



## Kinesiophobia, exercise capacity, peripheral muscle strength and physical activity in patients with hypertension: A cross-sectional study

Nihan KATAYIFÇI <sup>1,\*</sup>, İrem HÜZMELİ <sup>1</sup>, Döndü İRİŞ <sup>2</sup>, Fatih YALÇIN <sup>3</sup>

<sup>1</sup>Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Hatay Mustafa Kemal University, Hatay, Türkiye

<sup>2</sup>Department of Physiotherapy and Rehabilitation, Institute of Health Sciences, Hatay Mustafa Kemal University, Hatay, Türkiye

<sup>3</sup>Department of Cardiology, Tayfur Ata Sökmen Faculty of Medicine, Hatay Mustafa Kemal University, Hatay, Türkiye

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### Abstract

Functional limitations have recently been shown in patients with hypertension. However, the causes of kinesiophobia remain unknown. The aim was to compare functional exercise capacity, peripheral muscle strength, level of kinesiophobia, physical activity, fatigue, dyspnea, and quality of life in hypertension patients and healthy controls and to investigate the relationship between aforementioned outcomes in patients. Fifty-six patients and 45 matched controls were included. Functional exercise capacity [6 min. walking test (6MWT)], peripheral muscle strength (Dynamometer), kinesiophobia (Tampa Scale of Kinesiophobia), physical activity level [International Physical Activity Questionnaire (IPAQ)], perception of dyspnea (Modified Medical Research Council Dyspnea scale), fatigue (Fatigue Severity scale), and quality of life (Short Form-36 questionnaire) were evaluated. Demographic characteristics were similar in patients (54.58±11.33y,35M/21F) and healthy controls (51.11±7.42y,33M/12F) ( $p>0.05$ ). Peripheral muscle strength ( $p<0.05$ ), 6MWT, physical activity, and quality of life were significantly lower ( $p<0.05$ ); level of kinesiophobia ( $p<0.001$ ), perception of dyspnea ( $p<0.001$ ), and fatigue ( $p=0.001$ ) scores were higher in patients compared with controls. IPAQ ( $r=-0.556$ ,  $p<0.001$ ), quadriceps femoris ( $r=-0.429$ ,  $p=0.001$ ), hip flexor ( $r=-0.380$ ,  $p=0.004$ ), shoulder abductor ( $r=-0.410$ ,  $p=0.002$ ), elbow flexor ( $r=-0.364$ ,  $p=0.006$ ), hand-grip strength ( $r=-0.355$ ,  $p=0.007$ ), fatigue ( $r=0.434$ ,  $p=0.001$ ), SF-36 physical functioning ( $r=0.404$ ,  $p=0.002$ ), role limitations due to physical health ( $r=-0.370$ ,  $p=0.005$ ), energy/fatigue ( $r=-0.357$ ,  $p=0.007$ ), general health ( $r=-0.280$ ,  $p=0.036$ ) was related to kinesiophobia in patients. Patients had impaired functional exercise capacity, peripheral muscle strength, higher levels of kinesiophobia, perception of fatigue and dyspnea, reduced physical activity level, and quality of life compared with healthy controls. In addition, a higher degree of kinesiophobia was related to physical inactivity, weakened upper and lower extremity muscle strength, fatigue, and impaired quality of life in patients. Patients should be directed to cardiopulmonary rehabilitation.

**Keywords:** hypertension, kinesiophobia, physical activity, exercise capacity, muscle strength

### 1. Introduction

Hypertension, which affects about 25% of the general population and 65% of the elderly population, is one of the causes of mortality related to cardiovascular disorders (1). Therefore, it is important to determine and control target organ damage of hypertension (2). A decrease in exercise capacity has been shown in previous studies (3,4). In addition, exercise intolerance is associated with decreased skeletal muscle strength, physical inactivity, and cardiorespiratory fitness (2). Also, patients with cardiovascular diseases frequently experience fatigue; however, it is not known whether this occurs in patients with hypertension (5). Moreover, a recent meta-analysis showed that hypertension patients exhibit lower quality-of-life indicators than normotensives, particularly in the parameters connected to the physical domain (6).

Reduced physical activity is closely related to kinesiophobia (7). Kocjan found that a high level of kinesiophobia was significantly correlated with a high level of physical inactivity in patients with hypertension (7). However, whether muscle strength, fatigue or quality of life affects kinesiophobia is unknown.

Studies investigating the clinical symptoms of functional exercise capacity, peripheral muscle strength, physical activity level, kinesiophobia, quality of life, and fatigue in hypertension were not clear and insufficient. Therefore, this study's primary objective was to compare functional exercise capacity, peripheral muscle strength, kinesiophobia, fatigue, dyspnea, physical activity, and quality of life in patients with hypertension and healthy controls. The secondary objective

was to research the relationship between kinesiophobia, functional exercise capacity, peripheral muscle strength, fatigue, dyspnea, physical activity, and quality of life in patients with hypertension.

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## 2. Materials and methods

### 2.1. Patients

Fifty-six patients were referred to the department between December 2020 and November 2021, and 45 matched controls were included in the study. Hypertension patients aged between 18 and 80 years, with no changes in medication during the previous three weeks and being clinically stable for at least four weeks, were included in the study. Patients with severe musculoskeletal and neurological diseases, pulmonary diseases, acute myocardial infarction, malignancies, and complex arrhythmias were excluded.

The study, carried out in conformity with the Declaration of Helsinki, was approved by the Non-Interventional Clinic Research Ethics Committee of the Hatay Mustafa Kemal University (No: 2020/02). Written informed consent was obtained from all patients and controls to participate in the study.

### 2.2. Study design

A cross-sectional study was carried out. Assessment of functional exercise capacity, peripheral muscle strength, kinesiophobia, fatigue, dyspnea, comorbidity, PA level, and QOL of patients and controls were tested by a physiotherapist. A cardiologist evaluated the patients' clinical assessments. Physical and socio-demographic data were recorded.

The 6-minute walking test (6-MWT) was used to assess functional exercise capacity. The 6-MWT was performed according to ATS guidelines (8). For comparison, reference values were used (9). The 6-minute walking work (6-MW<sub>w</sub>) was calculated as the product of the most significant 6-MWT distance (in meters) and weight (in kilograms) (10). Quadriceps femoris, hip flexor, shoulder abductor, and elbow flexor muscle strength were assessed with a dynamometer (JTECH Power Track Commander, Baltimore, MD, USA). The percentage of predicted values was expressed (11). Handgrip strength was evaluated with a Jamar analogue hand dynamometer (PowerTrack II, JTECH Medical, Midvale, Utah, USA) (12). The left and right sides were measured three times, and the greatest value was recorded. The Tampa Scale of Kinesiophobia (TSK), which consists of 17 items, was used to assess kinesiophobia. The scale is scored between 17 and 68 points. Higher scores imply a higher level of kinesiophobia. A score above 37 defines a high level of kinesiophobia (13). The Fatigue Severity Scale (FSS), which includes nine items, was used to evaluate fatigue. Each item scores zero to seven, with a maximum score of 63. Scores above 36 indicate severe fatigue (14). Dyspnea was evaluated with The Modified Medical Research Council (MMRC) dyspnea scale. Dyspnea

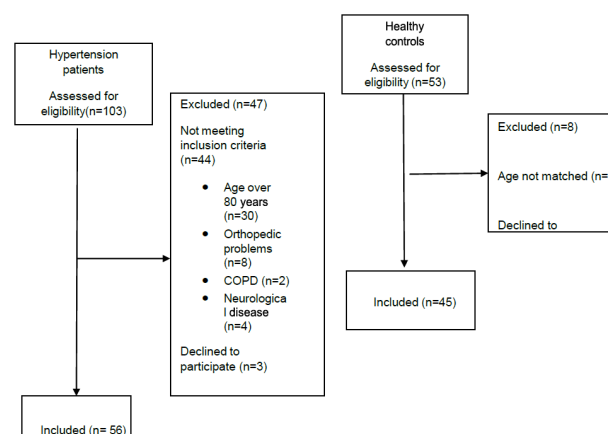
levels were graded from zero to four (15). The comorbidity level was assessed using the Charlson Comorbidity Index (CCI). The index contains 19 medical conditions. The total score indicates an index of severity (16). The International Physical Activity Questionnaire (IPAQ) short-form was used to assess PA level. The IPAQ includes walking time, moderate and vigorous-intensity activity, and sedentary activity information. Also, the scores were classified as inactive, minimally active, and sufficiently active due to the total score (17). The QOL was evaluated with the Short Form 36 (SF-36) questionnaire. The SF-36 includes eight dimensions: role limitations due to physical health, physical functioning, energy/fatigue, emotional well-being, pain, social functioning, role limitations due to emotional problems and general health. The score varies from 0 to 100. Higher scores indicate better QOL (18).

### 2.3. Statistical analyses

The statistical analyses were performed with IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp.). The G\*Power software was used to estimate the sample size. According to the results of a prior study (3), a total of 94 individuals was estimated (47 individuals in each group) to have a power of 80% for an  $\alpha$  value of 0.05 ( $d=0.530$ ). The Shapiro-Wilk test was used to test the normality of data. Normally distributed data were expressed as mean ( $\pm$ standard deviation). The Student's t-test was used to compare the groups' characteristics and reported a mean difference and 95% CI. The Mann-Whitney U test was used to compare non-distributed data shown as median (IQR). Nominal data were analysed with the Chi-square test. Pearson's and Spearman's rank correlation coefficients were used to calculate correlations between TSK, demographic, and clinical factors. A p-value of  $<0.05$  was considered statistically significant.

## 3. Results

Fifty-six patients with HT and 45 healthy controls were included and compared. The distribution of patients and controls is summarized in Fig. 1. Demographics and clinical characteristics of HT patients and healthy controls were similar ( $p>0.05$ ), except for the CCI ( $p<0.001$ ) score (Table 1).



**Fig. 1.** Flow diagram of the patients with hypertension and healthy controls

The distances covered during the 6-MWT, 6-MWT%, and 6MWw were significantly lower in patients than in healthy controls ( $p<0.001$ ) (Table 2, Fig. 2). Forty-two (75%) patients' predicted 6-MWT values were less than 80%. The parameters of the 6-MWT are given in Table 2. Measured and predicted quadriceps femoris, hip flexor, shoulder abductor, elbow flexor, and handgrip muscle strength were significantly higher in controls compared with patients ( $p<0.05$ , Table 3). The predicted muscle strength values that were less than 80% were in 54 (96.4%) patients for quadriceps femoris, in 21 (37.5%) patients for hip flexors, in 48 (85.7%) patients for shoulder abductors, and in 42 (75%) patients for elbow flexors. The TSK ( $p<0.001$ ), FSS ( $p=0.001$ ), mMRC ( $p<0.001$ ) scores and IPAQ

sitting duration ( $p=0.005$ ) were statistically significantly higher, and IPAQ total PA ( $p<0.001$ ), moderate ( $p=0.002$ ) and vigorous activity ( $p<0.001$ ) and SF-36 subscale scores ( $p<0.05$ ), except for social functioning, were higher in the controls compared with the patients (Table 4). Forty-four (78.6%) patients had a high level of kinesiophobia (TSK score  $>37$ ), and 23 (41.1%) patients reported severe fatigue. Thirty-five (62.5%) patients were inactive, 19 (33.9%) were minimally active, and two (3.6%) of the patients were sufficiently active. On the other hand, 18 (40%) of the controls were inactive, 31 (28.9%) were minimally active and 14 (31.1%) were sufficiently active ( $p=0.001$ ).

**Table 1.** Demographic characteristics of patients with hypertension and healthy control groups

Variables	Hypertension patients Mean $\pm$ SD Median (IQR)	Control Mean $\pm$ SD Median (IQR)	Mean difference %95 CI	p
Age (years)	54.58 $\pm$ 11.33	51.11 $\pm$ 7.42	3.47(-0.41-7.36)	0.079
Sex (female/male)	21/37.5%;35/62.5%	12/26.7%;33/73.3%		0.290
Weight, kg	81.65 $\pm$ 11.74	79.91 $\pm$ 10.29	1.74(-2.67-6.16)	0.436
Height, cm	168 (160.25-173)	167 (165-177)		0.304
BMI, kg/m <sup>2</sup>	29.14 $\pm$ 4.10	27.77 $\pm$ 3.20	1.36(-0.11-2.85)	0.070
Normal/over weighted/obese, n (%)	7/12.5%;29/51.8%;20/35.7%	9/20%;26/57.8%;10/22.2%		0.275
Smoking (pack.year)	3 (0-29.50)	1 (0-26)		0.316
Smoking (current/ex/non-smoker), n (%)	10/17.9%;21/37.5%;25/44.6%	10/22.2%;13/28.9%;22/48.9%		0.642
CCI score	2 (2-3)	0 (0-0)		<b>&lt;0.001*</b>
	n/%			
Medical history				
Diabetes mellitus	24/42.9%			
Hyperlipidemia	13/23.2%			
Chronic coronary syndrome	17/30.4%			

BMI: body mass index; CCI: Charlson Comorbidity Index; CI: confidence interval. \* $p<0.05$ .

**Table 2.** Comparison of 6-MWT parameters in patients with hypertension and healthy control

6-MWT parameters	Hypertension patients Mean $\pm$ SD Median (IQR)	Controls Mean $\pm$ SD Median (IQR)	Mean difference %95 CI	p
6-MWT distance, m	430.30 (344.40- 488.40)	604.80 (570-646)		<b>&lt;0.001*</b>
6-MWT distance, % predicted	71.14 (58.98-80.28)	96.89 (85.66-103.82)		<b>&lt;0.001*</b>
6MWw, kg·m	33281.96 $\pm$ 12146.11	48431.11 $\pm$ 7685.12	-15149.14 [(-19281.35)-(-11016.94)]	<b>&lt;0.001*</b>
Heart rate, beats/min (resting)	73(68-84.75)	79(71-89)		0.082
Peak heart rate, beats/min	101.96 $\pm$ 19.44	108.68 $\pm$ 23.10	-6.72 (-15.12-1.67)	0.115
Maximum heart rate, %	61.76 $\pm$ 11.45	64.57 $\pm$ 14.43	-2.80(-7.91-2.30)	0.278
Systolic blood pressure, mmHg (resting)	140 (140-140)	120 (110-120)		<b>&lt;0.001*</b>
$\Delta$ Systolic blood pressure, mmHg	10(5-20)	10 (7.50-30)		<b>0.153</b>
Diastolic blood pressure, mmHg (resting)	80 (70-86.75)	74(70-80)		0.111
$\Delta$ Diastolic blood pressure, mmHg	5(0-10)	6(0-10)		0.207
SpO <sub>2</sub> , % (resting)	98 (97-98)	98 (97-98)		0.986
$\Delta$ SpO <sub>2</sub> , %	0 (0-0)	0 (0-0)		0.260
Breathing frequency, breaths/min (resting)	21.50 (20-24)	21 (17-24)		0.188
$\Delta$ Breathing frequency, breaths/min	5.50 (4-8)	6 (4-8)		0.765
Dyspnea, 0–10 (resting)	0 (0-0)	0 (0-0)		0.203
$\Delta$ Dyspnea, 0–10	0 (0-2)	0 (0-1.50)		0.405
Fatigue, 0–10 (resting)	0 (0-0)	0 (0-0)		0.154
$\Delta$ Fatigue, 0–10	1(0-3)	0(0-3)		0.307

6-MWT: 6-minute walk test, SpO<sub>2</sub>: Oxygen saturation, 6MWw: 6-minute walk distance x body weight; CI: confidence interval. \* $p < 0.05$ .

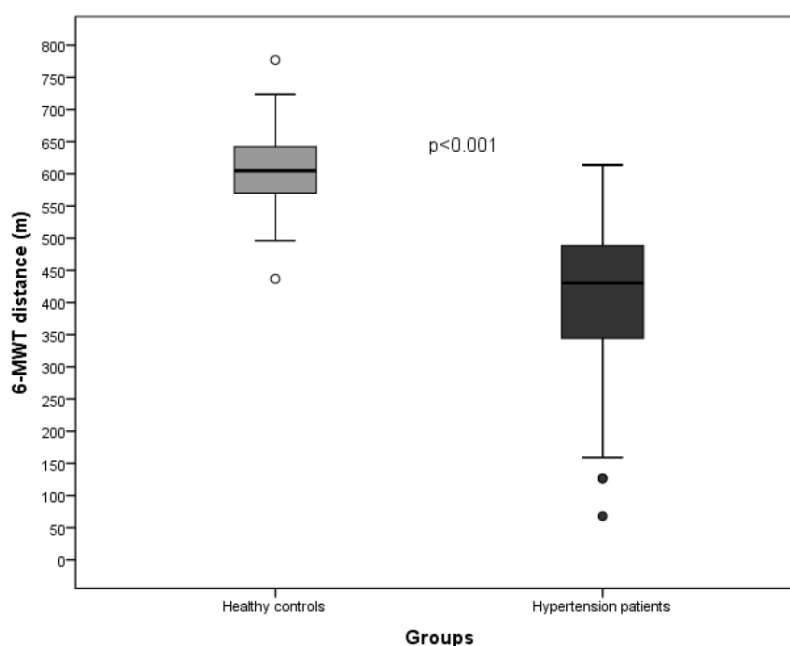


Fig. 2. Six-minute walk test distance of the patients with hypertension and healthy controls

Table 3. Comparison of peripheral muscle strength in patients with hypertension and healthy control

Variables	Hypertension patients Mean ± SD Median (IQR)	Control Mean ± SD Median (IQR)	Mean difference %95 CI	p
Quadriceps femoris (Right), N	169.60 (132-214.75)	184 (168-221.50)		0.021*
Quadriceps femoris (Left), N	149.90 (112.50-196.75)	184 (160-220)		0.005*
Quadriceps femoris, % predicted	35.29 (31-44.60)	43.61 (37-50.43)		0.002*
Hip flexors (Right), N	143.50 (110-178.25)	200 (172.50-218.50)		<0.001*
Hip flexors (Left), N	134 (114-179.75)	182 (158-215.50)		<0.001*
Hip flexors, % predicted	95.67±31.89	119.40±35.90	-23.72 [(-37.12)-(-10.32)]	0.001*
Shoulder abductors (Right), N	108.50 (84.70-123)	154 (116-193)		<0.001*
Shoulder abductors (Left), N	99 (80.65-128.75)	140 (113-176)		<0.001*
Shoulder abductors, % predicted	57.76 (43.38-72.27)	74.14 (66.20-91.88)		<0.001*
Elbow flexors (Right), N	129 (108.50-181.50)	169 (132-213)		0.005*
Elbow flexors (Left), N	130.50 (105-183.50)	158 (136-215.50)		0.008*
Elbow flexors, % predicted	64.12 (43.93-80.86)	78.47 (56.16-94.35)		0.019*
Hand grip strength (Right), P	69.30±25.53	84.53±22.56	-15.22 [(-24.86)-(-5.59)]	0.002*
Hand grip strength (Left), P	65.89±22.89	79.97±22.20	-14.08 [(-23.05)-(-5.11)]	0.002*

N: Newton; P: Pound; CI: confidence interval. \*p<0.05.

**Table 4.** Comparison of fear of movement, fatigue, dyspnea, physical activity level and Qol in patients with hypertension and healthy control

Variables	Hypertension patients Mean ± SD Median (IQR)	Control Mean ± SD Median (IQR)	Mean difference %95 CI	P
TSK score (17–68)	38 (35-41)	19 (17-23)		<0.001*
FSS score (1–7)	27.50 (14-50)	12 (6-29)		0.001*
MMRC score (0–4)	1 (0-2)	0 (0-0)		<0.001*
IPAQ (MET-min/week)				
<b>Total</b>	297 (165-767.25)	1140.00 (359.25-3421.50)		<0.001*
<b>Walking</b>				
Walking	272.25 (152.62-693)	462 (181.50-1386)		0.070
Moderate	0 (0-0)	0 (0-1140)		0.002*
Vigorous	0 (0-0)	0 (0-720)		<0.001*
Sitting (min/day)	360 (300-480)	240 (180-435)		0.005*
<b>SF-36 subscales (0-100)</b>				
Physical functioning	80 (55-90)	100 (90-100)		<0.001*
Role limitations due to physical health	87.50 (0-100)	100 (100-100)		<0.001*
Role limitations due to emotional problems	100 (0-100)	100 (100-100)		<0.001*
Energy/fatigue	60 (30-80)	75 (60-85)		0.009*
Emotional well-being	62.64±21.72	75.11±16.75	-12.46 [(-20.28)-(-4.65)]	0.002*
Social functioning	100 (75-100)	100 (81.25-100)		0.664
Pain	78.75 (55-100)	90 (77.50-100)		0.026*
General health	55 (41.25-70)	85 (65-90)		<0.001*

TSK: Tampa Scale of Kinesiophobia; FSS: Fatigue Severity Scale; MMRC: Modified Medical Research Council Dyspnea Scale; IPAQ, International Physical Activity Questionnaire; SF-36, Short-Form 36; CI: confidence interval. \*p < 0.05.

### 3.1. Correlations

Kinesiophobia was significantly correlated with total IPAQ score ( $r=-0.556$ ,  $p<0.001$ ), left quadriceps femoris muscle strength ( $r=-0.429$ ,  $p=0.001$ ), left hip flexor muscle strength ( $r=-0.380$ ,  $p=0.004$ ), left shoulder abductor muscle strength ( $r=-0.410$ ,  $p=0.002$ ), right elbow flexor muscle strength ( $r=-0.364$ ,  $p=0.006$ ), left elbow flexor muscle strength ( $r=-0.293$ ,  $p=0.028$ ), left handgrip strength ( $r=-0.355$ ,  $p=0.007$ ), right handgrip strength ( $r=-0.337$ ,  $p=0.011$ ), fatigue ( $r=0.434$ ,  $p=0.001$ ), SF-36 physical functioning ( $r=-0.404$ ,  $p=0.002$ ), role limitations due to physical health ( $r=-0.370$ ,  $p=0.005$ ), energy/fatigue ( $r=-0.357$ ,  $p=0.007$ ) and general health ( $r=-0.280$ ,  $p=0.036$ ).

### 4. Discussion

The main findings of the current study were: (1) functional exercise capacity and upper and lower extremity muscle strength are impaired; (2) kinesiophobia, fatigue, and dyspnea levels are increased; (3) PA level and QOL are reduced in HT patients compared with healthy controls, and (4) physical inactivity, weakened upper and lower extremity muscle strength, fatigue and impaired QOL are associated with a higher degree of kinesiophobia in HT patients.

Kinesiophobia was found to be a contributing factor to physical inactivity in patients with HT (19). It is known that controlled hypertension is related to decreased adverse events. Also, physical activity is one of the key factors to control hypertension (19). Nair et al. stated that 78% of the patients with HT had kinesiophobia. Also, kinesiophobia was negatively correlated with physical activity (20). Another study reported moderate intensity of kinesiophobia in patients with

HT, and kinesiophobia was associated with physical inactivity (7). In the current study, 78.6% of patients had a high level of kinesiophobia, consistent with the literature. In addition, to our knowledge, we indicated that kinesiophobia was related to not only physical activity but also upper and lower extremity muscle strength, fatigue and QOL in patients for the first time. A reduction in muscle strength may lead to physical inactivity, and muscle weakness and physical inactivity might cause kinesiophobia. Not only psychological parameters but also physical parameters should be considered for investigation and rehabilitation protocols for kinesiophobia in patients with HT.

It was reported that people with reduced mobility are more likely to develop hypertension (4). A study showed that the 6-MWT distance was lower ( $338.8\pm112.8$  vs.  $388.0\pm66.7$ ) in patients with HT than controls (3). In the present study, the 6-MWT distance was lower in patients with HT than in controls [ $430.30$  ( $344.40-488.40$ ) versus  $604.80$  ( $570-646$ )]. In addition, 6-MWw, an alternative method for assessing functional capacity for walking, accounts for bodyweight difference (10) and was lower in patients with HT than in healthy controls. The 6-MWw was more associated with peak  $VO_2$  than the 6-MWT distance in patients with COPD (10). The current study performed 6-MWw in patients with HT for the first time. Improving exercise capacity should be important to prevent or control hypertension.

Peripheral muscle strength abnormalities were shown in patients with HT (4, 21, 22). Cardiovascular disease mortality was related to lower levels of muscle strength in patients with HT (21); furthermore, as muscle strength increased, the

development of hypertension decreased (22). In the current study, both lower and upper extremity muscles were weakened in patients with HT. In addition, weakened proximal upper extremity muscles were also demonstrated for the first time. The effects of resistance training on mortality and peripheral muscle strength should be examined in patients with HT.

Fatigue is a frequent symptom among patients with CVD. It is a major symptom that affects activities of daily living and QOL (5). A study showed that more than 50% of patients with CVD (89.2% of the patients had hypertension) reported fatigue (23). It was stated that fatigue must be assessed in routine evaluations to decrease it in CVD patients (5). In the present study, 41.1% of patients with HT reported severe fatigue. Fatigue may be associated with peripheral muscle weakness, sedentary behaviour, and low functional capacity. Fatigue-related factors should be analysed in patients with isolated HT, and patients with severe fatigue should be referred to rehabilitation programs.

Dyspnea is reported in patients with HT; however, its origin is complex (24). Palhares et al. stated that 26.5% of the patients with HT indicated dyspnea (24). Another study showed that dyspnea was more common in female patients with HT than in males (25). In the present study, patients (66.1% MMRC1–2; 7.1% MMRC 3–4) had higher dyspnea perception than controls. Future studies investigating the effect of managing dyspnea perceptions in patient education programs are needed in patients with HT, and sex differences should be taken into account in assessment and rehabilitation programs.

A recent study stated that physical inactivity is responsible for up to 8% of deaths and non-communicable diseases assignable to physical inactivity (26). It is well-known that physical activity prevents hypertension, and compared with sedentary people, the risk of hypertension was reduced by 6% for people who met the minimum recommended physical activity levels of 150 min/week (10 MET hours/week) (27). In addition, as the amount of activity increases, the risk decreases (27). However, patients with HT were found to be more inactive compared to controls during the COVID-19 pandemic (28). In the current study, 62.5% of patients were inactive, 33.9% were minimally active, and only 3.6% of the patients was sufficiently active. The PA level was lower than in the healthy controls. Patients should be directed for PA counselling in cardiac rehabilitation programs to control hypertension.

Hypertension was found to be a contributing factor to decreased quality of life (6). Impaired quality of life causes barriers to adherence to treatment in patients with HT (29). Studies showed a reduction in quality of life in patients with HT (6, 29); however, we found that impaired quality of life was related to a higher degree of kinesiophobia in patients with HT for the first time in the current study. Physical inactivity, weakened muscle strength, and fatigue might contribute to decreased quality of life. A study stated that nine months of

physical activity interventions improved quality of life and blood pressure control in patients with HT (30). Factors affecting kinesiophobia should be considered while programming interventions to improve the quality of life in patients with HT.

The current study had some limitations. Cardiopulmonary exercise testing was not used due to technical difficulties. However, it should be used in further studies. In addition, patients' anxiety and depression levels, which may affect kinesiophobia, were not evaluated. A questionnaire was used to assess PA levels, but an accelerometer should be used in further studies.

This study showed that patients with HT had lower functional exercise capacity and upper and lower extremity muscle strength, higher levels of kinesiophobia, fatigue, dyspnea, and reduced PA level and QOL compared with healthy controls. In addition, a higher degree of kinesiophobia was related to physical inactivity, weakened upper and lower extremity muscle strength, fatigue, and impaired QOL. Patients with HT should be directed to cardiopulmonary rehabilitation, especially exercise training, PA counselling, and patient education with all other parameters. Further studies are needed to establish the influence of kinesiophobia on the outcomes of cardiopulmonary rehabilitation in patients with HT.

#### **Ethical Statement**

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Hatay Mustafa Kemal University (Date 2020/No.02).

#### **Conflict of interest**

The authors declare no conflict of interest.

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None to declare.

#### **Authors' contributions**

Concept: N.K., D.İ., F.Y., İ.H., Design: N.K., D.İ., F.Y., İ.H., Data Collection or Processing: N.K., D.İ., F.Y., Analysis or Interpretation: N.K., İ.H., Literature Search: N.K., Writing: N.K., D.İ., F.Y., İ.H.

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