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Original Article / Özgün Makale

Differences in pain, fatigue, and quality of life in patients with chronic venous insufficiency based on physical activity level

Kronik venöz yetmezliği olan hastalarda fiziksel aktivite düzeyine göre ağrı, yorgunluk ve yaşam kalitesindeki farklılıklar

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ABSTRACT

Background: This study aims to compare the effect of different physical activity levels on pain, fatigue, and quality of life in patients with chronic venous insufficiency.

Methods: Between October 2018 and February 2019, a total of 69 patients (4 males, 65 females; mean age 50 years; range, 19 to 73 years) who were diagnosed with chronic venous insufficiency and consulted for physiotherapy were included in the study. The physical activity level of the patients was determined using the International Physical Activity Questionnaire in three groups as light, moderate, or vigorous. Fatigue, pain, and QoL were assessed using the Fatigue Severity Scale, visual analog scale (during the night, activity, and rest), and Venous Insufficiency Epidemiological and Economic Study Quality/Symptom Scale, respectively.

Results: Of a total of 69 patients, 17 were in the light-intensity physical activity group, 32 in the moderate-intensity physical activity group, and 20 in the vigorous-intensity physical activity group. Perceived pain during activity and fatigue were significantly different between the light- and moderate-intensity physical activity groups ($p<0.05$). There was no significant difference in pain, fatigue, and quality of life scores between the vigorous-intensity physical activity group and the other two groups ($p>0.05$).

Conclusion: Our study results suggest that a moderate level of physical activity may be helpful to overcome symptoms such as pain and fatigue in patients with chronic venous insufficiency and to improve quality of life.

Keywords: Fatigue Severity Scale, International Physical Activity Questionnaire, physical activity, Venous Insufficiency Epidemiological and Economic Study Quality/Symptom Scale, visual analog scale, venous insufficiency.

ÖZ

Amaç: Bu çalışmada kronik venöz yetmezliği olan hastalarda, farklı fiziksel aktivite düzeylerinin ağrı, yorgunluk ve yaşam kalitesi üzerindeki etkisi karşılaştırıldı.

Çalışma planı: Ekim 2018 ve Şubat 2019 tarihleri arasında, kronik venöz yetmezliği tanısı konan ve fizyoterapiye başvuran toplam 69 hasta (4 erkek, 65 kadın; ort. yaş 50 yıl; dağılım, 19-73 yıl) çalışmaya alındı. Hastaların fiziksel aktivite düzeyleri, Uluslararası Fiziksel Aktivite Anketi ile hafif, orta ve ağır olmak üzere üç grupta belirlendi. Yorgunluk, ağrı ve yaşam kalitesi sırasıyla Yorgunluk Şiddeti Ölçeği, görsel analog ölçeği (gece, aktivite ve dinlenme sırasında) ve Venöz Yetmezlikte Epidemiyolojik ve Ekonomik Çalışma-Yaşam Kalitesi/Semptom Ölçeği ile değerlendirildi.

Bulgular: Toplam 69 hastanın 17'i hafif düzeyde fiziksel aktivite grubunda, 32'si orta düzeyde fiziksel aktivite grubunda ve 20'si ağır düzeyde fiziksel aktivite grubunda idi. Aktivite sırasında algılanan ağrı ve yorgunluk, hafif ve orta düzeyde fiziksel aktivite grupları arasında anlamlı derecede farklıydı ($p<0.05$). Ağır düzeyde fiziksel aktivite grubu ile diğer iki grup arasında ağrı, yorgunluk ve yaşam kalitesi açısından anlamlı bir fark yoktu ($p>0.05$).

Sonuç: Çalışma sonuçlarımız kronik venöz yetmezliği olan hastalarda ağrı ve yorgunluk gibi semptomlar ile başa çıkmak ve yaşam kalitesini artırmak için orta düzeyde fiziksel aktivitenin yararlı olabileceğini göstermektedir.

Anahtar sözcükler: Yorgunluk Şiddeti Ölçeği, Uluslararası Fiziksel Aktivite Anketi, fiziksel aktivite, Venöz Yetmezlikte Epidemiyolojik ve Ekonomik Çalışma-Yaşam Kalitesi/Semptom Ölçeği, görsel analog ölçeği, venöz yetmezlik.

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Chronic venous insufficiency (CVI) is a common, progressive chronic disease which may adversely affect mobility.[1] Pathophysiological processes linked to CVI can begin long before any visible damages to the large veins.[2] Symptoms may differ among patients, although the most commonly reported ones include limb pain, fatigue, heaviness, itching, night cramps, burning sensation, swelling, edema, and restless leg syndrome.[3,4]

Chronic venous insufficiency is characterized by persistent lower limb venous hypertension due to venous reflux or obstruction and a failure of calf muscle pump function.[5] In addition, a significant reduction in the dorsi and plantar flexion range of motion (ROM) has been reported, particularly in the more advanced form of chronic venous diseases (CVD).[6,7] The impairment of the calf muscle in patients with CVI may lead to an insufficient return of venous blood flow in the lower limbs.[8,9] In certain cases, CVI may also increase the degree of calf muscle deterioration, leading to an altered walking gait and reduction in general mobility.[10-12] To change this negative feedback mechanism, patients with this problem must be encouraged to participate in physical activity, despite the difficulties associated with leg disease to achieve the benefits of physical activity.[13,14]

Physical activity is defined as any bodily movement required to sustain life and produced by the skeletal muscles.[15] It can improve the health and quality of life (QoL) for patients with chronic diseases.[16] Intensity refers to the rate at which the physical activity is being performed or the magnitude of the effort required to perform an activity.[17] The total amount of caloric expenditure during physical activity is measured by the amount of muscle mass producing bodily movements and the intensity, duration and frequency of muscular contractions. The amount of energy expended by each individual is a continuous variable, ranging from light to vigorous.[18]

To express the intensity of physical activities, metabolic equivalents (METs) are commonly used. One MET is defined as the energy cost of sitting quietly and is equivalent to a caloric consumption of 1 kcal/kg/h. The MET is the ratio of an individual's working metabolic rate relative to the resting metabolic rate. Moderate-intensity physical activities (3-6 METs) such as brisk walking, dancing, gardening, housework, active involvement in games, general building tasks or carrying require a moderate amount of effort and noticeably accelerate the heart rate. Vigorous-intensity physical activities (>6 METs) such as running, walking and climbing, fast cycling, aerobics, fast swimming, competitive sports and games, heavy shoveling or digging or carrying more than 20 kg require a large effort and cause rapid breathing and substantial increase in the heart rate.[19] As a result, physical activity may exert positive effects on vascular leg disorders.[20] Therefore, patients with CVI are advised to be more active in their daily living environments.[21] The effects of various levels of physical activity on the most common symptoms of CVI have not been investigated, yet.

In the present study, we aimed to compare the effect of different physical activity levels on pain, fatigue, and QoL in patients with CVI.

PATIENTS AND METHODS

This study was conducted at Department of Physiotherapy and Rehabilitation, Gazi University, Faculty of Health Sciences between October 2018 and February 2019. A total of 69 patients (4 males, 65 females; mean age 50 years; range, 19 to 73 years) who were diagnosed with CVI by an experienced cardiovascular surgeon and consulted for physiotherapy were included in the study. *Inclusion criteria were as follows:* age between 18 and 75 years, having no diagnosis of systemic disease, or prior surgery, and having no psychological diagnosis. Patients who started any new medical treatment within the last month or had deep venous thrombosis were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Gazi University Ethical Commission (E.138533). The study was conducted in accordance with the principles of the Declaration of Helsinki. The severity of venous disease was described based on the internationally accepted Clinical manifestations, Etiological factors, Anatomic distribution of disease, Pathophysiological findings, in which a cardiovascular surgeon classified clinical signs of the disease using seven categories: C0 (no signs of venous disease), C1 (telangiectasias and reticular veins), C2 (varicose veins), C3 (swelling), C4 (subcutaneous changes: C4a is related to pigmentation and eczema changes, and C4b is related to lipodermatosclerosis and white atrophy of the skin), C5 (healed stasis ulceration), and C6 (open stasis ulceration). Additional symptoms including ache, pain, tightness, skin irritation, heaviness, muscle cramps, and other complaints were noted as previously described.[22] Only the patients between C1-C3 stages and with superficial insufficiency as assessed by a cardiovascular surgeon using ultrasound were included in the study.

The most frequent symptoms were pain, a feeling of heaviness in the legs, burning sensation, tired legs sensation, paresthesia, and cramps. The presence of

these symptoms and their associated intensity are known to be related, in most cases, to the stage of the disease and the degree of functional limitation.[23,24]

Outcome Measurements

Physical activity

The International Physical Activity Questionnaire (IPAQ) was developed by researchers from several countries with the support of the World Health Organization and Centers for Disease Control, a standardized tool to evaluate physical activity. Physical activity was assessed using the self-administered long (27-item) form of the IPAQ.[25] The IPAQ questionnaire lists activities and requests the duration and frequency of each activity engaged in over the past week. Durations are multiplied by known METs per activity and the results for all items are summed for the overall physical activity score. Scores for walking and for moderate and vigorous activities are the sums of corresponding item scores. Although sitting has been reported recently, it is not included in the physical activity score, as the IPAQ recommends.

The physical activity level was determined by the Turkish version of the IPAQ, which is a self-reported instrument. According to the IPAQ scores, patients were categorized into three groups as light, moderate, or vigorous.[26,27]

The IPAQ scoring protocol assigns the following MET values to walking: for moderate, and vigorous intensity activity 3.3 METs, 4.0 METs, and 8.0 METs, respectively.[28] This is expressed in the MET-min per week: MET level × min of activity × events per week.[29]

Fatigue

The fatigue level of the patients was evaluated with the Turkish version of the Fatigue Severity Scale (FSS) which is a self-reported scale that measures the severity of fatigue.[30] There are nine items and, for each question, the patient was asked to choose a number from 1 to 7 to indicate how much the patient agrees with each statement, where 1 indicates strong disagreement and 7 indicates strong agreement. A score of ≥4 indicates severe fatigue.[31]

Pain

The sensory dimension of CVI-related pain was assessed with a traditional 10-cm visual analog scale (VAS) (0= no pain; 10= worst pain), which has demonstrated good reliability and validity.[32] The patients mark the point on the line that corresponds best to their symptom severity or control status. They are instructed to put a cross on the straight line at the point that most accurately expresses their degree of pain during rest, activity and at night. When scoring the VAS, the position of the respondent's cross is assigned a score between 0 and 100. The scores can be, then, simply transferred to a 100-value scale using a millimeter tape measure.[33] To illustrate, VAS >5: uncontrolled, VAS 2-5: partly controlled, and VAS <2: well controlled.[34] Pain evaluation was performed in the same order for each patient by physiotherapists to compare pain during rest, activity, and at night.

Venous Insufficiency Epidemiological and Economic Study Quality/Symptom Scale (VEINES-QOL/Sym)

The VEINES-QOL/Sym is a unique scale consisting of 26 parts and two components developed to measure the effect of venous diseases about symptoms and QoL from the patient's perspective. It can be completed in about 10 to 15 min by patients; therefore, it is practical for routine use. It evaluates symptoms (10 items) at five different frequencies (daily, several times a week, once a week, once every few weeks or never), daily activity restrictions (nine items), frequency of leg problems (one item), change within the past year (one item), and psychological effect (five items). In questions about symptoms, daily limitations and psychological effects, the time includes the last four weeks. The scale has two scores. The VEINES-QOL score, with the sum of 25 items, shows the effect of CVD on QoL. The VEINES-Sym score, the sum of the venous symptoms (nine items) and the intensity of the pain felt (one item), provides information on the severity of venous symptoms. Lower scores indicate poorer QoL. The survey has been developed in English.[35,36] The Turkish version of the VEINES-QOL scale was shown to be valid and reliable.[37]

Statistical analysis

Statistical analysis was performed using the SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency. For the comparison of the difference between the groups, the Kruskal-Wallis test was used for three-group comparisons and the Mann-Whitney U test was used for two-group comparisons. A p value of <0.05 with 95% confidence interval (CI) was considered statistically significant.

RESULTS

Of a total of 69 patients, 17 were in the light-intensity physical activity group, 32 in the moderate-intensity physical activity group, and 20 in the vigorous-intensity physical activity group. There was

Table 1. The diagnosis and gender of patients based on physical activity level

	Light physical activity		Moderate physical activity		Vigorous physical activity	
	n	%	n	%	n	%
Diagnosis						
CVI	6	35.5	13	40.6	6	30
Lymphedema	3	17.6	9	28.1	7	35
CVI + lymphedema	8	47.1	10	31.3	7	35
Gender						
Female	16	94.4	30	93.8	19	95
Male	1	5.6	2	6.3	1	5

CVI: Chronic venous insufficiency.

no significant difference in age and gender among the three groups (p>0.05) (Table 1).

Although the median age was higher in the group with light-intensity physical activity group, there was no statistically significant difference among the groups. However, there was a statistically significant difference in the VAS scores for perceived pain during activity and FSS scores among the groups (p<0.05) (Table 2).

In addition, there was a statistically significant difference in the pain scores during activity and fatigue between the light- and moderate-intensity physical activity groups (p<0.05) in favor of the moderate-intensity group. However, there was no significant difference in pain, fatigue and QoL scores between the vigorous-intensity physical activity group and the other two groups (p>0.05) (Table 3).

Table 2. Differences between groups according to age, BMI, pain, fatigue, and QoL scores

	Light physical activity		Moderate physical activity		Vigorous physical activity			
	Median	IQR	Median	IQR	Median	IQR	Chi-square	*p*
Age (year)	60	50-65	51.5	32.25-59	41	33-55	4.568	0.102
BMI (kg/m^2)	31.40	27.45-36.05	25.62	23.64-29.73	27.23	25.46-35.49	5.214	0.074
VAS (cm)								
During activity	6.5	2-8,1	2	0-5	4	0-8,4	8.669	0.013*
During rest	4.8	0-6	0	0-3.6	2	0-4	3.361	0.186
At night	3	0-6.4	1	0-4	1	0-4	2.167	0.338
FSS (point)	49	44.25-55.75	37.50	32.25-49.25	40.5	32.5-57	6.485	0.039*
VEINES								
Sym (point)	37	32-49	43	36-48	40	31-43.25	2.990	0.224
QOL (point)	26	17-32	26	18.00-31.75	25	19.75-29.75	0.189	0.910

BMI: Body mass index, QoL: Quality of life, IQR: Interquartile range, VAS: Visual analog scale, FSS: Fatigue severity scale, VEINES: Venous insufficiency epidemiological and economic study quality/symptom scale, * p<0.05, Chi-square test.

Table 3. Differences between light, moderate, and vigorous level of physical activity groups

	Light-moderate physical activity		Vigorous-moderate physical activity		Vigorous-light physical activity	
	Z	*p*	Z	*p*	Z	*p*
VAS during activity	-2.890	0.004*	-1.812	0.070	-0.784	0.433
FSS	-2.649	0.008*	-0.791	0.429	-1.400	0.161

VAS: Visual analog scale, FSS: Fatigue severity scale, * p<0.05, Mann-Whitney U test.

DISCUSSION

To the best of our knowledge, this study is the first to investigate the effects of physical activity levels on pain, fatigue, and QoL in patients with CVI. Our study results showed that a moderate-intensity physical activity could significantly decrease pain during activity and fatigue. A recent study focuses on the relationship among the QoL, functional capacity, physical activity and performance levels of CVD and showed that, in patients with CVD, the QoL decreased when physical activity, functional capacity, and performance remained low. In addition, the authors reported that QoL had a low, but positive and significant correlation with physical activity ($r=0.178$; $p<0.05$).[38]

Physical activity is known to improve health and QoL in chronic diseases[15] and is associated with a remarkable decrease in cardiovascular mortality.[39] Strong evidence demonstrates that individuals who are more active have lower rates of all-cause mortality with decreased blood pressure, and exhibit a higher level of cardiorespiratory fitness and are more likely to achieve weight maintenance.[40] In CVI, physical activity may also have several potential positive effects which control symptoms, improve QoL, and decrease morbidities. As exercise and physical activity can improve the venous return, calf muscle pump,[5] and endurance,[11] the number of fast-twitch fibers (type II fibers),[6,41] functional sympatholysis,[42] and microvascular endothelial function.[43] One way to remediate CVI may be increasing the venous circulation, while modulating sympathetic vasoconstrictor activity with physical activity is the second way.[42]

In the present study, symptoms of CVI decreased in the moderate-intensity physical activity group compared to light- and vigorous-intensity physical activity. In addition, physical activity was found to be associated with reduced pain during activity, fatigue, and improved QoL. As mentioned above, the physical activity groups included walking, cycling, and dancing which require the use of lower limb functions. Physical activity due to lower limb exercises can stimulate the calf muscle pump, which supports the venous circulation. In particular, walking is beneficial as it causes the calf muscles to contract and expand by increasing the blood pump from the lower limb upward toward the heart.[44] When pump function becomes impaired, this can contribute to the development of edema in the lower limbs and other symptoms of CVI.[45] In a study, Heinen et al.[46] evaluated the level of walking and leg exercises among patients with venous leg ulcers. A total of 150 patients had leg ulcers caused mainly by venous insufficiency and 35% of the patients did not have a 10-min walk even once a week. Low levels of physical activity were established in patients with venous leg ulcers. This finding indicates the importance of physical activity in CVD.

In our study, we used the IPAQ to evaluate physical activity. Using this questionnaire, the duration and frequency of every individual's activity were assessed and the IPAQ scores were categorized into three groups as light, moderate, or vigorous. One of our main results highlights the importance of moderate level of physical activity to control fatigue, pain, and QoL in CVI patients. Of note, general public health recommendations are composed of at least 30-min moderate-intensity physical activity on most, preferably, all days of the week.[28,47]

It is known that the efficacy of at least 30-min moderate-intensity physical activity on at least five days of the week and have shown its beneficial effect on different physiological and clinical variables.[48] The international message of recent guideline is that health benefits can be only achieved, when a 150-min/week moderate-to-vigorous physical activity is achieved. This threshold and expert opinion-based message consistently demonstrate that a volume of physical activity of half (or even less) of 150-min/week recommendation may yield significant health benefits.[49] Observational, population-based studies have also suggested that this activity level is associated with a reduced risk of several chronic diseases and increased longevity.[50]

In the present study, we found the beneficial effect of moderate exercise on fatigue and pain for CVI patients. There are many factors which contribute to the association between the physical activity and fatigue. Individuals with CVI can continue their physical activity to avoid excessive fatigue.[51] Calf muscle fatigue, being the most essential factor of fatigue in CVI, may be a particularly important determinant in the compliance of CVI patients to perform physical activity. In previous studies, muscle fatigue was found to be strongly influenced by a failure of Ca^{2+} release and depressed NaC-KC-ATPase enzyme activity.[52,53] Another factor contributing to fatigue may be the increased lactic acid levels in skeletal muscles.[41] It has been thought that the pumping mechanisms of calf muscles and the vasodilatation of the vessels may not be effective enough in patients with a low level of physical activity. Additionally, increased levels of stress and forceful efforts may lead to insufficient time for recovery. However, moderate-intensity exercise was

shown to have a greater effect on reducing fatigue and increasing walking endurance than vigorous-intensity exercise. This outcome can be attributed to the nature of the mechanism of physiological changes as a result of exercise. It is well-known that regular exercise induces stress and must attain a certain level of stress for adaptation to occur.[54] Forty-two trials involving 3,816 participants showed that exercise resulted in significant reductions in fatigue (standardized mean difference 0.32, 95% CI 0.13 to 0.52) and a significant negative correlation was found between the aerobic exercise intensity and reduced fatigue.[55]

In CVI, immobilization of the limbs for two weeks leads to prolonged venous hypertension that can produce pain[10] due to impaired functional sympatholysis.[42] A moderate level of activity, but not low and high-level, may be an option to reduce CVI-related pain. The link between moderate physical activity and reduced pain incidence, intensity and/or pain sensitivity have indicated the requirement to select quantitative sensory test assessments.[56] Although the level of physical activity could be measured with certain devices to be more accurate, the IPAQ was used in our study, as in many clinics, due to unavailability of these devices in our facility. On the other hand, this limitation can be tolerated, as the IPAQ could be easily applied and adopted in clinical practice.

To date, no study has examined the most optimal level of physical activity in patients with CVI. Physical activity is an important factor for individuals with vascular leg problems.[20] In all previous reviews, all types and intensities of physical activity were collected and there has been a lack of evidence on the safety and efficacy of exercise in relation to dose.[57,58] Determining the most optimal level of physical activity to control CVI symptoms may be useful for the prevention of disease progression and its adverse consequences. In addition to physical activity recommendation, the effort level may have a critical role in this patient population. Therefore, the effects of different levels of physical activity on CVI symptoms should be investigated in further studies.

In conclusion, our study results suggest that a moderate level of physical activity may be helpful to overcome symptoms such as pain and fatigue in patients with chronic venous insufficiency with improved quality of life.

Declaration of conflicting interests

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