ORIGINAL ARTICLE

The association of fatigue severity with pain level, obesity indices and functional performances in women with knee osteoarthritis

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ABSTRACT

Introduction: Knee osteoarthritis is most common among women with obesity. It may lead to physical inactivity that, in turn, causes fatigue or lack of physical enthusiasm to perform meaningful daily activities. Hence, this study aimed to examine whether pain level, obesity indices and functional performances are associated with fatigue severity in women with knee osteoarthritis (KOA).

Materials and Methods: This cross-sectional study recruited women referred to physiotherapy to manage OA. The measurements included fatigue severity (fatigue severity scale); pain level (numerical rating scale); obesity indices (body mass index, fat %, waist circumference); functional performances (upper limb strength, lower limb strength, mobility, exercise capacity and quality of life). A simple linear regression analysis was used to determine which independent variable may be associated with fatigue severity.

Results: Ninety-six women with unilateral KOA participated in this study (Mean age, 55.70, Standard Deviation, SD 6.90) years; Mean fatigue severity, 34.51, SD 14.03). The simple linear regression analysis showed that pain level (β=4.089, *p*<0.001), fat % (β=0.825, *p*<0.001) and QoL (β=0.304, *p*<0.001) were significantly associated with fatigue. After controlling for pain level, only fat % was significantly associated with fatigue (β=0.581, *p*=0.005).

Conclusion: Pain level, fat %, and QoL appear to be associated with fatigue severity in women with KOA. In addition, pain symptoms may interact with factors associated with fatigue severity.

KEYWORDS:
Functional performance, osteoarthritis, obesity, pain, quality of life

INTRODUCTION

Knee osteoarthritis (KOA) is a degenerative joint disease associated with ageing, female sex, obesity, and repetitive joint trauma.[1] Women diagnosed with KOA are at much higher rates than men. It was found that about 18% of women had symptomatic KOA, and only about 9.6% of men had similar conditions.[2] KOA severely impacted women due to differences in anatomy, kinematics, and hormonal influences.[3] Furthermore, women with KOA present for treatment in more advanced stages and have more debilitating pain than their male counterparts.[3]

Pain sensation, the most dominant symptom of KOA, has been shown to limit functional and physical activities such as walking, sitting to standing, performing household chores, climbing stairs and sitting upright.[4-6] Ultimately, lack of physical activity might lead to poor exercise tolerance or fatigue that is defined as an unpleasant and subjective feeling of tiredness, exhaustion or lack of energy.[7] A previous study has shown that fatigue is associated with the life aspects of people with osteoarthritis.[8] About 40% of people with OA reported clinically meaningful levels of fatigue that resulted in significant disruptions to their regular social, leisure time, and activities of daily living.[9]

Based on the prior knowledge of factors associated with osteoarthritis, understanding what factors may influence fatigue warrants further study, as fatigue is an established factor leading to physical inactivity. However, to date, a limited number of studies have identified factors that influence fatigue in individuals with KOA. One study reported the associations between pain and fatigue levels, symptom interference, and physical activity in adults with KOA.[9] However, this study was limited to understanding pain and fatigue-related activities that interfere with physical activity over a day. It is not well established if other factors may associate with fatigue in women with KOA. Since KOA is a progressive degenerative process, management of KOA should include education, exercise and weight loss,[10] that can be targeted to promote pain relief and increase exercise tolerance. However, besides understanding the relationship between pain and fatigue, further investigation on other factors, such as obesity indices and functional performances (e.g., strength, mobility, exercise capacity and quality of life), may provide insights into the association of these variables with the level of fatigue.

Therefore, to provide evidence for clinical practice, this study aimed to measure whether fatigue severity was associated with pain level, obesity indices (body mass index, fat percentage, waist circumference) and functional performances in women diagnosed with KOA.

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Table I: Participants' characteristics (N=96)

Variables	Fatigue Severity Mean (SD)			*p*-value
	ALL (N=96)	Low (n=47)	High Severity (n=49)	
Age (years)	55.70 (6.90)	54.98 (6.75)	54.39 (7.04)	0.320
Height (m)	1.55 (0.53)	1.56 (5.32)	1.54 (5.25)	0.170
Bodyweight (kg)	70.16 (12.13)	68.91 (11.74)	71.35 (2.49)	0.327
BMI (kg/m2)	29.14 (5.00)	28.34 (4.95)	29.90 (4.99)	0.128
Fat %	40.04 (6.41)	38.07 (6.06)	41.93 (6.23)	0.003**
WC (cm)	94.62 (11.11)	94.27 (10.85)	94.96 (11.45)	0.761
Pain level	2.63 (1.51)	2.11 (1.13)	3.12 (1.67)	0.001**
Fatigue	34.51 (14.03)	22.32 (7.24)	46.20 (7.60)	<0.001**
UL strength (kg)	18.83 (5.09)	18.29 (5.87)	19.35 (4.20)	0.309
LL strength (s)	13.11 (5.64)	13.06 (4.81)	13.15 (6.38)	0.940
Mobility (s)	11.65 (2.98)	11.21 (2.36	12.08 (3.45)	0.158
ES (m)	304.54 (56.38)	307.68 (57.73)	301.54 (55.49)	0.596
QoL	23.65 (18.16)	13.58 (10.96)	28.34 (19.01)	0.002**

Note: t-test significant at *p<0.05 and **p< 0.01; SD – Standard Deviation
UL - upper limb, LL - lower limb
WC: Waist circumference
UL: Upper limb
LL: Lower limb
EC (please change ES to EC): Exercise capacity
QoL: Quality of life

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study was conducted among women with KOA who were referred for physiotherapy management. Patients included in the study were diagnosed with unilateral knee OA according to a radiographic grade, aged 40 to 65 years old, understood Malay or English and had a referral from a medical doctor. Patients with knee arthroplasty, pregnant, had knee motion limitation (<70° of knee flexion) or knee deformity associated with KOA, had other medical problems (e.g., rheumatic disease, cardiovascular problem, gastrointestinal tract disease, or neurological problem), and had recent surgery (<6months) were excluded from the study. This study was approved by the Research Ethics Committee of Universiti Teknologi MARA (UiTM) on 3rd September 2019 (Approval no. 600-IRMI (5/1/6)). Informed consent forms were obtained from all participants after a briefing about the study procedure.

Instrumentations

Fatigue severity was assessed using the Fatigue Severity Scale (FSS). The FSS is a self-administered questionnaire with nine items related to how fatigue affects motivation, exercise, physical functioning, and interference with work, family, and social life, based on a seven-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The minimum score is 9, and the maximum score is 63; the higher the score, the greater the fatigue severity.[11] The score at the 50th percentile was used to group participants into low and high fatigue levels. The FSS has high validity and reliability in assessing fatigue levels and how it will affect the patients' daily activity.[12]

The current level of pain intensity was measured using the Numerical Rating Scale (NRS). The NRS is a scale of 0, which indicates no pain, to 10, which indicates the worst pain. The participant was asked to choose the number that best represented the pain level of their affected knee. The NRS has excellent test-retest reliability with intra-class correlation coefficients of 0.95, a standard error of measurement (SEM) of 0.48 and a minimum detectable change of 1.33.[13]

We measured the participant's height and body weight to calculate the body mass index (BMI). These measurements were taken twice by the same investigator to minimise inter-rater error. The participant's body weight was measured using a TANITA weighing scale (Japan) and recorded to the nearest 0.1 kg. The height was measured using the SECA Model Body (Germany) with the head horizontal to the Frankfurt plane to the nearest 0.1 cm. Both measurements were taken with shoes off. Body Mass Index (BMI) was calculated using the body weight in kilogram (kg) divided by the square of height in metres (m^2).

A bioelectrical impedance analysis (BIA) machine (TANITA BC418) was used to measure the body fat percentage (%). The participant stood on the footpads of the BIA platform while grasping the handles and was reminded to remain still and relaxed, as the measurement results appeared in less than 30 seconds. The waist circumference (in cm) was measured using a non-elastic cloth tape in standing with feet shoulder-width apart. The measurement was taken over the bare skin between the costal margin and the top of the iliac crest at the level of the smallest waist diameter, approximately between the lower ribs level and the iliac crest. The participant was asked to remove their clothing except for light underwear. The measurement was recorded to the nearest 0.5cm based on the tape resolution.

The upper limb strength represented by the handgrip was assessed using the Jamar Analogue Hand Dynamometer, which has good reliability and validity for measuring handgrip strength.[14] The participant was instructed to sit with elbows in 90° flexion parallel to the trunk. Then, the participant was asked to squeeze the dynamometer as hard as possible. The assessment was repeated thrice on each

Table II: The Pearson correlation of fatigue with pain level, obesity indices, and functional performances (N=96)

		r (p-value)										
		1	2	3	4	5	6	7	8	9	10	11
1	Fatigue level	1	0.165 (0.108)	0.467** (<0.001)	0.120 (0.244)	0.375** (<0.001)	-0.019 (0.858)	0.053 (0.607)	-0.028 (0.786)	0.200 (0.050)	-0.083 (0.419)	0.459** (<0.001)
2	Age	0.165 (0.108)	1	0.305** (0.002)	-0.149 (0.148)	-0.032 (0.754)	0.079 (0.444)	-0.313** (0.002)	0.225* (0.028)	0.234 (0.050)	-0.202 (0.419)	0.338** (0.007)
3	Pain level	0.467** (<0.001)	0.305** (0.002)	1	0.132 (0.201)	0.283** (0.005)	0.113 (0.271)	-0.096 (0.351)	0.169 (0.100)	0.339** (0.001)	-0.121 (0.241)	0.585** (<0.001)
4	Body mass index	0.120 (0.244)	-0.149 (0.148)	0.132 (0.201)	1	0.633** (<0.001)	0.722** (<0.001)	0.119 (0.250)	0.147 (0.152)	0.015 (0.884)	-0.193 (0.059)	0.296* (0.018)
5	Fat %	0.375** (<0.001)	-0.032 (0.754)	0.283** (0.005)	0.633** (<0.001)	1	0.375** (<0.001)	0.150 (0.145)	0.024 (0.820)	0.059 (0.571)	-0.060 (0.560)	0.250* (0.048)
6	Waist circumference	-0.019 (0.858)	0.079 (0.444)	0.113 (0.271)	0.722** (<0.001)	0.375** (<0.001)	1	0.041 (0.691)	0.127 (0.217)	-0.007 (0.949)	-0.187 (0.068)	0.309* (0.014)
7	Upper limb strength	0.053 (0.607)	-0.313** (0.002)	-0.096 (0.351)	0.119 (0.250)	0.150 (0.145)	0.041 (0.691)	1	0.229* (0.025)	-0.039 (0.703)	0.195 (0.056)	-0.447 (<0.001)
8	Lower limb strength	-0.028 0.786	0.225* (0.028)	0.169 (0.100)	0.147 (0.152)	0.024 (0.820)	0.127 (0.217)	-0.229* (0.025)	1	0.725** (<0.001)	-0.419** (<0.001)	0.460** (<0.001)
9	Mobility	0.200 (0.050)	0.234 (0.050)	0.339** (0.001)	0.015 (0.884)	0.059 (0.571)	-0.007 (0.949)	-0.039 (0.703)	0.725** (<0.001)	1	0.420** <0.001)	0.387** (0.002)
10	Exercise capacity	-0.083 (0.419)	-0.202 (0.419)	-0.121 (0.241)	-0.193 (0.059)	-0.060 (0.560)	-0.187 (0.068)	0.195 (0.056)	-0.419** (<0.001)	-0.420** <0.001)	1	-0.391 (0.002)
11	Quality of life	0.459** (<0.001)	0.338** (0.007)	0.585** (<0.001)	0.296* (0.018)	0.250* (0.048)	0.309* (0.014)	-0.447 (<0.001)	0.460** (<0.001)	0.387** (0.002)	-0.391 (0.002)	1

Note: Pearson correlation coefficient, r, significant at p<0.05* and p<0.001**

Table III: Crude and adjusted (pain level) simple linear regressions of fatigue level

Variable	SLR[a]			SLR[b]		
	β[c]	s.e.	*p*-value	β[d]	s.e.	*p*-value
Age	0.34	0.21	0.108	0.05	0.20	0.795
Pain level	4.09	0.80	<0.001**			
Body mass index	0.34	0.29	0.244	0.17	0.26	0.520
Fat %	0.82	0.21	<0.001**	0.58	0.20	0.005**
Waist circumference	-0.02	0.13	0.858	-0.09	0.12	0.433
Upper limb strength	0.15	0.28	0.607	0.27	0.25	0.283
Lower limb strength	-0.07	0.26	0.786	-0.27	0.23	0.236
Mobility	0.95	0.48	0.050	0.22	0.46	0.625
Exercise capacity	-0.02	0.03	0.419	-0.01	0.02	0.768
Quality of life	0.30	0.07	<0.001**	0.15	0.09	0.084

SLRa: Simple linear regression; SLRb: Simple linear regression adjusted for pain level; s.e.: Standard error; βc: Crude regression coefficient; βd: Adjusted regression coefficient; Regression coefficient is significant at p<0.001**

hand, with a 1-minute rest between attempts. The average score from all measurements was recorded as the final score, in which the higher the value, the greater the handgrip strength. In the handgrip test-retest assessment, 5 to 45 days after baseline, the interclass correlation (ICC) was 0.81.[15]

The lower limb strength was measured using the five times sit-to-stand test (5STS). The participant was instructed to sit with arms folded across the chest and the back against the chair of about a standard height (43-45cm) with a backrest. Then, the investigator instructed, "I want you to stand up and sit down five times in a row, as quickly as you can when I say "GO". Be sure to stand up fully and try not to let your back touch the chair back between each repetition. Do not use the back of your legs against the chair". The time was started once the investigator said GO and stopped once the participant's body touched the chair following the fifth repetition. The score (recorded using a stopwatch) was the amount of time (to the nearest decimal in seconds) it takes a participant to transfer from a seated to a standing position and back to sitting for five times. The shorter the time to complete the test, the stronger the lower limb strength.

The time up and go test (TUG) measures mobility and balance, that is, the ability to stand up from an armchair (seat height of about 46cm), walk a distance of three metres, turn around, and return to sitting in the same chair again without physical assistance.[16] The time required to complete the test was recorded in seconds using a stopwatch. The TUG has been shown to have excellent intra-rater and inter-rater reliability, with ICC values greater than 0.95.[17]

The 6-minute walk test (6MWT) is a sub-maximal exercise test used to measure exercise capacity and the ability to walk over a longer distance.[18] Based on the American Thoracic Society (ATS) Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories guidelines,[19] the participant was instructed to walk for six minutes on a hard, flat, indoor surface and with standardised verbal support while allowing rest in the procedure. The test-retest reliability of the 6MWT among patients with knee OA was excellent, with ICC 0.991 (95% confidence interval; 0.986–0.994).[20]

QoL was measured using the Western Ontario McMaster University Osteoarthritis Index (WOMAC), a widely used self-administered health status measure for assessing pain, stiffness, and function in patients with OA of the hip or knee. Each dimension of the questionnaire assesses the clinical severity of the disease; five questions for pain, two for stiffness and 17 for physical functions. The participant was requested to rate the score of each dimension. In this study, the total score was analysed based on the overall level of quality of life (QoL), in which a higher score indicates a higher level of pain, stiffness and functional limitation. WOMAC is a reliable and valid instrument for evaluating the severity of KOA.[21]

Data Collection Procedures

The study began with the recruitment process of participants in the physiotherapy clinic. The potential participants were approached by the researcher and briefed about the purpose and procedure of the study. The inclusion and exclusion criteria were checked, and those eligible signed an informed consent form. Then, the participants completed all measurements of fatigue level, QOL, obesity indices and functional performances, except for exercise capacity (6MWT). The participants continued the measure for the 6MWT on the second or third day based on their preferences. The sequence of the measurements was organised, starting with the easiest test to avoid fatiguing the participants. All data collected were kept in a secure cupboard that only the main researcher could access it.

Statistical Analysis

Data were analysed using SPSS version 26. A p-value of <0.05 was considered significant. The data were presented using means and standard deviations for all participants and between those with low and high levels of fatigue using the cut-off of 36 based on the 50th percentile of fatigue score. The t-test analysis was conducted to determine the significant differences in the variables of interest between participants with different fatigue levels. A Pearson correlation analysis was used to determine the relationship between fatigue severity (dependent variable) and pain level, obesity indices and functional performances. In addition, the partial correlation was used to determine the relationship of fatigue severity with obesity indices and functional performances while controlling the effect of pain. The stepwise regression analysis included variables significantly correlated with fatigue severity to determine whether the variables predicted fatigue severity. The sample size was calculated using the GPower application.[22] A total of 96 samples was sufficient to provide a moderate effects size (0.15) with an α error of 0.05 to achieve a minimum of 80% power for a regression model. From the regression analysis, the Durbin-Watson value was 1.2, indicating the assumption of independent errors was met. In addition, there is also an absence of multicollinearity of the independent variables, as the variation inflation factors were from 1.0-1.5.[23]

Ethics Approval and Informed Consent

The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Universiti Teknologi MARA (Approval number: 600-IRMI (5/1/6).

RESULTS

Ninety-six women participated in this study (mean age=54.76 (Standard Deviation, SD5.54 years). Table I shows the measurement characteristics of all participants, in which we included participants' age and those categorised as low and high fatigue levels. The t-test analysis indicated that only pain level, body fat %, and QoL differed significantly (All $p < 0.05$) between the low and high fatigue levels. The participants with a low level of fatigue presented with a lower pain level, lower body fat percentage and better QoL.

The results of the Pearson correlation analysis, as shown in Table II, indicated that only pain ($p<0.001$), fat % ($p<0.001$) and QoL ($p<0.001$) were correlated with fatigue severity. The simple linear regression analysis (Table III) of age, pain level, BMI, fat %, waist circumference, upper limb strength, lower limb strength, mobility, exercise capacity and QoL showed only pain level ($p<0.001$), fat % ($p<0.001$) and QoL ($p<0.001$) were significantly associated with fatigue. After controlling for pain level as the possible confounding factor, only fat % remained significantly associated with fatigue ($p=0.005$) (Table III).

DISCUSSION

This study evaluated whether fatigue severity is associated with pain level, BMI, fat %, waist circumference, upper and lower limb strength, mobility, exercise capacity and QoL in women diagnosed with KOA. We found that the mean for fatigue level among the participants in this study was 34.51 (SD14.03), which can be considered within the borderline range between low and high levels of fatigue. However, about 51% (n=49) presented with a high level of fatigue severity. According to a previous study, a high perception of general fatigue may indicate that the energy to expend in association with chronic pain may negatively impact subsequent physical activity.[24]

Pain level was associated with fatigue severity and may interact with the association between body indices and fatigue severity and between functional performances and fatigue severity. Previous studies have shown that pain interaction with fatigue leads to limitations in daily activities,[25] and mobility.[8] Pain triggered during movement may create fear among the patients, further restricting their participation in regular physical activity that ultimately cause poor exercise tolerance or undue fatigue during physical activities. On the other hand, physical inactivity may lead to muscle weakness, further increasing the sensation of pain,[26] as weak muscles may not absorb the impact of knee loading on the knee joint. Severe pain is usually associated with a chronic condition, as chronic pain has been shown to increase the energy cost of walking.[27] Accordingly, increasing pain is accompanied by various mitigation strategies that may affect energy differently.[28] Understanding this may have implications for clinical practice; for instance, exercise can be done after taking pain killer or during the best time of the day when pain is felt the least, as well as breaking down the exercise duration into a few sessions so that pain can be controlled. In addition, non-weight-bearing exercises such as swimming or static cycling should be recommended to prevent excessive joint loading. In terms of obesity indices, we found only body fat % that was significantly higher in the participants with a high fatigue level and significantly associated with fatigue severity. However, it is also important to note that the means for all the obesity indices (BMI, body fat percentage, waist circumference) in all participants and participants with low and high fatigue levels exceeded the healthy cut-offs. These results support that most of the participants with KOA had excessive body weight or were obese, an established risk factor for KOA. A previous study reported that a higher BMI would increase knee joint loading, resulting in adverse effects associated with joint inflammation and stress on the articular cartilage beyond its natural ability,[29] thus resulting in degenerative changes.[5] However, BMI may not be the best predictor of fatigue severity compared to body fat percentage, as women tend to have a generalised fat mass around their bodies that increases body weight. A previous study suggested that with every 1 kilogram of total body fat increase, the risk of cartilage defect will become higher and thus may increase the pain sensation that subsequently limits physical activity.[30]

Regarding functional performances, even though there were no significant differences in all measures except for QoL, we noticed that participants with a higher fatigue level also presented with a lower mean in all measures of functional performance than those with a lower fatigue level. The upper limb strength was slightly higher in the participants with a high fatigue level because the hand compensates for the lower extremities' declining functions. It has been suggested that walking pattern in people with KOA may be altered in association with a painful knee that is energetically costly and exacerbate the average reduction of energy reserve.[28] In addition, individuals with KOA may reduce their habitual gait speed below the rate that minimises energy consumption, given the U-shaped relationship between gait speed and energy consumption.[28] This explains the reduction in mobility and exercise capacity performance, as both measures have walking components and require the participants to complete the tests as fast as possible with their habitual gait speed. Furthermore, reduced quadriceps strength associated with arthritic pain can influence the gait pattern by decreasing the gait speed, which correlates with a shorter swing phase and longer support time.[31] In addition, the longer time to complete the five times sit-to-stand test that reflects lower limb strength could be explained by the arthrogenic muscle reaction that inhibits the excitability of the quadriceps' motoneuron pool as a consequence of the pain experienced.[32] The interaction between the independent variables may have led to poor QoL among the participants, as indicated by a much poorer WOMAC score in the study, ultimately associated with fatigue severity. This study has some limitations. Firstly, the sample size for this study was calculated with a power of 80%, which may have contributed to the non-significant findings in the majority of the independent variables in predicting fatigue severity. Secondly, we did not measure the duration of the KOA as this could influence fatigue severity due to the duration of physical inactivity. On the other hand, this study provided some insights into the importance of conducting future studies to unravel further explanations of the various factors that may influence fatigue severity to provide guidelines for intervention to promote long-term adherence to physical activity.

CONCLUSION

In conclusion, the findings of this study showed that pain level, fat % and QoL were likely to be associated with fatigue severity. However, it is also important to note that obesity indices should be the target for intervention as most participants presented with a pathological level of obesity indices. Future studies with a larger sample size and a consideration of the influence of the duration of KOA should be explored. In addition, a longitudinal study would be more suitable to study how pain severity impacted fatigue with disease progression, providing more information to healthcare providers and patients. These findings may implicate the practice of healthcare providers, especially physiotherapists, to focus on pain management, weight management and modification of exercise and physical activity.

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CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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REFERENCES

1. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019; 393: 1745-59.
2. Valdes AM, Stocks J. Osteoarthritis and ageing. Eur J Rheumatol 2018; 3: 116-23.
3. Hame SL, Alexander RA. Knee osteoarthritis in women. Curr Rev Musculoskelet Med 2013; 6: 182-7.
4. Baert IA, Meeus M, Mahmoudian A, Luyten FP, Nijs J, Verschueren SM. Do psychosocial factors predict muscle strength, pain, or physical performance in patients with knee osteoarthritis? J Clin Rheumatol 2017; 23: 308-16.
5. Lespasio MJ, Piuzzi NS, Husni ME, Muschler GF, Guarino AJ, Mont MA. Knee osteoarthritis: a primer. Perm J 2017; 21: 16-183.
6. Nawito ZO, El-Azkalany GS, El-Sayad M. Nottingham health profile assessment of health-related quality of life in primary knee osteoarthritis patients: Relation to clinical features and radiologic score. Egypt Rheumatol 2018; 40: 265-8.
7. Rose DM, Seidler A, Nübling M, Latza U, Brähler E, Klein EM, et al. Associations of fatigue to work-related stress, mental and physical health in an employed community sample. BMC Psychiatry 2017; 17: 1-8.
8. Murphy SL, Alexander NB, Levoska M, Smith DM. Relationship between fatigue and subsequent physical activity among older adults with symptomatic osteoarthritis. Arthritis Care Res 2013; 65: 1617-24.
9. Murphy SL, Niemiec SS, Lyden AK, Kratz AL. Pain, fatigue, and physical activity in osteoarthritis: the moderating effects of pain- and fatigue-related activity interference. Archi Phys Med Rehabil 2016; 97 Suppl: S201-9.
10. Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis: A Review. JAMA 2021; 325: 568-78.
11. Cross M, Lapsley H, Barcenilla A, Brooks P, March L. Association Between Measures of Fatigue and Health-Related Quality of Life in Rheumatoid Arthritis and Osteoarthritis. Patient 2008; 1: 97-104.
12. Amtmann D, Bamer AM, Noonan V, Lang N, Kim J, Cook KF. Comparison of the psychometric properties of two fatigue scales in multiple sclerosis. Rehabil Psychol 2012; 57: 159-66.
13. Alghadir AH, Anwer S, Iqbal A, Iqbal ZA. Test-retest reliability, validity, and minimum detectable change of visual analog, numerical rating, and verbal rating scales for measurement of osteoarthritic knee pain. J Pain Res 2018; 11: 851-56.
14. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011; 40: 423-9.
15. Wolinsky FD, Miller DK, Andresen EM, Malmstrom TK, Miller JP. Reproducibility of physical performance and physiologic assessments. J Aging Health 2005; 17: 111-24.
16. Steffen TM, Hacker TA, Mollinger L. Age-and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. Phys Ther 2002; 82: 128-37.
17. Hafsteinsdóttir TB, Rensink M, Schuurmans M. Clinimetric properties of the Timed Up and Go Test for patients with stroke: a systematic review. Top Stroke Rehabil 2014; 21: 197-210.
18. Bennell K, Dobson F, Hinman R. Measures of physical performance assessments: Self-Paced walk test (SPWT), stair climb test (SCT), Six-Minute walk test (6MWT), chair stand test (CST), timed up & go (TUG), sock test, lift and carry test (LCT), and car task. Arthritis Care Res 2011; 63 Suppl: S350-70.
19. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166: 111-7.
20. Ateef M, Kulandaivelan S, Tahseen S. Test–retest reliability and correlates of 6-minute walk test in patients with primary osteoarthritis of knees. Indian J Rheumatol 2016; 11: 192-6.
21. Salaffi F, Leardini G, Canesi B, Mannoni A, Fioravanti A, Caporali R, et al. Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. Osteoarthritis Cartilage 2003; 11: 551-60.
22. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. Behav Res Methods 2009; 41: 1149-60.
23. Rehman AS, Mamoon D. Does new public management practices lead to effective public welfare responses in Pakistan. Turk Econ Rev 2018; 5: 150-73.
24. Fawole HO, Dell'Isola A, Steultjens MP, Riskowski JL, Chastin SF. Temporal associations between physical activity, mental activity and fatigue dimensions in knee osteoarthritis: an exploratory intensive longitudinal study. Fatigue: Biomed Health Behav 2020; 8: 32-48.

25. Alikari V, Sachlas A, Giatrakou S, Stathoulis J, Fradelos E, Theofilou P, et al. Fatigue in arthritis: a multidimensional phenomenon with impact on quality of life. InGeNeDis 2016; 2017: 243-56.
26. Luc-Harkey BA, Safran-Norton CE, Mandl LA, Katz JN, Losina E. Associations among knee muscle strength, structural damage, and pain and mobility in individuals with osteoarthritis and symptomatic meniscal tear. BMC Musculoskelet Disord 2018; 19: 258.
27. Coyle PC, Schrack JA, Hicks GE. Pain energy model of mobility limitation in the older adult. Pain Med 2018; 19: 1559-69.
28. Foucher KC, Aydemir B, Huang CH. Walking energetics and fatigue are associated with physical activity in people with knee osteoarthritis. Clin Biomech 2021; 88: 105427.
29. Weiss E. Knee osteoarthritis, body mass index and pain: data from the Osteoarthritis Initiative. Rheumatol 2014; 53: 2095-99.
30. Kulkarni K, Karssiens T, Kumar V, Pandit H. Obesity and osteoarthritis. Maturitas 2016; 89: 22-8.
31. Spinoso DH, Bellei NC, Marques NR, Navega MT. Quadriceps muscle weakness influences the gait pattern in women with knee osteoarthritis. Adv Rheumatol 2019; 58: 26.
32. Kim D, Park G, Kuo LT, Park W. The effects of pain on quadriceps strength, joint proprioception and dynamic balance among women aged 65 to 75 years with knee osteoarthritis. BMC Geriatr 2018; 18: 1-6.