Evaluation of Patients with Lower Extremity Peripheral Artery Disease by Walking Tests: A Pilot Study

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Abstract
Peripheral arterial disease (PAD) directly affects the quality of life, patients experimenting limited walking ability and disability. The purpose of the current study was to investigate the walking and climbing patterns of patients with lower extremity PAD in relation with several risk factors, applied on Romanian population. A cohort non-randomized design was conducted and all eligible subjects who self-referred for medical care since March 2016 until February 2017 at the Second Surgery Department, County Clinical Emergency Hospital of Cluj-Napoca were included. The eligible patients were older than 18 years, with leg pain and Rutherford grade from I to IV. The following tests were applied to each subject included in the study to investigate the capacity to walk as far as possible in six minute (6 minute walking test), the capacity to climb stairs (climbing stairs test) and the capacity to walk on a treadmill (treadmill test) until the pain occurred. Twenty-four patients with mean age of 65.08±8.53 years were investigated. Almost 81% of patients were with chronic pain, 46% were overweight, and 79% were smokers. The results on applied walking tests were as follows: 279.17±70.58 meters to 6-minutes walking test, 77.50±21.80 stairs and 182.50±73.34 meters on treadmill test. The results of the walking tests significantly correlate with each other (ρ>0.93, p<0.0001), and all applied tests significantly correlate with toe gangrene (ρ>|0.52|, p<0.01) and toe disarticulation (ρ>0.62, p<0.002). It can be concluded that any of the applied walking test proved reliable instrument, able to identify the patients with most severe PAD.

Keywords: claudication, peripheral arterial diseases, reliable tool, walking tests

Introduction
Atherosclerosis affects up to 10% of the Western population older than 65 years (Selvin and Erlinger, 2004). Peripheral artery disease is an obstructive disease caused by the process of atherosclerosis, characterized by a narrowing of the peripheral vessels like legs arteries, mesenteric arteries, brain arteries, but most commonly in the arteries of the legs, PAD being highly similar to coronary artery disease (Gerhard-Herman et al., 2016). Predicted mortality for PAD patients with claudication is approximately 30% at 5 years, 50% at 10 years, and 70% at 15 years (Norgren et al., 2007).

As symptoms, claudication occurs during physical activity and is relieved after a short rest later pain develops because of inadequate blood flow. Under resting conditions, normal blood flow to extremity muscle groups averages 300-400 mL/min. Once the exercise begins, blood flow increases as much as 10-fold as a consequence of the increase in cardiac output and compensatory vasodilation at the tissue level. This allows the increase in oxygen demand to be met. When exercise ceases, blood flow returns to normal within minutes (Domínguez, 2017).

Surgical treatment options, are typically reserved for patients with more severe disease or those in whom nonsurgical management (vasodilators, platelet antiaggregants or prostaglandin treatments) fails, including: bypass surgery and endovascular therapy (e.g. stents, balloons, or atherectomy devices). Whereas open surgery dominated the treatment options two decades ago, endovascular
management of PAD has become exponentially more popular since then (Rowe et al., 2009). Overall, recommendations for selecting a treatment modality may depend on the patient's life expectancy and comorbid conditions, as well as on the extent of the occlusive disease (Antoniou et al., 2013).

Three tests, named 6-minute walking test, climbing stairs test, treadmill test, were used in the evaluation. These tests have been initially developed to assess the physical fitness in healthy subjects (Balke, 1963) and then applied to test the exercise tolerance in chronic respiratory disease and heart failure (ATS 2002; Guyatt et al., 1985). The 6-minute walking test (6MWT) has highly reliable measurements, which are in direct correlation with the functional and hemodynamic severity of PAD (Montgomery and Gardner, 1988). The treadmill test allows to accurately estimate walking distances (Saska et al., 2010), while the climbing stairs test reveals the severe cases of PAD (Atul Jain et al., 2012).

The selected tests for the current study exhibit good test-retest reliability, whereas other walking tests such as timed up and go, sit and stand test, 4 m gait speed test, lack conclusive data to support their practical use. In the last 10 years there has been a growing interest among medical practitioners towards the walking tests and the body of evidence regarding these tests’ practical relevance is on the ascending path. For example, lower results during one of the walking tests is strongly correlated with longer hospitalization and mortality in people with chronic respiratory disease (Holland et al., 2014), but there is further necessity for studies to evaluate their relevance and utility in PAD.

The purpose of our study was to investigate the walking pattern of patients with lower extremity PAD in relation with body mass index, metabolic and cardiovascular co-morbidities and smoking status as risk factors in a Romanian cohort.

Materials and Methods

The overall evaluation was an observational study conducted between March 2016 and February 2017 on convenient sample of subjects hospitalized at the Second Surgery Clinic, Emergency County Hospital in Cluj-Napoca, Romania.

Patients with Rutherford grade between I (mild claudication) and IV (ischemic rest pain with ulceration and gangrene) were included in the study according to the following criteria: ankle pressure (ABI = ankle-brachial index) < 0.9, age > 18 years old and leg pain. These were eligible for participation in the study, and were included in the study depending on the time-frame granted for the data collection before treatment. Patients with absence of PAD (ABI > 0.90), inability to obtain an ABI measure, asymptomatic PAD (Rutherford grade 0), exercise tolerance limited by other factors than leg pain (dyspnea, active cancer, renal disease, liver disease, coronary disease) were excluded from the study.

The inclusion and exclusion criteria applied in this study are presented in Fig. 1.

For this cohort, the following data were recorded: the demographic characteristics (gender, age, living area (rural/urban) and education), risk factors (body mass index, smoking status, and co-morbidities such as type II diabetes, arterial hypertension, ischemic heart disease, other cardiac diseases and stroke if exists), signs and symptoms of peripheral arterial disease (continuous pain, toe gangrene etc.), and surgical interventions (toe disarticulation, necrectomy etc.). The flowchart of the applied design is presented in Fig. 2.

Three different walking tests were applied to each subject included in the cohort: 6-minute walking test (record the individual capacity to walk as far as possible in six minute), climbing stairs test (record the individual capacity to climb a number of stairs until the pain occurs), and treadmill test (record the individual capacity to walk on a treadmill until the pain is felt).

The 6-minute walking test is conducted by placing two poles at a distance of 30 m between them, whereas a full lap is considered a round of 60 walk. Then it is recorded how many laps each patient can undergo and the participant can stop to rest if needed (this data is also recorded).

Treadmill walking test is conducted as follows: the test begins with the treadmill set to a low speed (1 km per hour) at 10% incline, and every 3 minutes the speed is increased by 0.5 km/hour. The test continues for a maximum of 30 minutes (usually attainable only by well-trained individuals) or until the patient quits or develops signs or symptoms of ischemia or an arrhythmia.

For climbing stairs test, the time (in seconds) taken to ascend and descend a flight of stairs (2-6) is recorded. The number of stairs will depend on the patient's condition, as well as on the extent of the occlusive disease. The flowchart of the applied design is presented in Fig. 2.

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rest if needed, but the time keeps going. Using a handrail and walking aid is also permitted if needed, but this should be recorded. Timing begins on the signal to start and terminates when the participant returns with both feet to the ground level.

The study was conducted according to the principles of the Declaration of Helsinki and was approved by the Ethical Committee of our university (no. 66/14.03.2016). All patients agreed to participate and signed an informed written consent.

The data were analyzed according to type and distribution. The frequencies as absolute and percentage were reported for qualitative data. Shapiro-Wilk test was used to test the normal distribution of quantitative data. Quantitative data were summarized as arithmetic mean and standard deviation for normally distributed data; otherwise median and interquartile range (defined as (Q1-Q3) where Q1 = 25th percentile and Q3 = 75th percentile) were used. Z test with continuity correction (Zc) was used to test the significance of marginal proportions:

\[ Zc = \frac{[(p-p0)+c]/\sqrt{p0*(1-p0)/n}}{,} \]

where ‘p’ and ‘p0’ are the proportions to compare, ‘c’ is the correction factor and is -1/(2*n) if p>p0, 1/(2*n) if p<p0, and 0 if |p-p0|<1/(2*n)).

The association between the results of different applied walking tests was tested with Spearman rank correlation coefficient (ρ). Statistical analysis was conducted with Statistica program (v. 8, StatSoft) at a significance level of 5%.

Table 1. Demographic characteristics of the investigated cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± stdev)</td>
<td>65.08±8.53</td>
</tr>
<tr>
<td>Gender (no. (%))</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>22 (91.67)</td>
</tr>
<tr>
<td>Women</td>
<td>2 (5.88)</td>
</tr>
<tr>
<td>Environment, rural (no. (%))</td>
<td>12 (50.0)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Medium studies</td>
<td>12 (50.00)</td>
</tr>
<tr>
<td>Intellectuals</td>
<td>12 (50.00)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean±stdev)</td>
<td>25.40±4.03</td>
</tr>
</tbody>
</table>
Results

A cohort of twenty-four patients aged between 48 and 81 years have been included in the study. As expected, due to the characteristics of the disease, a significant higher percentage were men (Z-statistic = -14.40, p-value < 0.0001). Half of the patients were overweight (11 patients) or obese (one patient). Demographic characteristics of the cohort are presented in Table 1.

The duration of the disease varied from 1 to 156 weeks with a median of 23 weeks and an interquartile range of (2.75 - 42.00).

Most of the patients were with continuous pain at the inclusion in the study (17 (78.83%), Z-statistic = -4.49, p-value < 0.0001). Most of the patients included in the study were smokers (19 (79.17%), Z-statistic = -7.04, p-value < 0.0001).

Excepting ischemic heart disease, all other investigated co-morbidities were significant from statistical point of view (Table 2). Three patients (12.50%) were with gangrene and four had a by-pass (16.67%).

The summary of the applied tests is presented in Table 3. Significant association has been observed between applied walking tests (Fig 3).

All applied walking tests correlated significantly with toe gangrene (p < 0.02), p-value < 0.01 and toe disarticulation (p < 0.06, p-value < 0.002), cases in which the values were lower as compared with performances when gangrene or disarticulation is not present (Table 4).

Discussion

The assessment of patients with PAD using three walking tests was successfully conducted. The patient’s mean age was 65 years, result similar to that reported by Criqui and Aboyans (2015) in their study where it was highlighted that PAD is uncommon in patients with age before 50 years and have a pick at 80 years.

It is well known that PAD occurs more frequent in men compared with women, demonstrated also by the hereby results (see Table 1). Although this gap inclines to decrease and to even the proportions, there are still regions, like Romania disparity between sexes (Malik et al., 2004; The PARTNERS program, 2001).

The current study revealed a 50-50% distribution regarding environment and education level. In specialty literature predominates the rural environment and medium level of education of the patients (Shammas, 2007). The obtained result is similar to the one reported in the scientific literature (Ciocan et al., 2017).

Half of the patients in the studied cohort were at the border between normal weight and overweight (Table 1). It is known that obesity is frequently observed among subjects with PAD in association with atherosclerosis (Gorter et al., 2004; NCEP Expert Panel, 2001).

The study revealed that the median period of time from the first severe symptoms to the hospital presentation ranged between 1 to 156 weeks, a quarter of patients presented to the hospital after 42 weeks. No studies that measured this time frame were found in the available scientific literature. This period influences the stage of disease at admission, more severe symptoms making the patient seek professional help earlier (McDermott et al., 2001; Conte et al., 2015; Ratchford, 2017).

As expected, smoking is directly linked with PAD, most of the patients in the cohort being smokers (p < 0.0001). PAD patients are smokers, the frequency identified in our study being similar with the one reported by other studies (Anderson et al., 2001; Conen et al., 2011). It is known that smoking affects arteries and speeds the development of atherosclerosis (Cui et al., 2006), leading also to a fast decrease in the quality of life (Fritschi et al., 2013).
Diabetes, arterial hypertension and cardiac rhythm disorders were co-morbidities observed in our cohort (Table 2). Blood hypertension and type II diabetes were present to the majority of the investigated patients, while on the opposite, the cardiac rhythm disorders were less frequent observed. Diabetes is known as the strongest predictor of PAD and the association of these two diseases leads to amputation faster (Athyros et al., 2004; Cerqueira et al., 2008; Shammas, 2007). Selvin shows in the National Health and Nutrition Survey (NHANES) that arterial hypertension is strongly correlated with PAD (Selvin and Efringer, 2004). Rhythm disorders decrease the patient’s biologic balance and affect the quality of life (Feringa et al., 2006; Qureshi et al., 2015).

Half of the patients in the cohort succeeded to walk 300 meters to the 6 minutes walking test, results similar with other studies reported in the scientific literature. In Tsai’s study and other studies, the mean of meters walk in 6 minutes walking test was equal with 350 meters (Tsai et al., 2002; Beatty et al., 2012; Nash, 2012).

Regarding the climbing test, the current study revealed a median of 88 stairs, showing that half of patients included in the study succeeded to climb 88 stairs. As the subjects are evaluated on stairs of 16-20 cm height, the results are expected to be equivalent. There were not identified in the available literature, any studies that evaluated the number of stairs climbed by patients with PAD.

The results related with treadmill test show that, patients need to stop after 11 minutes, and the median distance walked was equal to 212.5 meters (Table 3). In Hiatt’s study, also confirmed by other studies, is revealed that if a patient walks on a Treadmill 3 hour per week during 12 weeks, his/her performance improves within 24 months and the improvements are even higher compared to the strength training (3 hours/week of resistive training of five muscle groups of each leg) (Hiatt et al., 1994; Libby et al., 2007; Regensteiner et al., 2002). This underlines the importance of exercises in the evolution of PAD and that a sedentary life style will badly influence the natural course of the disease (Craft et al., 2008; Acampa et al., 2016; Gibbons et al., 2002).

The performances in the applied tests decrease, as expected, in the presence of toe gangrene or disarticulation (Table 4) with significant correlation between walking performances and toe gangrene or disarticulation (p<0.002). Major events occurring in the natural evolution of the disease, like toe gangrene and toe disarticulation affects the ability of walking, translating in a poor result during tests, conclusion supported by other researchers (Ciocan et al., 2015).

As expected, a positive, very good association, statistically significant was observed between pairs of applied walking tests (Fig. 1). The highest association was observed between 6 minutes walking test and climbing stairs test (correlation equal with 0.94). This result showed that, from a clinically point of view, any of these investigated tests are good in the evaluation of patients with PAD. The efficiency of 6 minutes walking test and Treadmill test had also been demonstrated on patients with cardiac diseases (Enright, 2003; Wise and Brown, 2009).

The investigated walking and climbing tests are not investigated enough in lower limb arterial diseases. Studying this may provide an important glimpse in the physical examination of arterial patients at admission and extended also after any medical strategy, either surgical or non-surgical, in order to evaluate its efficiency. Not only is it a reliable instrument to objectively assess the PAD patients’ capacity to use their limbs and determine to what extend PAD has affected them, but they are also an extremely cheap and fast tool. Walking tests can further be used to evaluate one’s response to treatment, therefore enabling the physician to choose the best suited treatment strategy for each individual, with the best functional result respectively.

The current study is a pilot study and developing this area is essential for further results regarding walking tests.

Conclusions

Testing patients with lower extremity peripheral artery using walking and climbing tests brings an objective measure on the functional capacity of the patients of using their affected patients’ lower limbs. The obtained results show that half of the investigated patients with PAD were able to walk 300 steps in 6 minutes, 212 steps in 11 minutes according to treadmill test and were able to climb 88 stairs until the pain imposed resting. The performances in these tests decreased in the presence of toe gangrene or disarticulation. Any of the applied walking tests proved equally reliable instruments able to identify the patients with most severe PAD.

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References


