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Aerobic capacity and fatigability are associated with activity levels in women with hip osteoarthritis

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Abstract

Physical activity is important for physical function and pain relief in people with lower extremity osteoarthritis (OA). Unfortunately, people with OA are not as active as their peers without OA. The objective of this study was to determine whether aerobic capacity and fatigability are associated with physical activity in women with hip OA. We conducted a cross-sectional analysis of 36 women with hip OA. We assessed aerobic fitness as predicted VO_2 max from a six-minute walk test. We assessed fatigability using a treadmill test. Finally, we assessed self-reported physical activity using the UCLA activity scale, and quantified steps per day and activity intensity using accelerometers. We used Pearson correlations to determine associations. We used regression analysis to determine whether fatigability mediated the association between aerobic fitness and physical activity. On average, subjects were moderately active via the UCLA score (5.2 ± 1.3 out of 10). Aerobic fitness ($R = 0.582$, $p < 0.001$) and fatigability ($R = 0.516$, $p = 0.003$) were significantly correlated with UCLA scores. However, aerobic fitness was the best predictor of UCLA scores, as well as sedentary time, and time spent in light activity. Fatigability was not a mediator between aerobic fitness and UCLA scores. Aerobic fitness and fatigability may be modifiable barriers to physical activity in people with OA. Future interventional studies should examine whether improving aerobic fitness improves physical activity or fatigability.

Keywords

hip osteoarthritis; physical activity; aerobic fitness; fatigue

Introduction

People with osteoarthritis (OA) are at risk for low physical activity and for failing to meet physical activity recommendations.¹⁻³ This is a serious problem because physical activity is

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Author Contribution Statement

KCF contributed to the conception and design of the study, data analysis and interpretation, and drafting the article. BA contributed to data analysis, acquisition of data, data analysis and interpretation, and drafting the article. CH, MH, and SJC contributed to acquisition of data or provision of data, analysis and interpretation of data, and revising the article critically. All authors provided final approval of the version to be submitted.

critical for healthy aging. Physical activity promotes cardiovascular health, cognitive health, and living independence.⁴⁻⁶ Moreover, increasing physical activity is beneficial for those suffering from OA because physical activity has positive effects on physical function and pain.⁷⁻⁹ OA is associated with increased cardiovascular morbidity and mortality,^{10, 11} in part through its adverse effect on mobility.^{12, 13} Together, these findings suggest that improving physical activity is an important goal in the care of the older adult with OA. However, the reasons for reduced physical activity in people with OA are not well understood.

Fatigue is one factor that can contribute to lower physical activity in older adults generally.¹⁴⁻¹⁶ Fatigue is a common symptom associated with OA,^{17, 18} and has been linked to lower physical activity in people with OA.^{14, 19} Fatigability is a separate but related construct.^{20, 21} While fatigue can arise from a number of mental and physical sources, fatigability refers to the process of becoming more fatigued with activity. Fatigability has been associated with lower physical activity in general samples of older adults²² but has not yet been related to physical activity in people with OA.

Separately, energy availability, or specifically the reduction in energy availability associated with aging, has been proposed as a factor limiting physical activity in older adults.²³ It has been postulated that people who require more energy relative to their total energy capacity for activities of daily living, such as walking, have less energy reserve and are therefore less likely to participate in physical activity.²⁴ This hypothesis is dubbed the energetic model of mobility limitation.²³ Wert and colleagues linked energy cost of walking to physical function in older adults with slow gait,²⁴ however to our knowledge, the impact of aerobic capacity (energy availability) on physical activity has not been studied in OA.

There is a dearth of successful physical activity interventions for people with OA. Many have taken a behavioral approach,²⁵ and have not taken into account the specific physical impairments that may characterize OA. Perhaps, as a result, these approaches have had mixed results.²⁵ New targeted interventions are needed to improve physical activity in this unique population and to create such new interventions, more insight is needed into the factors that limit physical activity in people with OA. Hence, the rationale for this study is that fatigability may be a modifiable factor associated with physical activity in people with OA and could thereby provide a new target for intervention. As stated above, fatigability has been shown to be a key limiting factor in physical activity in older adults,²² and has been shown to be modifiable in other populations.²⁶ Further, there is literature demonstrating reduced aerobic capacity in people with OA and that aerobic capacity is modifiable in people with OA.²⁷ Thus establishing a relationship between fatigability and physical activity, and between fatigability and aerobic capacity in people with OA could uncover a mechanism contributing to reduced physical activity in this group and a framework for interventions. As a first step, in this study we sought to establish potential associations among fatigability, aerobic capacity, and physical activity in a subset of people with OA.

The primary purpose of this study was to investigate the association between fatigability and physical activity in women with hip OA. We focus on women in this study because some studies show that older adult women are at higher risk for low levels of physical activity than older adult men.²⁸⁻³⁰ The secondary purpose was to investigate whether or not aerobic

capacity, a potentially modifiable factor, is associated with fatigability and physical activity. This would suggest that fatigability may be amenable to treatments targeting aerobic capacity. We hypothesized that insufficient energy capacity (poorer aerobic capacity) could adversely affect physical activity through its effect on fatigability. Thus, the specific hypotheses tested were that in women with hip OA (i) increased fatigability is associated with decreased physical activity levels, (ii) lower levels of aerobic capacity are associated with decreased physical activity levels, and (iii) fatigability mediates the association between aerobic capacity and physical activity.

Methods

Participants

This Level I prospective study was approved by the Institutional Review Board of the University of Illinois at Chicago. We recruited women from local surgical practices, radio and public transport advertising, and an IRB-approved contact list obtained from medical records. Inclusion criteria were doctor-diagnosed hip OA. Exclusion criteria included other actively symptomatic joints, history of total joint replacement within 2 years, inability to walk without assistive devices, and any medical condition that interfered with gait or the ability to safely complete the protocol. Data from 36 women who satisfied enrollment criteria and provided written informed consent to participate were used in this study (Table 1).

Clinical Status

The Hip disability and Osteoarthritis Outcome Score (HOOS) was used to characterize clinical status of participants. HOOS is a patient-reported assessment about the participant's hip and hip-associated problems.³¹ The HOOS questionnaire consists of 5 subscales: Pain, Symptoms, Function in activities of daily living (ADL), Function in Sport and Recreation (Sport/Rec), and hip-related quality of life (QOL) in which higher scores indicate fewer hip-related problems or symptoms.

Fatigability

We modified a fatigability test that was previously developed and validated in older adults.³² The major change between the original fatigability test and the test as administered in this study was that we used a treadmill and asked people to walk for a set time rather than a set distance. Participants were aware that fatigability was being assessed. Women walked on a treadmill for 10 minutes, after a 2-3 minute acclimation period. They began walking at their preferred speed. Every 2.5 minutes they were given the opportunity to reduce or increase their speed to their comfort but were encouraged to do their best with regard to walking speed throughout the evaluation. Participants were asked to indicate verbally or using hand gestures whether they wanted the speed increased or decreased. Speed was changed accordingly by the investigator in 0.2 m/s increments until the participant indicated that they should stop. Environmental factors were the same for all participants. The performance fatigability score was calculated as the average speed during the 10-minute period divided by the speed during the first 2.5 minutes. Lower scores reflected increased levels of fatigability.

Aerobic capacity

Aerobic capacity was assessed by predicting the VO_2max from a treadmill-based six-minute walk test using a published regression equation.³³ For the six-minute walk test, participants were asked to walk for as far as possible. They could adjust speed as needed but were encouraged to maximize distance. Heart rate was measured during the test. The regression equation estimates VO_2max based on heart rate, body mass, and distance walked. Calculated VO_2max was then normalized to body mass and reported as $\text{ml}/\text{min}\cdot\text{kg}$.

Physical activity

Physical activity was our primary outcome measure. Physical activity was characterized in three ways. First, we used the UCLA activity score.³⁴ This score is widely used in this population and has been validated against pedometers.^{34, 35} The UCLA activity score assesses self-reported activity level ranging from a score of 1 – “Wholly inactive; dependent on others; cannot leave residence” to 10 “Regularly participate in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking.” Thus both perceived frequency and perceived intensity are included in this scale. Next, participants were provided with an accelerometer-based activity monitor (ActiGraph wGT3X-BT, ActiGraph, Pensacola, FL) to be worn for 7 days. We used manufacturer-provided software to extract average number of steps per day to represent quantity of activity. We also extracted intensity of activity characterized as percent sedentary time, percent time spent in light, moderate, or vigorous activity.

Statistical Analysis

We used SPSS version 26 (IBM Corp, Armonk, NY, USA) for all analyses. First, descriptive statistics were computed for all variables. Next, before testing the hypotheses, we assessed the effect of age, BMI, and HOOS pain scores on all variables of interest to determine whether they should be included as covariates in our analyses. Where the associations were statistically significant at the level of 0.05, we used regression analyses including these terms to verify that they did not confound the primary associations sought.

To test hypothesis (i), that increased fatigability is associated with decreased physical activity levels we used Pearson correlations to assess associations between performance fatigability scores and UCLA scores. (By convention based on Cohen’s recommendations, a medium correlation coefficient was defined as between 0.3 and 0.5 and a large correlation coefficient was defined as higher than 0.5.³⁶) To test hypothesis (ii), that lower levels of aerobic capacity are associated with physical activity, we again used Pearson correlations to assess associations between predicted VO_2max and UCLA scores. In both cases we used regression analysis including any potentially confounding terms (i.e. age, BMI, or pain) to verify these associations as stated above. Finally, to test hypothesis (iii) that fatigability mediates the association between aerobic capacity and activity levels we used nonparametric bootstrapping analysis with bias-corrected confidence estimates.³⁷ The 95% confidence interval of the indirect effect was obtained with 1000 bootstrap resamples and the mediation was considered significant if the confidence interval of the indirect effect did not cross zero.

Results

UCLA scores ranged from 2, representing “mostly inactive or restricted to minimum activities of daily living” to 8, representing “sometimes participates in impact sports...” (mean 5 ± 1 , representing “sometimes participates in moderate activities...”) Based on the ActiGraph measures, participants walked 4440 to 16,967 steps per day (mean 9697 ± 3436 steps per day) and spent $43.1 \pm 15.2\%$ of time sedentary, $43.7 \pm 9.7\%$ of time in light activity, and $13.2 \pm 7.8\%$ of time in moderate activity. No participants engaged in vigorous activity. UCLA scores were significantly correlated with sedentary time (-0.376 , $p = 0.041$), but not with light activity ($R = 0.318$, $p = 0.087$), moderate activity time ($R = 0.350$, $p = 0.058$) or number of steps per day ($R = 0.243$, $p = 0.195$). Age and BMI were not associated with UCLA scores, quantity or intensity of physical activity ($R = -0.021$ to 0.307 , $p = 0.087$ to 0.910).

HOOS profiles indicated a moderate level of impairment in all domains (Figure 1). There were significant associations between some physical activity variables and HOOS scores (Table 2). UCLA scores were associated with HOOS ADL function, Sport/Rec Function, and Hip Related Quality of Life. Steps per day were associated with all domains of the HOOS. More sedentary time and lower UCLA scores were associated with worst sport/rec function and quality of life. Notably, no domains of the HOOS were associated with light activity time. Further, pain was associated with percent of time in moderate activity, along with ADL and sport/rec function, and hip related quality of life.

There was a significant correlation between fatigability scores and UCLA scores. More fatigable women reported less physical activity (Figure 2). Fatigability was not associated with quantity or intensity of accelerometer-based activity measures at a statistically significant level ($p = 0.122$ to 0.432).

Aerobic capacity, as measured by predicted VO_{2max} , ranged from 8.9-42.9 (mean 21.6 ± 9.5) ml/kg*min. Aerobic capacity was significantly associated with UCLA scores with women with lower aerobic capacity reporting less physical activity levels (Figure 3). Aerobic capacity was also associated with percent sedentary time ($R = -0.477$, $p = 0.006$), and percent light activity time ($R = 0.501$, $p = 0.004$). There was no association between aerobic capacity and steps per day ($p = 0.264$) and there was a weak but not statistically significant association between aerobic capacity and percent moderate activity time ($R = 0.302$, $p = 0.094$). Notably, lower aerobic capacity was related to increased fatigability scores ($R = 0.619$, $p < 0.001$, Figure 4).

Finally, we sought to determine the combined influence of aerobic capacity and fatigability on physical activity and whether fatigability functioned as a mediator between aerobic capacity and physical activity. Together aerobic capacity and fatigability predicted UCLA scores with an R^2 of 0.404 (adj $R^2 = 0.360$, $SEE = 0.969$, $p = 0.001$). We note, however, that aerobic capacity was the stronger predictor of UCLA scores with a standardized coefficient of 0.464 compared to a standardized coefficient of 0.236 for fatigability. Moreover, the coefficient for fatigability was not statistically significant ($p = 0.215$). Further, there was not

a significant indirect effect of aerobic capacity on UCLA through fatigability ($b = 0.018$, $SE = 0.018$, 95% CI $[-0.020, 0.055]$).

Discussion

This study characterized physical activity in a group of women with hip OA and investigated potentially modifiable physical predictors of physical activity. The main purpose of this study was to investigate the association between fatigability and physical activity, and to test whether aerobic capacity could be a modifiable factor associated with fatigability and physical activity. Our hypothesis was partially supported. Fatigability was associated with self-reported physical activity as assessed through the UCLA score. Aerobic capacity was independently associated with physical activity and there was no evidence that fatigability mediated this association. Moreover, when aerobic capacity and fatigability were both used as predictors in the same regression model, the coefficient representing fatigability was no longer statistically significant. This suggests that aerobic capacity is a key contributor to physical activity in women with hip OA.

Several studies have shown that people with OA have reduced aerobic capacity compared to healthy controls. Values in the literature range from ~12-16 ml/min*kg for people with hip OA vs. ~17-21 ml/min*kg for controls.^{38, 39} Most of these studies, however, have been performed in people with advanced disease. One study showed that those with mild to moderate symptoms do not necessarily show a decrease in aerobic capacity.⁴⁰ With a mean aerobic capacity of 21.6 ± 9.5 ml/min*kg, our cohort of participants do not necessarily exhibit reduced aerobic capacity. This is in line with their moderate level of impairment as assessed via HOOS scores. However, it is important to note that there are various ways to assess aerobic capacity (e.g. submaximal or maximum effort cycling tests, six-minute walk test, etc.); different methods were used in each study, so direct comparison is difficult.

Aerobic capacity was independently associated with physical activity. A potential mechanism by which reduced aerobic capacity could reduce physical activity is via the energetic model of activity limitation.²³ This model posits that people whose energy cost of walking is high relative to their total energy capacity have less energy reserve for physical activity. Thus, this model suggests that reduced total energy capacity is implicated in lower physical activity levels in older adults. Since OA is associated with reduced aerobic capacity – total energy capacity – this mechanism could be an explanation for reduced physical activity in women with hip OA.

This study adds to the growing body of work linking fatigability to physical activity in various ways in people with OA. Momentary self-reported fatigue, induced fatigue, and self-reported fatigue have been linked to reduced physical activity in people with hip OA.^{14, 19, 41, 42} Fatigue or fatigability are also found to predict subsequent physical activity.^{19, 43} This is the case even when confounders such as pain and physical function are included in regression models.⁴¹ The contribution of the present work is the use of a performance-based fatigability measure to assess the effects of movement-associated fatigue. This is important because other factors associated with OA, such as sleep-related problems, and depression could be linked to self-reported fatigue.⁴⁴ Fatigability, movement-associated fatigue may be

a more direct determinant of physical activity limitation compared to the construct of fatigue. Moreover, if linked to modifiable factors, fatigability may in turn be modifiable. Indeed, in this study aerobic capacity, which is modifiable in OA,^{25, 27} was associated with fatigability. The present findings suggest, however, that targeting aerobic capacity may be the most direct way to improve physical activity.

Although this was a cross-sectional study, findings suggest that fatigability could be modifiable by targeting aerobic capacity. It is further expected that this would have positive effects on physical activity. This is important because it is well established that exercise improves physical function in OA.^{7, 8, 45, 46} Moreover, exercise has a positive impact on OA biomarkers in animal studies,⁴⁷ and in some human studies.^{47, 48} Unfortunately, current interventions to improve physical activity in people with OA have had limited effectiveness.²⁵ The present findings emphasize the importance of aerobic fitness and suggest that improving fitness may have positive effects on physical activity as well.

In contrast with physical activity as represented by UCLA scores, accelerometer-based physical activity was not associated with aerobic capacity and fatigability. HOOS scores, however, were significantly associated with several aspects of accelerometer-based physical activity. Notably, pain was associated with average number of steps per day and moderate activity times. This is in contrast with studies of knee OA and of mixed hip and knee cohorts. In a study using data from the Multicenter Osteoarthritis (MOST) Study, pain was not highly associated with walking quantity.⁴⁹ The impact of momentary pain on physical activity in women with hip or knee OA was studied in a series of work by Murphy and colleagues.^{14, 15} In one study, pain was found to be associated with physical activity once momentary fatigue was accounted for in regression models.¹⁵ A later study from this group found that older women with hip or knee OA higher levels of pain actually had higher levels of activity early in the day when they had low levels of pain interference.¹⁴ In these studies, results were not reported separately by affected joint so it is not possible to determine whether or not the results were different in women with hip OA compared to women with knee OA. In any case, the relationship between pain and physical activity in OA is complex and is governed by a variety of physical and psychological factors. More work is needed to understand factors related to physical activity specifically in hip OA.

The discordance in results between the association between fatigability and UCLA scores and ActiGraph data suggests that these tools may be measuring different constructs related to physical activity. We expect that the UCLA score and the ActiGraph are measuring different aspects of the construct of physical activity. There are several aspects of physical activity including quantity, intensity, duration, type. The ActiGraph primarily reflects walking activity so could miss other types of activities that are important to participants that may be picked up by the UCLA score. The fact that there were only moderate correlations between UCLA scores were more closely associated with objectively measured physical activity intensity and no correlation with steps per day suggests that the UCLA score may be a better indicator of perceived intensity than perceived quantity of activity. We also note that the UCLA score assesses overall perceived/desired physical activity levels rather than a snapshot of one week's worth of activity that may not be fully representative of a longer timespan. Murphy et al., reported that fatigability was associated with increased self-pacing

behaviors, wherein participants slowed down, took breaks, or otherwise paced their activity levels.⁵⁰ While self-pacing was not assessed in the present study, it is possible that variation in self-pacing behaviors could confound the ActiGraph measures, but would not be as likely to affect the UCLA measures, as the latter assesses an overall perceived level of physical activity. Studies using the UCLA score to characterize physical activity should keep this in mind when interpreting findings. Combinations of both subjective and objective frequency and intensity measures may be needed to fully characterize physical activity in an OA population.

With the cross-sectional design of this study, we cannot rule out an alternative framework, in which reduced physical activity leads to deconditioning and reduced aerobic capacity which could in turn increase fatigability. However, based on the existing literature in older adults, we believe that our proposed hypothesis is the most plausible. It has already been established that reduced energy capacity or increased effort in walking is associated with reduced physical activity in older adults, via the energetic model.^{23, 51} Because of literature showing that people with OA have reduced aerobic capacity,^{38, 39} it seems likely that the energetic model could be applied here as well. We concede that it is not possible to determine the initiating event regarding aerobic capacity and physical activity. However, because improving one necessarily improves the other, it may be reasonable to attempt to improve the capacity for physical activity by addressing aerobic capacity.

There were several important limitations to consider when interpreting these results and their generalizability. First selection bias may have been an issue. For inclusion in the study participants needed to be able to tolerate the fatigability test by being able to walk on a treadmill without assistive devices. This introduced a risk of biasing the study toward higher functioning individuals. However, we do not believe this was the case. The wide range of HOOS scores and UCLA scores indicate that a broad spectrum of functional levels were represented. Second, we note that we did not assess radiographic severity of OA. Thus, we do not know how physical activity may vary with radiographic severity. While other studies have shown, that physical function does not vary strongly with radiographic severity of OA,⁵² whether or not radiographic severity of OA impacts physical activity has yet to be determined. Third, there is no consensus on how to assess fatigability, other than that performance measures are necessary.^{50, 53} In addition, others who have used the same type of fatigability assessment have modified it to suit their experimental design.^{26, 50, 54} As a result, we cannot make direct numerical comparisons between our results and others that have been described in the literature. Finally, only women were included in this study. The rationale was that being female is a risk factor for having lower physical activity in older adults,^{29, 55} as well as for having osteoarthritis. Future studies should evaluate men as well and should specifically examine potential sex differences in physical activity predictors.

In conclusion, we found that performance-based fatigability was associated with physical activity engagement in women with hip OA. Moreover, aerobic capacity was associated with fatigability and physical activity. Although 40% of the variance in physical activity level was explained by aerobic capacity and fatigability together, aerobic capacity was the best predictor of activity levels. It is also important to note that a substantial amount of variance can be accounted for by factors not considered in this study. Among these may be behavioral

factors addressed in many other approaches to improving physical activity in this population.²⁵ Addressing physical factors such as aerobic capacity and fatigability may improve the effectiveness of behavioral interventions. This study is important because physical activity is associated with better outcomes in OA.⁷⁻⁹ Further OA is associated with increased cardiovascular mortality,^{10, 11} which in turn has low physical activity as a risk factor. Although this was a cross-sectional study, these results suggest that addressing aerobic capacity, could be an avenue to improve physical activity in women with hip OA, with potential additional benefits to fatigability. Longitudinal and interventional studies are needed to determine whether targeting aerobic capacity results in an increase in physical activity levels in women with hip OA.

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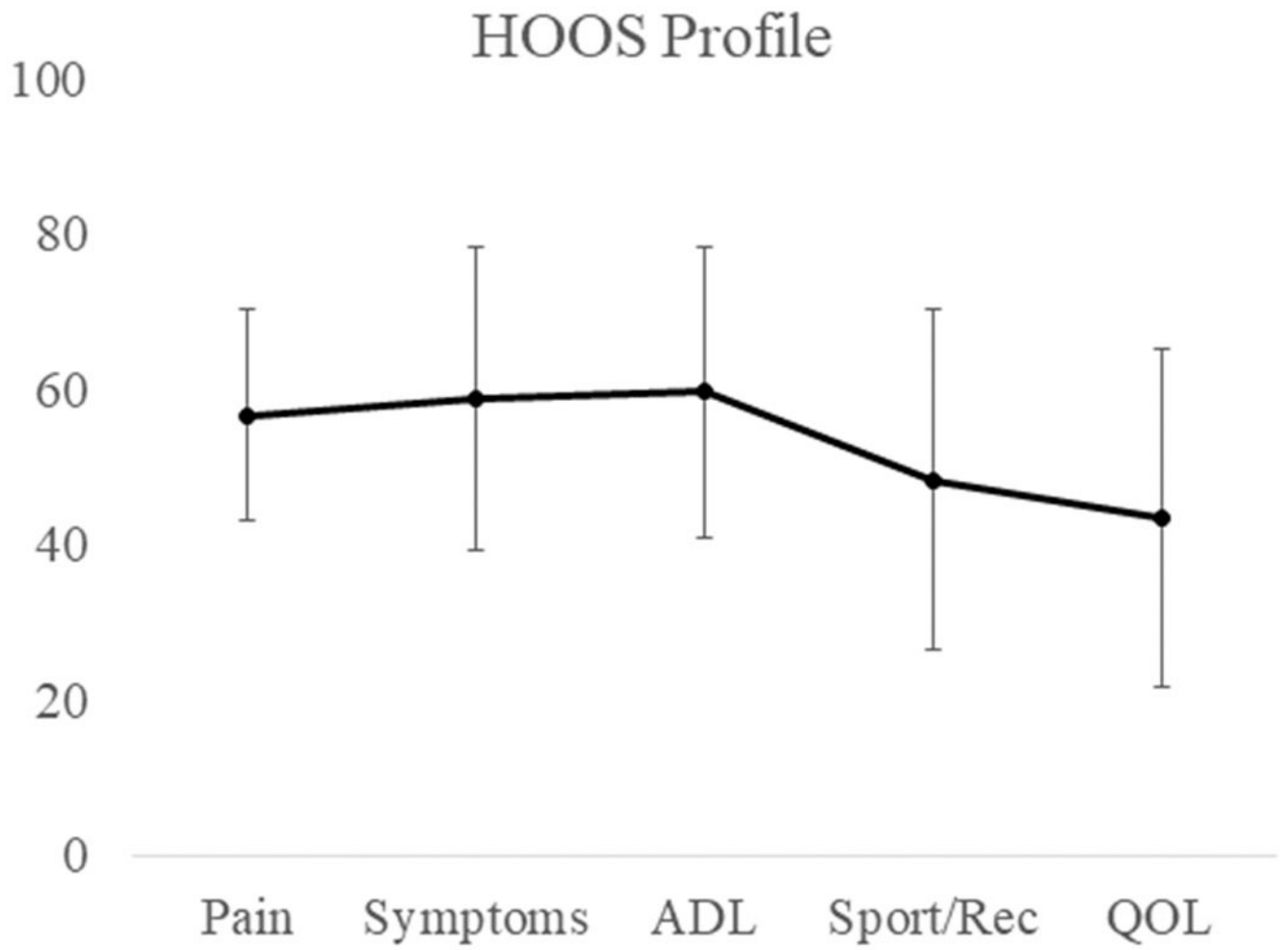


Figure 1. HOOS profiles (mean \pm standard deviation). Lower scores indicate a greater level of impairment.

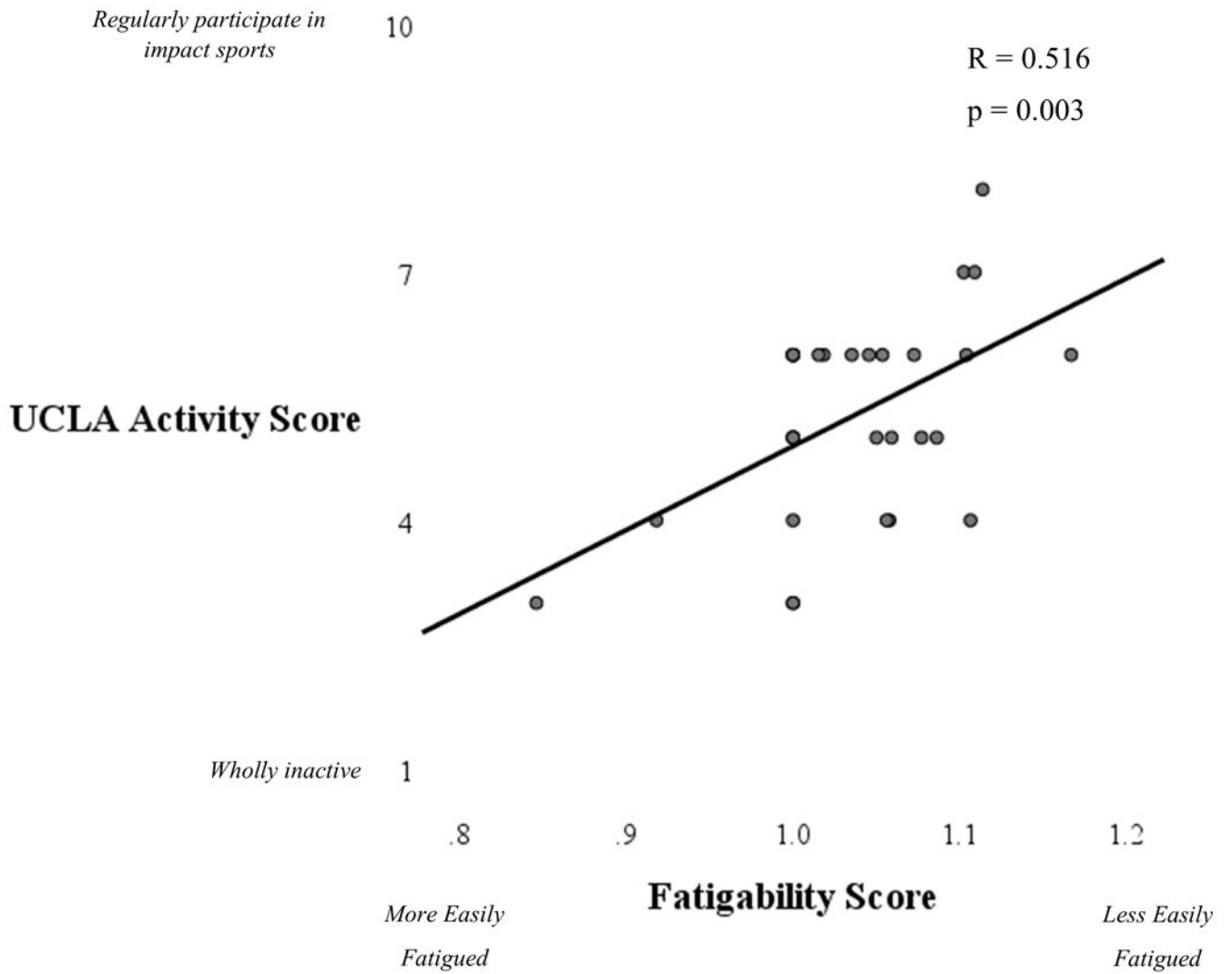


Figure 2. Scatterplot illustrating the association between fatigability and activity levels. Women with OA who were more fatigable (lower scores) had lower activity levels.

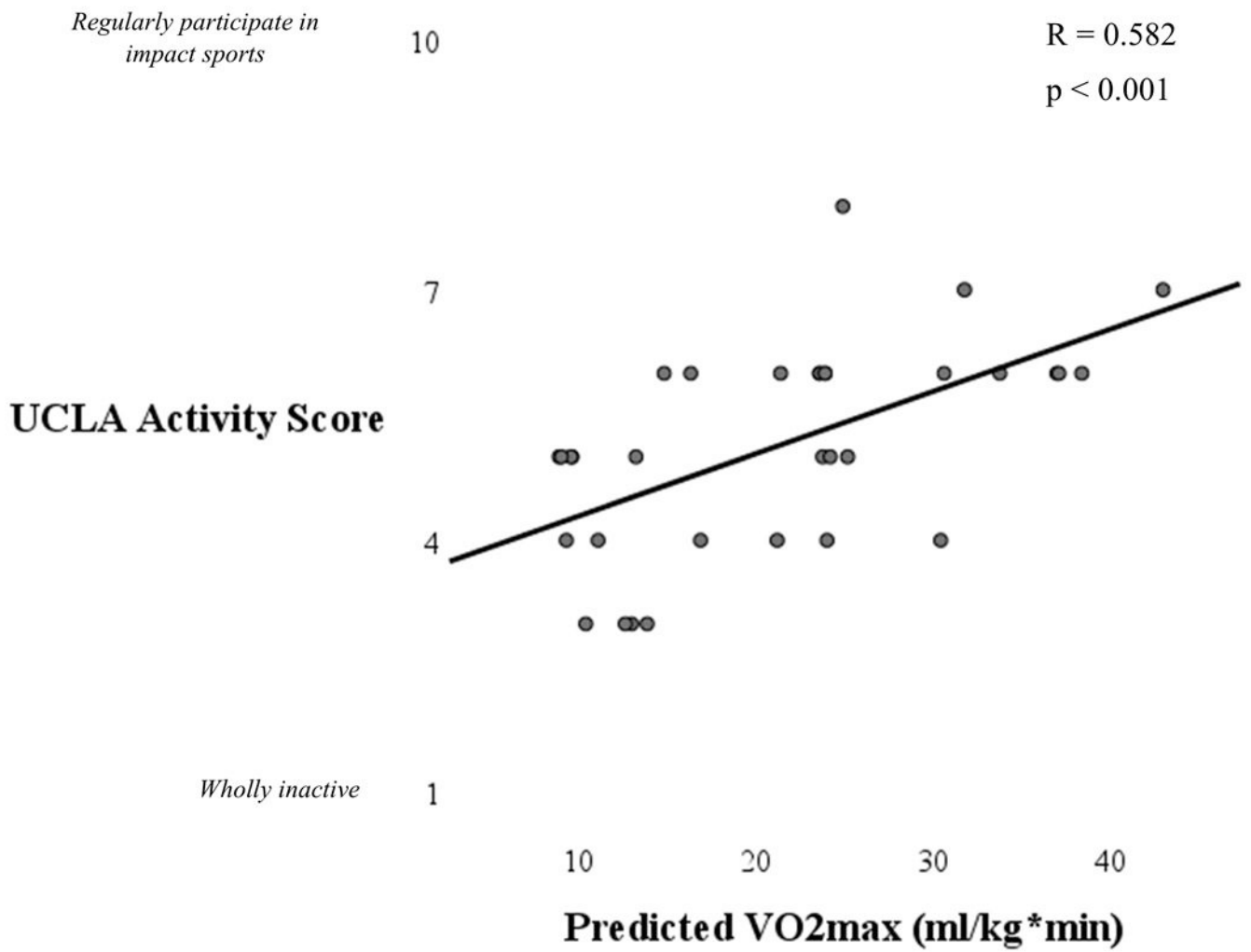


Figure 3. Scatterplot illustrating the association between aerobic capacity and activity levels. Women with OA who had lower aerobic capacity had lower activity levels.

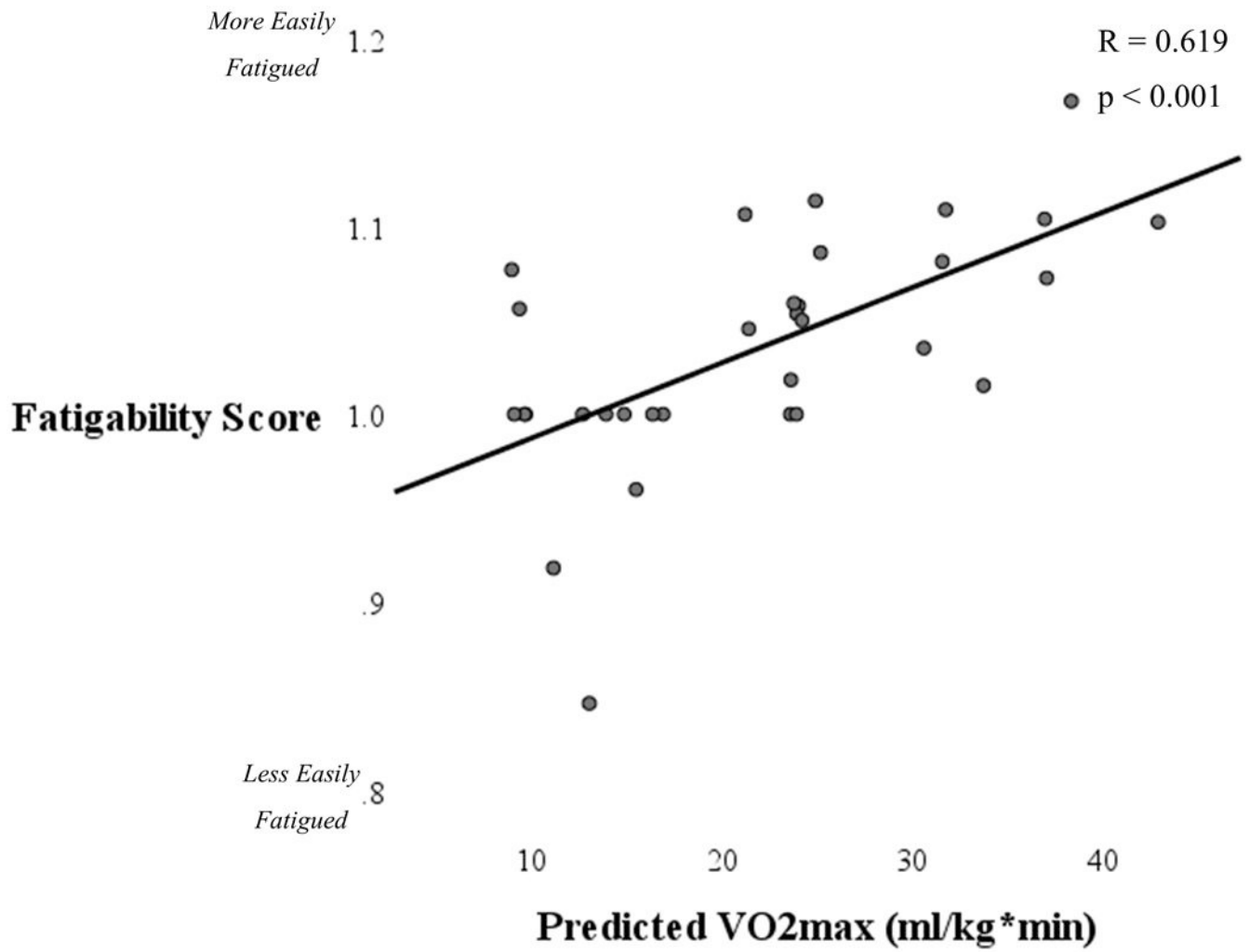


Figure 4. Scatterplot illustrating the association between aerobic capacity and fatigability. Women with OA who had lower aerobic capacity were more fatigable.

Table 1.

Characteristics of (N = 36) women with hip OA

	Mean ± SD
Age (years)	60.3 ± 9.3
Body Mass Index (kg/m²)	29.9 ± 5.8
Aerobic Capacity (ml*kg)	21.2 ± 10.1
UCLA scores	5.0 ± 1.3

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Table 2.

Associations between physical activity variables and HOOS domain scores

	Pain	Symptoms	Function: ADL	Function: Sport/Rec	Quality of Life
UCLA Score	R = 0.275 p = 0.121	R = 0.086 p = 0.633	R = 0.357 p = 0.041	R = 0.475 p = 0.005	R = 0.467 p = 0.006
Steps per day	R = 0.443 p = 0.013	R = 0.402 p = 0.025	R = 0.506 p = 0.004	R = 0.460 p = 0.009	R = 0.419 p = 0.019
%Sedentary time	R = -0.245 p = 0.185	R = -0.253 p = 0.170	R = -0.325 p = 0.074	R = -0.384 p = 0.033	R = -0.370 p = 0.041
%Light activity time	R = 0.095 p = 0.613	R = 0.127 p = 0.497	R = 0.157 p = 0.400	R = 0.223 p = 0.229	R = 0.262 p = 0.155
%Moderate activity time	R = 0.356 p = 0.049	R = 0.332 p = 0.068	R = 0.435 p = 0.014	R = 0.468 p = 0.008	R = 0.391 p = 0.030