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***Original Article** / Özgün Makale*

The metabolic efficiency of walking is reduced in patients with intermittent claudication

İntermitan klodikasyonu olan hastalarda yürümenin metabolik etkinliği azalır

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Background: We aimed to determine the differences in the preferred walking speed, oxygen cost of walking and their correlations, comparing the intermittent claudication (IC) questionnaire, claudication pain scale and Borg scores in the patients with IC and the healthy subjects.

Methods: Twelve healthy subjects (group 1) and 12 patients with IC (group 2) participated in our study, one healthy control subject and three patients with IC were excluded from the study because of exclusion criteria, and remain 20 participants were evaluated (n=11 in group 1, n=9 in group 2). The participants walked on a treadmill at pre-determined speeds for the measurements of oxygen cost of walking by indirect calorimetry method. The IC questionnaire was administered prior to the test.

Results: The mean walking speed in group 1 was 77.8±11.4 m/min and 67.2±10.5 m/min in group 2 ($p<0.05$). The mean oxygen cost of the walking trial in healthy subjects was 0.14±0.02 mL/kg/m and 0.18±0.04 mL/kg/m in the patient group ($p<0.05$). In group 2, there was no correlation between the IC questionnaire score and oxygen cost, preferred walking speed, claudication pain scale score, and Borg score. The oxygen cost of walking was significantly correlated with the maximal walking distance (MWD) ($p<0.05$). There was a significant correlation between the initial claudication distance and Borg score and claudication pain scale score ($p<0.001$).

Conclusion: The metabolic efficiency of gait and the preferred walking speed may be reduced in PAD patients. Our study results suggest that oxygen cost of walking, preferred walking speed, Borg score, claudication pain scale score, initial claudication distance and MWD are objective parameters which can be used in monitoring the ambulatory limitation of PAD patients with IC.

Key words: Intermittent claudication; questionnaires; treadmill test.

Amaç: Bu çalışmada intermitan klodikasyon (İK) olan ve sağlıklı bireylerin tercih ettikleri yürüme hızı, yürüme oksijen maliyeti açısından görülen farklar ve aralarındaki ilişki araştırıldı ve İK anketi, klodikasyon ağrı skalası ve Borg skorları karşılaştırıldı.

Çalışma planı: Çalışmamıza 12 sağlıklı birey (grup 1) ve İK'li periferik damar hastalığı (PDH) olan 12 hasta (grup 2) katıldı, bir sağlıklı birey ve üç İK'li hasta dışlanma kriterleri nedeniyle çalışmadan çıkarıldı ve kalan 20 katılımcı değerlendirildi (grup 1 n=11, grup 2 n=9). Katılımcılar, indirekt kalorimetri yöntemi ile yürüme oksijen maliyeti ölçümü için önceden belirlenen hızlarda koşu bandında yürütüldü. İntermitan klodikasyon anketi test öncesi uygulandı.

Bulgular: Grup 1'in ortalama yürüme hızı 77.8±11.4 m/dk., grup 2'nin 67.2±10.5 m/dk idi ($p<0.05$). Sağlıklı bireylerin ortalama yürüme oksijen maliyetleri 0.14±0.02 mL/kg/m, hasta grupta ise 0.18±0.04 mL/kg/m idi ($p<0.05$). Grup 2'de İK anket skoru ile oksijen maliyeti, tercih edilen yürüme hızı, klodikasyon ağrı skalası skoru ve Borg skoru arasında ilişki yoktu. Yürüme oksijen maliyeti ile maksimum yürüme mesafesi (MYM) arasında anlamlı ilişki vardı ($p<0.05$). Klodikasyon mesafesinin, Borg skoru ve klodikasyon ağrı skalası skoru ile anlamlı ilişkisi vardı.

Sonuç: Periferik damar hastalığı olan hastalarda, yürümenin metabolik etkinliği ve tercih edilen yürüme hızı azalabilir. Bu çalışma yürüme oksijen maliyetinin, tercih edilen yürüme hızının, Borg skorunun, klodikasyon mesafesinin ve MYM'nin, İK'li hastaların hareket kısıtlılığını izlemek için kullanılabilecek objektif parametreler olduğunu göstermektedir.

Anahtar sözcükler: İntermitan klodikasyon; anketler; koşu bandı testi.

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Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis in the lower extremities that affects a large proportion of the middle-aged population.[1-3]

Intermittent claudication (IC) is the most common symptom of PAD, and it affects approximately 40% of PAD patients.[4,5] While walking, the increased blood demand of the muscles in the lower extremities cannot be supplied by the occluded arterial system, which may cause the symptom of claudication. In addition, altered antioxidant capacity was also reported because of hypoxia.[6] Claudication leads to severe limitations in walking ability, which may result in decreased physical functioning.[1] Crowther et al.[3] declared that the kinematics of walking in IC patients is different than for healthy subjects.

The severity of disease and physical activity of patients with IC can be determined using both quantitative [ankle-brachial index (ABI), invasive or noninvasive radiological monitoring, and initial and maximal claudication distances] and qualitative parameters (the IC questionnaire together with other questionnaires) that can be used for assessing the quality life of patients with IC.[7] It is clear that the diagnosis of IC and the assessment of its treatment outcomes should rely on objective and quantitative criteria. Hiatt[8] reported that the treatment of IC should target an improvement in exercise capacity. To assess walking capacity, the initial claudication distance and the maximal walking distance are assessed for the evaluation of walking capacity, and the maximal walking distance is an important parameter that can be used for classifying the severity of a PAD based on the Fontaine or Rutherford classifications.[9]

The preferred walking speed (PWS) is a gait parameter that may have implications for determining overall gait performance.[10] In addition, the oxygen cost of walking is another gait parameter that revealed gait metabolic efficiency.[11] The energy consumption measurement while exercising on the treadmill is a reproducible method that can be adjusted by medical and surgical treatments of IC. However, exercise testing needs expensive laboratory equipment along with trained staff, and the requirements of an exercise laboratory preclude its use in daily clinical practice.[1] The oxygen cost of walking may lead to a discrimination between the normal and pathological gait.[11,12] Thus, the PWS and the oxygen cost of walking may provide objective and quantitative data for patients with IC.

The IC Questionnaire is an instrument for determining the quality of life in PAD patients with PAD-IC[13] while the Borg score and claudication pain scale serve as valuable tools for the assessment of perceived exertion and pain, respectively.[14,15]

The purpose of this study was to determine the differences in the PWS and oxygen cost of walking in both a group of patients with IC and in a healthy control group and determine how they correlate with the IC questionnaire, claudication pain scale, and Borg scores.

PATIENTS AND METHODS

Patients

Twelve healthy subjects (group 1) and 12 patients with IC (group 2) participated in our study. One healthy control subject and three patients with IC were excluded from the study because of the mentioned exclusion criteria below. The data of 11 subjects in group 1 and nine subjects in group 2 was evaluated in this study. The healthy control subjects in group 1 were sedentary (performing moderate or vigorous physical activities not more than 30 minutes on most days of the week).[16] Ethical approval was obtained from the institutional ethical committee, and all participants provided written informed consent for inclusion in the study.

Statistical power analysis (MedCalc Software 11.3.3, Mariakerke, Belgium) was used to establish the appropriate sample size. According to the power analysis of the pilot study performed in our laboratory on patients with PAD-IC and healthy individuals, the minimal required sample size for each group was calculated as eight subjects (Oxygen costs were used in the power analysis; oxygen cost for group 1 = 0.14±0.01 mL/kg/m and for group 2 = 0.18±0.04 mL/kg/m).

Inclusion criteria

Newly diagnosed patients with no previous medical treatment for PAD-IC participated in our study. Patients with Fontaine stage IIa and IIb lower-extremity PAD were chosen if they had an ABI of ≤0.90. This was determined via invasive (digital subtraction angiography) and/or non-invasive tests (Doppler ultrasound imaging or magnetic resonance angiography).[1-9]

Exclusion criteria

Individuals with Fontaine stage III and IV PAD, acute infectious disease, orthopedic problems, gait abnormalities, recent lower extremity injuries, or metabolic disorders (thyroid function disorders, diabetes mellitus, etc.) along with those taking medications that may affect their energy expenditure were excluded from the study. In addition, any patients that the clinician strongly suspected of having a cardiovascular disease were excluded. Moreover, those with any contraindication for the exercise testing after an examination of their medical history, physical examination, and electrocardiography testing were also not included.

Vascular testing

The measurements of the systolic pressures of the brachial arteries, dorsalis pedis, and posterior tibial arteries were obtained bilaterally while the patients were in the supine position for 15 minutes using a handheld vascular Doppler device (Datascope IABP Doppler DS900 8 MHz, Huntleigh, UK] and a standard sphygmomanometer (Erka, Kallmeyer Medizintechnik GmbH, Germany). The ABI was calculated by dividing the lowest systolic blood pressure in the ankle into the higher of the brachial systolic pressures for each lower limb.[17]

Questionnaire

Each of the participants filled out the IC questionnaire (Turkish version) prior to the treadmill walking trials.[18] This questionnaire is a disease-specific questionnaire for the assessment of health-related quality of life in patients with IC.[13] The validation and reliability of the Turkish version of the IC questionnaire was achieved by Ketenci et al.,[18] and the score is assessed by using a 0-100 scale in which 0 represents the best possible score and 100 indicates the worst possible health condition.[13]

The treadmill walking protocol

The metabolic measurements while walking on the treadmill were gathered in an exercise laboratory at Mersin University, the Department of Physiology, Yenişehir campus. The subjects came to the exercise laboratory on two occasions. The PWS determination and habituation trial to the treadmill walking were completed on the first visit. On the second visit, the subjects only performed the walking trial on the treadmill to measure oxygen cost.

All subjects completed a standardized familiarization session on the treadmill for at least 10 minutes.[19] The elevation of the treadmill was set at a 0% grade, and the subjects were instructed to not hold onto the handrails while walking. The PWS of each subject was determined by overground locomotion prior to the treadmill walking tests for oxygen cost measurement to determine the PWS. The subjects were asked to walk at a natural pace along a 14-meter walkway, and the time for each trial was determined by using two infrared timing gates placed at the second and 12^{th} meters. The PWS (meters/second) was calculated by dividing the distance walked (10 meters) by the average time of three walking trials.

Measurements of walking capacity

The subjects were instructed not to eat or drink (except for water) for at least 12 hours before the testing and not to perform any kind of physical exercise on the test day.[20] Each subject walked on the treadmill for seven minutes using a predetermined overground PWS to measure the energy expenditure of walking. The indirect calorimetry method was used to determine the energy expenditure measurements of the walking trials on the treadmill (CareFusion Corporation, San Diego, California, USA). Gas samples were collected breath-by-breath through a face mask (Hans-Rudolph, Shawnee, Kansas, USA) during oxygen consumption measurements of walking. The last two minutes of oxygen data for each trial were taken as the steady state and averaged at 10-second intervals for analysis.[21]

The Borg scale is a 15-grade scale for rating perceived exertion that ranges from 6 (no exertion) to 20 (maximal exertion). It was applied at every two minutes of each walking trial in both groups.[14] The claudication pain scale was assigned to determine the participants' perception of claudication pain. It was determined via a five-point scale (0: no pain, 1: onset of pain, 2: moderate pain, 3: intense pain, 4: maximal pain).[15]

The initial claudication distances and maximal walking distances that the patients could walk just before stopping because of pain were recorded, and the walking trials were stopped if the subjects were able to walk more than one kilometer.

Statistical analyses

All statistical analyses were carried out using the SPSS version 11.5 for Windows (SPSS Inc., Chicago, Illinois, USA). All measurements were expressed as mean and standard deviation (SD). Group differences in all variables were assessed by the Mann-Whitney U-test. Spearman's correlation was used to test the statistical significance of any possible correlation, and the significance level was set at $p<0.05$.

RESULTS

The mean and SD of the demographic and anthropometric data of the subjects in each group is summarized in Table 1. The groups were similar in age, height, weight, and body mass index (BMI) ($p>0.05$). In group 1, 54.5% of the patients were current smokers while the figure was higher in group 2 at 88.9%. All the subjects with PAD-IC had a distal type of lower extremity arterial disease, and their mean ABI was 0.74±0.12.

The mean PWS was 77.76±11.41 m/min and 67.20±10.54 m/min for groups 1 and 2, respectively.

Table 1. Demographic and anthropometric data of the groups

Variables	Healthy subjects (n=11)	PAD-IC patients (n=9)	*p*
Age (years)	50.5±9.4	58.7±9.1	>0.05
Height (m)	170.3±15.2	165.1±6.1	>0.05
Weight (kg)	81.1±13.2	70.1±9.5	>0.05
BMI (kg/m^2)	27.9±3.2	25.7±3.4	>0.05
Mean ABI	1.1±0.1	0.7 ±0.1	<0.05

PAD-IC: Peripheral arterial disease with intermittent claudication; PAD: Peripheral arterial disease; BMI: Body mass index; ABI: Ankle-brachial index.

(Figure 1), and the difference between the PWS in the groups was statistically significant (p<0.05). The mean oxygen cost of the walking trial was 0.14±0.02 mL/kg/m for the healthy subjects and 0.18±0.04 mL/kg/m for the PAD-IC group (Figure 2). There was also a significant difference in the mean oxygen cost of the walking trail between the patients with IC and the control group (p<0.05). The mean Borg score for the walking trial in group 1 and group 2 was 9.12±1.32 and 12.64±1.02, respectively, and the difference was significant (p<0.05).

In the treadmill walking trials, the mean initial claudication distance was 204.6±179.74 meters, and the mean maximal walking distance was 668.67±417.19 meters in the PAD patient. In group 2, the self-reported initial claudication distance was 266.67±171.39 meters. According to this distance, 66.6% of the patients were in Fontaine stage IIa while the results of the recorded initial claudication distance while walking on the treadmill revealed that 33.3% of the patients were in Fontaine stage IIa.

The IC questionnaire score in group 1 was 3.61±2.02 and 15.94±11.09 in patients with IC, and there was a statistical difference between the groups (p<0.05). The mean claudication pain scale score was 1.82±1.20 in patients with IC. There was no correlation between the IC questionnaire score and the oxygen cost, PWS, claudication pain scale score, Borg score, or initial-maximal claudication distance in the PAD-IC patients (p>0.05). The oxygen cost of walking had significant correlation with the maximal walking distance (r=-0.75; p<0.05), but there was no correlation between the oxygen cost of walking and the IC questionnaire score, PWS, claudication pain scale score, Borg score, or initial claudication distance in group 2 (p>0.05). The Borg score had a significant correlation with the claudication pain scale score (r=0.94; p<0.001) while the initial claudication distance had significant correlations with the Borg score (r=-0.93; p<0.001) and claudication pain scale score (r=-0.90; p<0.001).

DISCUSSION

This study demonstrated that the metabolic efficiency of walking for patients with PAD-IC was lower than that for the healthy control group. In addition, the Borg score and claudication pain scale score were strongly correlated with the initial claudication distance.

The PWS in patients with PAD-IC

The quality of life in patients with IC is diminished because of ambulatory limitations.[7-22] In our study, the patients with IC preferred lower speeds than the healthy control group. Since the PWS is a gait parameter that can be used for assessing the overall gait performance,[10] we suggest that the PAD may have affected the gait performance of our patients with IC. Scherer et al.[23] postulated that there was no difference in the PWS between IC patients and their healthy control group. Myers et al.[7] pointed out that the PWS of IC patients was higher than their control subjects. It is difficult to explain

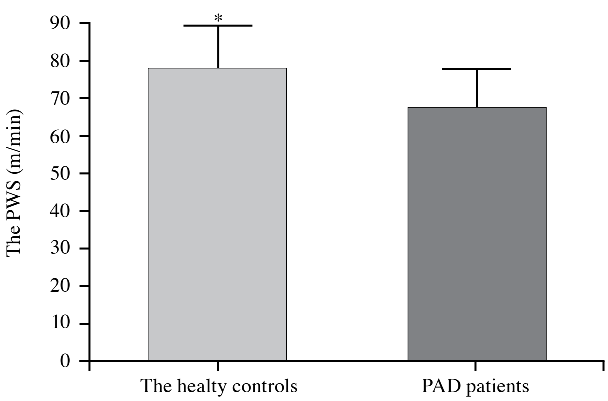

Figure 1. Means and standard deviations of the preferred walking speeds of both groups. * Statistically significant (p<0.05); PWS: Preferred walking speed.

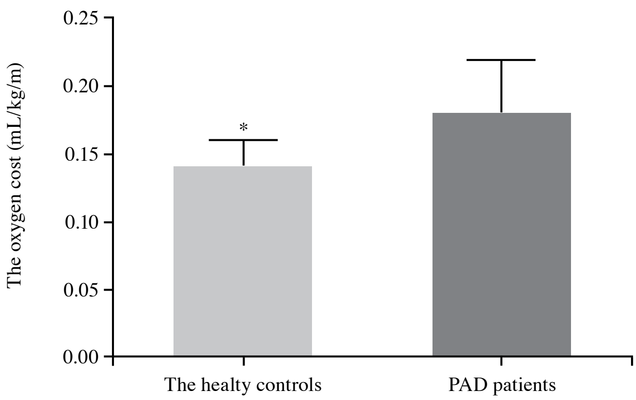

Figure 2. Means and standard deviations of the oxygen cost of walking of both groups. * Statistically significant (p<0.05); PAD: Peripheral arterial disease.

the higher PWS in claudicant patients while postulating ambulatory limitations. In accordance with our results, Crowther et al.[3] and Gardner et al.[24] reported a lower PWS than their healthy subjects. The PWS was not reported as a predictor of quality of life in patients with claudication in Myers et al.'s study.[7] To summarize, it can be assumed that the PWS is a good predictor of gait performance. As declared before, altered gait performance may affect the patients' quality of life.[22]

The oxygen cost of walking

The oxygen cost of walking is an another gait parameter that revealed gait efficiency. The age and BMI of the subject have an effect on the oxygen cost of walking;[11] therefore, we tried to match these parameters between the groups in our study. The oxygen cost of walking in healthy subjects is 0.15 mL/kg/m in people between 20 and 59 years of age,[11] and it may lead to discrimination between the normal and pathological gait.[11,12] We preferred to use the PWS instead of a fixed walking speed in our study. As previously explained, the oxygen cost is lowest at the PWS and increases with a lower or higher PWS (U-shape).[25] The lower PWS in the IC group led to a higher oxygen cost in the present study that could be considered as a decreased metabolic efficiency of walking. Crowther et al.[3] postulated that the kinematics of walking for IC patients is different than for healthy subjects. This may lead to higher oxygen cost in IC patients. The PWS and the oxygen cost of walking can help to differentiate between normal healthy subjects and PAD-IC patients. Thus, these two variables can be used for assessing the outcomes of the different treatment policies associated with PAD-IC patients.

The maximal walking distance of the PAD-IC patients

There was a negative correlation between the oxygen cost of walking and the maximal walking distance in our study. This result implies that when the patients walk more efficiently (lower oxygen cost), the maximal walking distance will be longer. The severity of the PAD can be assessed by using the Fontaine or Rutherford classifications, and the maximal walking distance is an important parameter that can be used in both types of classification.[9] The maximal walking distance and oxygen cost relationship may serve as important variables in determining the severity of the PAD. Determining the maximal walking distance at the PWS in daily living environments is rather difficult; hence, it can only be obtained easily by using the treadmill in the laboratory. The determination of maximal walking distance on the treadmill walking trial is the gold standard method for patients with PAD-IC.[9,27]

The Borg score

The Borg score was used to determine the perceived exertion while walking on the treadmill in both groups. A high Borg score showed that the intensity of the walking trial at the PWS was higher for the patients than for the healthy controls. We found that there was a positive correlation between the Borg score and the claudication pain scale score. This correlation demonstrated that the pain that occurred while walking on the treadmill affected the perceived exertion in PAD-IC patients. In accordance with our results, it was pointed out that exercise-induced ischemic pain decreases the peak exercise performance during treadmill exercise testing.[26] Additionally, the higher oxygen cost of the walking and the higher perceived exertion can serve as the main reasons for lesser mobilization in PAD-IC patients. The initial claudication distance can be easily recorded in the treadmill testing. In our study, this distance had a negative correlation with both the Borg score and the claudication pain scale scores. When the initial claudication distance was shorter, the scores of both scales were higher. This result implies that both scores were influenced by the initial claudication distances.

The IC questionnaire of the patients with PAD-IC

The score of the IC questionnaire was not correlated with any of the variables in our study. According to the self-reported initial claudication distance, 66.6% of the patients were able to walk more than 200 meters. The initial claudication distance recorded while walking on the treadmill proved that 33.3% of the patients were able to walk farther than that. This discrepancy can be attributed to the perception of a higher quality of life, which may lead to lower IC questionnaire scores in those with PAD-IC. This data clearly established that qualitative parameters, for instance self-reported initial distance, should be validated by quantitative methods, such as the determination of the initial claudication distance on the treadmill walking test.

A limitation of our study was the low number of participants. This was primarily due to the exclusion of IC patients with diabetes since PAD-IC is highly comorbid with diabetes mellitus (DM) and other cardiovascular diseases.[17]

In conclusion, the metabolic efficiency of walking and PWS are decreased in PAD-IC patients. Our results suggest that the oxygen cost of walking, PWS, Borg score, scores on the claudication pain scale, initial claudication distance, and maximal walking distance are objective parameters that can be used to monitor the ambulatory limitations of patients with PAD-IC.

Declaration of conflicting interests

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