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Original Research Article

Impedance plethysmography as an alternative method for the diagnosis of peripheral arterial disease

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ARTICLE INFO

Article history:

Received 11 April 2014

Accepted 21 November 2014

Available online 27 November 2014

Keywords:

Impedance plethysmography

Ankle-brachial index

Peripheral arterial disease

ABSTRACT

Background and objective: In the diagnosis of peripheral artery disease (PAD), the ankle-brachial index (ABI) is considered as the standard, and other noninvasive methods have received too little attention. Therefore, the aim of the study was to determine the diagnostic accuracy of impedance plethysmography in diagnosing PAD and to compare this method with other methods.

Materials and methods: A total of 66 patients with a mean age of 76.1 ± 9.6 years who had been treated for various cardiovascular diseases at Kaunas Clinical Hospital during 2011–2012 were enrolled into the study. All the patients were screened for PAD. Impedance plethysmography was performed with a new-generation Niccomo™ device. The receiver operating characteristic analysis was employed to determine the diagnostic accuracy of 4 parameters of impedance plethysmography: crest time (CT), crest width (CW), pulse amplitude (P_{ampl}), and alternating blood flow (ABF).

Results: There were a significant correlation between the ABI and the CT ($r = -0.699$, $P < 0.001$), between the ABI and the ABF ($r = 0.552$; $P < 0.001$), and between the ABI and the P_{ampl} only among men ($r = 0.652$; $P < 0.001$). No correlation was found between the ABI and the CW. Among all the parameters, the CT had the highest sensitivity and specificity (73.2% and 96.0%, respectively). Other parameters had the following sensitivities and specificities: ABF, 61.0% and 96.0%; and P_{ampl} , 90.0% and 20.0%, respectively.

Conclusions: Impedance plethysmography, especially its parameter CT, is an alternative non-invasive method in diagnosing PAD and could be used for the screening of patients with PAD.

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Peer review under the responsibility of Lithuanian University of Health Sciences.



<http://dx.doi.org/10.1016/j.medic.2014.11.007>

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1. Introduction

Peripheral artery disease (PAD) is a common pathological condition. It is estimated that the disease affects 10% and 20% of the general population [1]. The typical symptoms of intermittent claudication are experienced only by one-third of the patients, whereas in the majority (around 50%) of cases, the course of the disease remains asymptomatic [2,3].

Every clinic should have noninvasive diagnostic tools that would allow making rapid, simple, sufficiently accurate, time- and cost-effective screening of patients in order to early detect the disorders of the peripheral artery system. The measurement of the brachial index (ABI)/Doppler test is the most widely used test. It is rather simple to perform and is reported to have a sensitivity of around 95% and a specificity of almost 100% for the diagnosis of PAD [4]. Moreover, the ABI is an indicator of atherosclerosis at other vascular sites and recognized as a prognostic marker for future cardiovascular events and functional impairment [5,6].

To date, the diagnostics of PAD by different noninvasive methods has received too little attention over the world. Though the ABI is assumed as the standard for the screening of patients with PAD [4,5], our analysis has shown that it is applied rather rarely [7]. In medical practice across the world, impedance plethysmography is used for the assessment of blood flow in the lungs, heart, and aorta [8,9]. The first studies and publications about impedance plethysmography appeared in 1988–1993. Impedance plethysmography was successfully used to register periodic, heart activity-dependent pulse-wave velocity in limbs [10]. Limb impedance shows peripheral vascular response to the quantity and velocity of circulating blood [11] and peripheral vascular resistance. In 1990, a study by Jindal et al. investigated patients with the diagnosis of PAD who underwent impedance plethysmography, and the results obtained were compared with arteriographic findings. The results of impedance plethysmography were found to correlate very well with arteriographic findings [11]. However, there are no comparative studies that also examined the patients without the symptoms of PAD, when the ABI >0.9, as well as the patients without any symptoms.

Having reviewed the PubMed database of 2001–2011, we failed to find any articles describing diagnostics of PAD by the noninvasive diagnostic method of impedance plethysmography. Therefore, the aim of this study was to evaluate the diagnostic accuracy of impedance plethysmography in diagnosing arterial circulation disorders in the legs and to compare the sensitivity and specificity of this method with those of other noninvasive and invasive diagnostic methods.

2. Materials and methods

The study was conducted at Kaunas Clinical Hospital during 2011–2012. A total of 66 patients who had been treated for various cardiovascular diseases were enrolled into the study. Clinical data and data of medical history were collected from medical records and patients' interviews. The patients with cardiovascular diseases (CVD) were screened for PAD. The diagnosis of permanent atrial fibrillation (AF) was made based

on subject's ECG or a history of rhythm disorders documented in medical records. Permanent AF was diagnosed according to the American College of Cardiology/American Heart Association/European Society of Cardiology definitions [12]. Previous ischemic stroke was documented in medical records, or the diagnosis of ischemic stroke was established by a neurologist and confirmed by computed tomography findings. The diagnosis of arterial hypertension (AH) was made based on the mean arterial pressure (MAP) of >140/90 mm Hg or a history of AH documented in medical records.

The ABI was recorded by using a 5-MHz Doppler ultrasound device (Elite model No. 100, Nicolet Vascular Inc., USA) in both the legs of all subjects. It was measured in the supine position after 10-min rest. Systolic blood pressure was measured at the level of the brachial artery of each arm and the posterior tibial and/or dorsalis pedis arteries of each leg. The measurements were performed 3 times, and the mean ABI was assessed. PAD was diagnosed in subjects with the ABI of <0.9 at least in one leg. Arterial circulation was assessed by using impedance plethysmography in the supine position to avoid interference caused by the venous blood influx.

The findings were recorded by using a new-generation Niccomo™ device, which is a tool for the noninvasive monitoring of hemodynamic parameters using the methods of impedance cardiography and impedance plethysmography. The 4 parameters of impedance plethysmography with the reference values defined in the manual of Niccomo™ software were analyzed [13]: crest time (CT) (reference value, <180 ms), crest width (CW) (reference value, <80 ms), pulse amplitude (P_{amp}) (reference value, >0.7‰), and alternating blood flow (ABF) (reference value, >2.2%/min). While evaluating the associations between the ABI and parameters of impedance plethysmography, the severity of PAD according to Lawall and Diehm matched to those proposed by the manufacturer [14].

A device with a Doppler and color Doppler function, and a 5–10-Hz frequency linear transducer were used for the ultrasound examination of the arteries of the legs. During the examination, atherosclerotic plaques, changes in blood flow velocity, and changes in the Doppler spectrum were assessed. Blood flow velocity was measured at the groin and popliteal levels. If arteries were occluded, patients were referred to a vascular surgeon for consultation. In case of nonhealing wounds, necrosis, and pain at rest, angiography was performed.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 19.0. The following clinical parameters were analyzed: age, body mass index, hypertension, coronary artery disease, atrial fibrillation, and blood pressure. Continuous variables were expressed as a mean and standard deviation. The samples of continuous variables were checked for normality using the Kolmogorov–Smirnov test. Associations between continuous variables were tested by the Student *t*-test and the ANOVA method for variables with normal distribution and the Mann–Whitney and Kruskal–Wallis tests for nonnormally distributed variables. The chi-square test was employed to analyze associations between categorical variables.

In the study, the receiver operating characteristic (ROC) analysis was used. Spearman correlation was used for analysis of qualitative variables. The difference was considered to be statistically significant when a *P* value was less than 0.05.

3. Results

The mean age of the patients was 76.1 ± 9.6 years. There were 59.1% of men and 40.9% of women hospitalized due to various cardiovascular diseases: 30.2% had ischemic stroke; 71.2%, ischemic heart disease; 57.6%, arterial hypertension; 28.8%, previous myocardial infarction; 39.4%, permanent atrial fibrillation; and 24.2%, PAD. The majority of the patients with PAD were admitted to the hospital for the verification of diagnosis or for vascular reconstructive surgery to treat critical limb ischemia.

The patients had one or more prevalent cardiovascular diseases. The mean ABI of the patients was 0.8 ± 0.36 . More than half (62.1%) of the patients subjects had an ABI of <0.9 , 31.8% had the ABI within a reference range, and 6.1% were found to have arterial calcification (ABI of ≥ 1.40).

With the help of the ROC analysis, the new cutoff values of 0.415% and 12.5%/min for two parameters of impedance plethysmography – P_{amp1} and ABF, respectively – were determined. These new cut points could be used for the diagnosis of peripheral artery disease because the areas under the ROC curve (AUC) for P_{amp1} and ABF were 0.7 and 0.8, respectively ($P < 0.002$ and $P < 0.001$, respectively). Other two parameters – CT and CW – had the same cut points as the reference values. The analysis of specificity and sensitivity for all 4 parameters of impedance plethysmography showed that the CT had the highest sensitivity and specificity among all the parameters (Table). Other parameters had lower specificity and sensitivity with the lowest sensitivity and specificity being for the CW.

The correlation analysis showed a significant negative correlation between the ABI and the first parameter, CT: a decrease in the ABI was associated with an increase in the CT ($r = -0.699$, $P < 0.001$) (Fig. 1). The analysis of men and women separately also revealed that a lower ABI was associated with a longer CT ($r = -0.695$ and $r = -0.683$ for men and women, respectively; $P < 0.001$). A significant positive correlation was found between the ABI and the ABF ($r = 0.552$; $P < 0.001$) and between the ABI and the P_{amp1} only among men ($r = 0.652$; $P < 0.001$). However, the ABI did not correlate significantly with the CW.

The analysis of the 3 patients' groups (with the ABI values <0.9 ; $0.9-1.39$; and ≥ 1.4 , respectively), the CT was found to be significantly longer in 30 patients (68.6%) with the ABI value <0.9 implying PAD as compared with the subjects with the ABI value within the reference range. Among the patients having the ABI within the reference range ($0.9-1.39$), 19 subjects (96%) had a normal CT, which did not exceed 180 ms ($P < 0.001$).

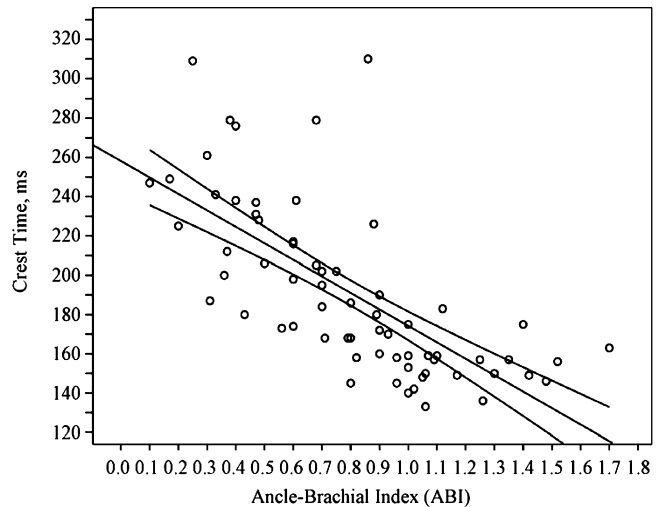


Fig. 1 – Correlation between the ankle-brachial index and crest time, the parameter of impedance plethysmography. Linear regression equation: $y = 258.147 - 83.906x$, where y is CT and x is ABI ($r = -0.699$; $P < 0.001$).

Arterial calcification (ABI, ≥ 1.4) was documented in 5 subjects. In this case, the CT was also less than 180 ms.

When the patients were divided into more groups, i.e., those with an ABI of ≤ 0.4 , $0.41-0.75$, and $0.9-1.39$, the association between the ABI and the CT remained significant ($P < 0.001$) (Fig. 2). In the subgroup of patients with a normal ABI value ($0.9-1.39$), 21 patients (91.3%) had the CT below 180 ms, and only 2 subjects (8.7%) had the CT interval above 180 ms ($P < 0.001$). Meanwhile, even 12 subjects (100%) with an ABI of ≤ 0.4 and 13 subjects (76.5%) with an ABI of $0.41-0.75$ were found to have a longer CT (>180 ms), compared with the patients having a normal ABI.

The significance of changes in the second parameter, CW, is doubtful as the analysis of the overall study population or patients divided into different groups based on the ABI showed no significant associations between the CW and the ABI.

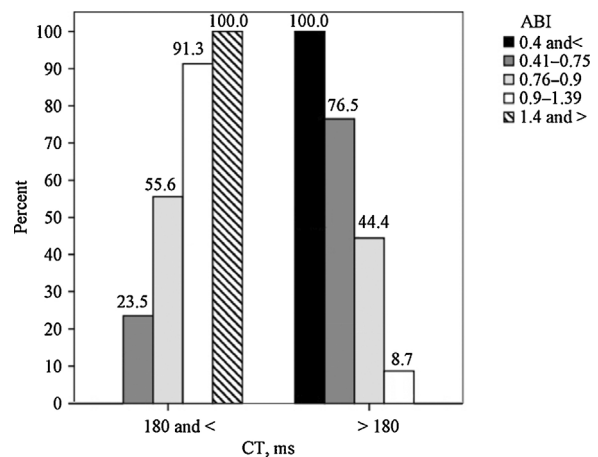


Fig. 2 – Association between the parameter of impedance plethysmography – crest time (CT) – and the ankle-brachial index (ABI) by different groups ($P < 0.001$).

Table – Sensitivity and specificity of all 4 parameters of impedance plethysmography.

Parameter and its reference value	Sensitivity, %	Specificity, %
CT <180 ms	73.2	96.0
CW <80 ms	58.5	12.0
ABF $<12.5\%/min$	61.0	96.0
P_{amp1} $<0.415\%$	90.0	20.0

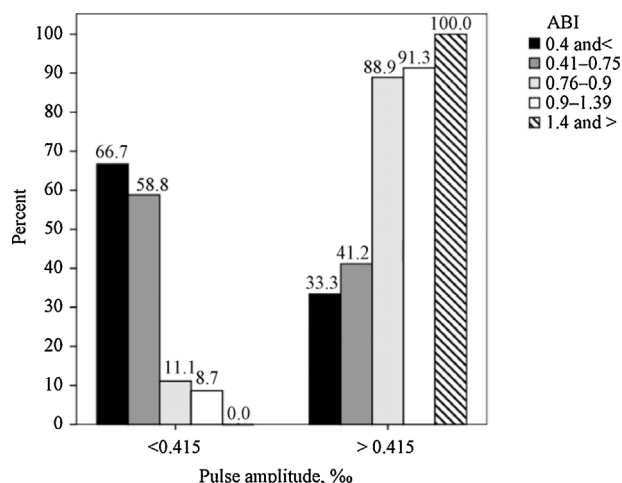


Fig. 3 – Association between the parameter of impedance plethysmography – pulse amplitude (P_{ampl}) – and the ankle-brachial index (ABI) by different groups ($P < 0.001$).

The third parameter, P_{ampl} , showed significant associations with the ABI ($P < 0.001$) (Fig. 3). In the analyses of subgroups with the ABI value ≤ 0.4 ; 0.41–0.75; and 0.76–0.9, 8 patients (66.7%), 10 patients (58.8%), and 1 patient (11.1%), respectively, had the P_{ampl} value of $<0.415\%$ ($P < 0.001$).

With consideration of the new value of the fourth parameter, ABF, even 25 patients (61%) with diagnosed PAD (ABI < 0.9) were found to have an ABF value of $<12.5\%/min$, and among the patients with a normal ABI value (0.9–1.39), 24 (96%) had ABF greater than $12.5\%/min$.

A total of 18 patients due to a bad condition of peripheral arteries underwent angiography. Vessel occlusion was most common in the group of patients having an ABI of <0.75 . The results of angiography showed that the CT had a sensitivity and a specificity of 100% when $>70\%$ stenosis in the femoral artery or its complete occlusion was determined. The ABF showed the same sensitivity, but the specificity was only 50%. When the lesion was present at the level of the popliteal artery, the CT showed a sensitivity of 100% and a specificity of 50%, but the ABF showed a sensitivity of 90% and no specificity.

4. Discussion

PAD impairs leg functioning, especially in people aged more than 55 years, but is rather rarely diagnosed in a primary healthcare setting [6,15,16]. In the PARTNERS study, the percentage of patients with newly diagnosed PAD alone accounted for 55%, whereas the proportion of patients with newly diagnosed PAD and other accompanying CVD made up 35% (9). It is worth noting that the low awareness rates of existing PAD worsen the control of risk factors and the quality of preventive treatment [17,18].

In our previous study, asymptomatic PAD was diagnosed in 37% of all the patients examined. In women, asymptomatic PAD was diagnosed more often than in men (33.3% vs. 19%) [7]. Based on the findings of other studies, the course of the disease remains asymptomatic in up to 50% of patients [19,20]. In 2010,

a study to evaluate the treatment of patients with atherothrombosis in a primary health care setting was conducted in Germany. The results of studies confirmed that patients with PAD posed big challenges for physicians due to a great variety of complaints. However, in comparison with previous studies, diagnostics and organization of treatment of PAD in such patients seem to be improved [21].

Literature reports that an early detection of a decreased ABI, adequate control of risk factors, and timely treatment may prevent or delay life-threatening outcomes of CVD [5,16]. The ABI, the same as arterial blood pressure, should be measured on a regular basis in an outpatient setting. Therefore, the significance of noninvasive methods is unquestionable [5,17].

Impedance plethysmography is another noninvasive method, which is safe, simply done, requires no special staff training and might be used much wider in diagnostics of PAD. However, to our knowledge, all the studies employing this method were published only during 1981–1990. Many studies compared impedance plethysmography with invasive angiographic methods or methods used to measure blood circulation in large blood vessels, aorta, and iliac arteries [3,22]. Early investigations of arterial occlusive disease of the legs and comparisons with invasive angiographic tests were described by Parulkar et al. already in 1981 [23]. Impedance plethysmography was used to identify the exact site of vascular occlusion [21] and to determine the status of collateral blood flow and distal arterial runoff [3,23]. The majority of later investigations were also related to invasive methods.

In 1990, the study by Jindal et al. reported a very good sensitivity and specificity of impedance plethysmography for diagnosing PAD. The investigators analyzed the blood flow index and differences in the pulse-wave arrival time and compared them with angiographic and reconstructive vascular methods. Impedance plethysmography had a sensitivity of 97.5% and a specificity of 98.1% [11]. According to their opinion, the test has only one limitation: it cannot be used to identify the exact anatomic location of the block in the affected blood vessel.

It is difficult to tell why no studies describing and employing this method in the diagnostics of PAD have been carried out since 1990 until now. Moreover, there are no studies analyzing the possibilities of this method in performing the screening of patients with PAD. As medical equipment has improved considerably over the time, researchers decided to compare contemporary impedance plethysmography with the ABI in screening the patients due to possible PAD. In addition, this method could be used in cases when the measurement of the ABI fails in patients due to severe pain during the measurement, large damaged areas of leg skin, and certain conditions after reconstructive operations.

As the ABI is sufficiently informative, easy to measure, and not cost- and time-consuming, it is used most widely. Besides these methods, oscillometry can be used to determine lesions in peripheral arteries as well. The comparison of this method with the ABI measured by Doppler ultrasound showed the AUC to be greater (0.87–0.95) than that determined by oscillometry (0.80–0.93) [24,25].

In our study, impedance plethysmography was used to measure blood circulation in the ankle of a more affected leg. A comparison between the ABI and the parameters of

impedance plethysmography was made. The CT parameter was found to be one of the main parameters indicative of an arterial circulation disorder. In case of impaired arterial circulation, the CT was >180 ms. In the patients with an ABI value of <0.9 , a significant association between abnormal CT parameter values indicative of arterial lesions was observed ($P < 0.001$).

When men and women were analyzed separately, the results remained the same irrespectively of gender ($P < 0.001$). An association between the CT and the site of vascular occlusion identified by angiography was found ($P < 0.05$). The CT had a sensitivity of 73% and a specificity of 96%. With a decrease in the P_{ampl} value, a significant decrease in the ABI value was found ($P < 0.001$). A positive significant correlation between the ABI and the P_{ampl} was found only among men.

The ABF parameter is directly related to the ABI changes too. With an increase in the ABI value, the ABF parameter increased correspondingly. When the ABI was <0.9 , even 25 subjects (61%) were found to have an ABF value of $<12.5\%/min$ ($P < 0.001$). Its sensitivity and specificity were 61% and 96%, respectively ($P < 0.001$).

The significance of noninvasive tests in angiology and vascular surgery is increasing each year. Due to advanced two-dimensional ultrasound scanners and highly skilled physicians-investigators, this test method is used in vascular surgery to examine the anatomy of blood vessels affected by atherosclerosis and to identify possible sites of occlusion both during preoperative and postoperative periods. It may be more complicated to perform in overweight and obese patients or when arteries are calcified [26].

Previous studies in literature also confirms the fact that impedance plethysmography is sufficiently precise for identifying the site of an affected segment. A study by Feigelson et al. that employed plethysmography to detect arterial flow reported a specificity of 99%, but the sensitivity was only 39%. In this study, only half of participants had an isolated occlusive disease of the posterior tibial artery [27]. In our study, the sensitivity was higher. Therefore, impedance plethysmography is another test method that is sufficiently effective for early diagnostics of PAD. Its benefit is a possibility to diagnose segmental circulatory disorders. Our study suggests that impedance plethysmography could be used for monitoring the patients after revascularization, especially when it is necessary to prevent compression in the leg or multiple skin lesions. The accuracy of the ABI in predicting revascularization failure is poor, because the ABI is a global estimator of whole-limb perfusion and cannot distinguish between graft failure and progression of PAD in native arteries [5].

The limitations of this study should be mentioned as well. The selection of patients was not randomized. The sample sizes (especially in the subgroups) were relatively small. These results apply only to a white population, and no follow-up results after revascularization are available.

5. Conclusions

The findings have shown that impedance plethysmography, especially its parameter CT, is an alternative noninvasive method in diagnosing PAD and could be used for the screening of patients with PAD.

Conflict of interest

The authors state no conflict of interest.

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