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Association of body composition and physical activity with pain and function in knee osteoarthritis patients: a cross-sectional study

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ABSTRACT

Objective The objective of this study is to delineate disparities between patients with knee osteoarthritis (KOA) based on obesity status, investigate the interplay among body composition, physical activity and knee pain/function in patients with KOA and conduct subgroup analyses focusing on those with KOA and obesity.

Design Cross-sectional study.

Setting Residents of eight communities in Shijiazhuang, Hebei Province, China, were surveyed from March 2021 to November 2021.

Participants 178 patients with symptomatic KOA aged 40 years or older were included.

Main outcomes and measures The primary outcome measure was knee pain, assessed using the Western Ontario and McMaster Universities Osteoarthritis Index-pain (WOMAC-P) scale. Secondary outcome measures included function, evaluated through the WOMAC-function (WOMAC-F) scale and the Five-Time-Sit-to-Stand Test (FTSST). Data analysis involved t-tests, Wilcoxon rank-sum tests, χ^2 tests, linear and logistical regression analysis.

Results Participants (n=178) were 41–80 years of age (median: 65, P25–P75: 58–70), and 82% were female. Obese patients (n=103) had worse knee pain and self-reported function (p<0.05). In general patients with KOA, body fat mass was positively associated with bilateral knee pain (β=1.21 (95% CI 0.03 to 0.15)), WOMAC-P scores (β=0.25 (95% CI 0.23 to 1.22)), WOMAC-F scores (β=0.28 (95% CI 0.35 to 1.29)) and FTSST (β=0.19 (95% CI 0.03 to 0.42)), moderate-intensity to low-intensity physical activity was negatively associated with bilateral knee pain (β=–0.80 (95% CI –0.10 to –0.01)) and Skeletal Muscle Index (SMI) was negatively associated with WOMAC-F scores (β=–0.16 (95% CI –0.66 to –0.03)). In patients with KOA and obesity, SMI was negatively associated with FTSST (β=–0.30 (95% CI –3.94 to –0.00)).

Conclusion Patients with KOA and obesity had worse knee pain and self-reported function compared with non-obese patients. Greater fat mass, lower muscle mass and lower moderate-intensity to low-intensity physical activity were associated with increased knee pain and poor self-reported function. More skeletal muscle mass was associated with the improvement of objective function.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used body fat percentage as a criterion for obesity, describing the characteristic differences between patients with knee osteoarthritis (OA) and obesity and non-obesity.
- ⇒ This study used subgroup analysis to investigate the effects of body composition and physical activity on outcomes in patients with knee OA and obesity.
- ⇒ The severity of knee OA was not determined and analysed.
- ⇒ The use of self-reported questionnaires may lead to recall bias.
- ⇒ The study design of cross-sectional studies will limit causal explanations of the relationships between variables.

INTRODUCTION

Knee osteoarthritis (KOA) constitutes a significant chronic, degenerative and profoundly disabling affliction prevalent among middle-aged and elderly populations.[1] Knee pain, stiffness and mobility disorders are the main symptoms of the disease, which profoundly affect quality of life.[2] Acknowledged by the WHO as one of the 'three killers' detrimentally affecting human health.[3] Regrettably, the escalating pace of the ageing process has led to an annual increase in the number of individuals afflicted by KOA.[4 5]

Knee pain and compromised physical function significantly impact the daily lives of individuals grappling with KOA. Notably, those experiencing bilateral knee pain encounter heightened challenges in executing routine activities compared with their counterparts with unilateral knee pain.[6] The constraints on physical function, particularly in terms of mobility, not only propel patients towards surgical interventions but also impose substantial financial burdens on both families and society. In the context of China, the projected figure for total knee arthroplasty procedures is expected to reach 400 000 by 2020.[7] KOA presently stands as the 11th leading cause of global disability,[8] with forecasts indicating its ascendancy to the top spot in global disability rankings by 2030.[9] Understanding modifiable factors influencing knee pain and function is imperative, as it holds the key to delaying disease progression and extending the functional longevity of the knee.

Research findings have consistently demonstrated that sociodemographic characteristics,[10] encompassing age, gender, cognitive function[11] and personality traits,[12] play pivotal roles in influencing knee pain and functional outcomes. Despite evidence establishing obesity as a risk factor for knee pain and function,[13] the intricate relationship between obesity and these outcomes remains inadequately understood. This knowledge gap arises from the prevalent use of body mass index (BMI) as the primary index for investigating the association between obesity and KOA.[14 15] Unfortunately, BMI lacks the precision to differentiate between muscle mass and fat mass,[16] leading to the potential misclassification of individuals with higher fat mass and lower lean mass as non-obese.[16] A more meaningful approach involves stratifying patients into the obese and non-obese categories based on body fat percentage and subsequently scrutinising the distinctions between these two groups.[17]

Body composition analysis emerges as a valuable method for assessing and monitoring changes in both muscle mass and fat mass.[18] Among the techniques available for this purpose, bioelectrical impedance analysis (BIA) stands out as a widely employed and clinically advantageous approach. Notably, BIA is non-invasive, cost-effective, swift, portable, reproducible and safe, rendering it particularly suitable for clinical settings.[18] The fundamental principle underlying BIA is the division of the body into conductive fluids, muscular components and non-conductive adipose tissue.[19] In the course of measurement, a minute electrical current is transmitted through the body via electrodes. In instances where the fat ratio is elevated, the measured biological resistance registers a corresponding increase, and conversely. BIA proves versatile in quantifying various parameters of body composition, including but not limited to muscle mass, fat mass, phase angle, body capacitance, resistance and reactance.

Body composition is strongly associated with knee pain and physical function among patients with KOA, even in those with a normal BMI.[20] However, body composition has shown inconsistent associations with knee pain and physical function in patients with KOA in previous studies. Davis *et al*[16] reported that lower fat mass and higher muscle mass were associated with better physical performance in patients with KOA, whereas muscle mass had no correlation with physical performance in other studies.[21] Chinese scholars have delved into the impact of body composition on KOA risk across genders.[22] Only a limited number of researchers[23] have reported a positive correlation between muscle mass and strength around the knee joint in elderly women grappling with KOA. Given that knee pain and diminished knee function stand as pivotal challenges for patients with KOA, comprehending the intricate relationship between body composition and these outcomes holds profound significance.

Physical activity/exercise are widely endorsed for the management of KOA, given their proven efficacy in improving patient outcomes, including enhanced symptom relief, increased mobility, better quality of life and positive effects on mental health.[24 25] Notably, existing literature has highlighted that active participation in physical activity can relieve knee pain and improve knee function.[26]However, evidence on physical activity and its relationship with knee pain and physical function in China is quite limited. Therefore, our study endeavours to elucidate the distinctions between obese and non-obese patients with KOA, unravel the intricate interplay between body composition, physical activity and knee pain/function among patients with KOA, and further conduct subgroup analyses to delineate these relationships specifically within the subset of patients with KOA and obesity.

METHODS

Study design and population

This study is a cross-sectional study, and the sample size is evaluated according to the empirical principle. Multifactor regression analysis generally requires that the sample size of the event outcome should be 5–10 times the number of independent variables.[27] With six independent variables in this study, and considering the 36.4% prevalence rate of KOA in Chinese individuals over 40 years old,[28] the calculated sample size ranges from 138 to 165 participants. The study was conducted in eight communities in Shijiazhuang, Hebei Province, China, spanning from May 2021 to November 2021. Convenience sampling was employed to recruit a total of 178 patients, categorised into non-obese group (75 patients) and obese group (103 patients). Symptomatic KOA was defined as knees meeting both criteria: (1) Frequent knee symptoms, which means pain or stiffness persisted for at least 1 month during the past 12 months and and (2) A diagnosis of KOA established through electronic medical records and clinician self-reports diagnosing OA.[29] Inclusion criteria encompassed patients aged 40 years or older, exhibiting symptomatic KOA, with stable physical conditions, clear consciousness and the ability to cooperate with data collection. Exclusion criteria comprised individuals (1) had a BMI greater than 40 kg/m^2, (2) underwent total knee replacement and (3) had other serious functional and organic diseases such as cancer, severe coronary heart disease, hypertension, etc. Reasons for excluding patients with a BMI greater than 40 kg/m^2 include the following: individuals with a BMI exceeding 40 are classified as morbidly obese.[30] Studies have shown that morbidly obese patients with KOA had more structural and metabolic changes,[31 32] and to ensure the homogeneity of the study subjects, we excluded individuals with a BMI greater than 40 kg/m^2.

Data collection

Sociodemographic characteristics, encompassing age, gender, education level and marital status, along with anthropometric variables such as height, body weight and BMI, were meticulously documented at the study's baseline. Additionally, comprehensive clinical data, including knee pain, self-reported function and objective physical function, were systematically gathered. Furthermore, data pertaining to physical activity levels and body composition were also methodically collected during the baseline assessment. It is worth noting that in order to ensure the availability and authenticity of the data, the self-reported questionnaire data were collected by way of interview.

Knee pain and function

Bilateral knee pain was ascertained through a single inquiry: 'Which side of your knee joint is experiencing pain?' The assessment of knee pain used the pain subscale derived from the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-P), comprising five questions. Each item was rated on a scale ranging from 0 to 4, with higher scores indicative of more severe pain, leading to total scores ranging from 0 to 20. To enhance comparability, normalised scores for each subscale were calculated using the formula: standardised scores=(actual score/highest possible score)×100.[20] Higher scores indicate worse knee pain.

Physical function evaluation encompassed both self-reported function and objective physical function assessments. Self-reported function was measured through the function subscale of the WOMAC (WOMAC-F), consisting of 17 questions. Each item was rated on a scale from 0 to 4, with higher scores indicating poorer function, resulting in total scores ranging from 0 to 68. To facilitate standardised comparisons, normalised scores for each subscale were computed using the formula: standardised scores=(actual score/highest possible score)×100.[20] Elevated scores on this subscale signify a decline in self-reported physical function. Objective physical function was evaluated through the Five-Time-Sit-to-Stand Test (FTSST).[33] This requires patients with KOA to cross their arms across their chest, ascend from a chair, return to a seated position and repeat five times as quickly as possible. Each participant completed the exercise twice, with a 1 min break between each test. The average of the two tests was used. The longer it takes, the worse the function.

Anthropometric and body composition

Height and body weight were meticulously measured using standard methods, with precision extended to the nearest 0.1 kg and 0.1 cm, respectively. BMI was defined as the ratio of body weight to height squared (kg/m^2). Obesity was defined as BMI≥28.0 kg/m^2.[34] Parameters of body composition were obtained from an InBody 770 (BioSpace, Seoul, Korea) device. Key metrics, including body fat mass (BFM, kg), per cent BFM, appendicular skeletal muscle mass (ASM, kg), fat-free mass (FFM, kg) and Skeletal Muscle Index (SMI, kg/m^2), were collected for statistical analyses. BFM was computed as total weight minus FFM, with the latter encompassing muscles, bones, organs and body fluids. The percentage of BFM (%) was determined as BFM divided by total weight, multiplied by 100%.[35] Obesity, based on BFM percentage, was established with cut-off points of ≥35% for women and ≥25% for men.[17] The SMI was calculated as the ratio of ASM, mass to height squared.[36]

Physical activity

Physical activity was assessed using the short version of the International Physical Activity Questionnaire (IPAQ-S).[37] While the IPAQ-S is a third of the length of the long form, it encompasses all pertinent categories of daily life and work movements and demonstrates equivalent psychometric properties to its lengthier counterpart.[38] Research indicates that individuals with KOA commonly display distinctive physical activity patterns, including inactivity, avoidance of vigorous physical activity and prolonged periods of sitting. Notably, the IPAQ-S has been validated as a sufficient tool for evaluating physical activity levels in patients with KOA.[39,40] Consequently, we opted for the IPAQ-S to assess physical activity in patients with KOA. Patients with KOA were prompted to disclose both the total time (in minutes) and frequency (times per week) of three specific activity types engaged in over the preceding week, across four domains (occupational, commuting, domestic and leisure activities). The calculation of physical activity involved multiplying the frequency by duration, thereby quantifying the minutes dedicated to vigorous, moderate and walking activities each week. Additionally, the IPAQ version also includes a question about the time spent on sedentary activity. Associative recall was used to collect data on patients' physical activity. To avoid misassigning patients to the 'high' physical activity group, we applied the data truncation principle.[41] The data truncation principle means if the daily time of a certain intensity physical activity exceeded 3 hours, it was recoded to 180 min. The principle allows a maximum of 21 hours (1260 min) per week of physical activity of each intensity to be reported.

Bias

The use of self-reported questionnaires has the potential to introduce recall bias. Furthermore, measurement bias may exist among objective functional raters. In order to reduce information bias, we implemented associative recall methods aimed at minimising recall bias. For instance, in assessing moderate physical activity, patients were queried about activities at work that elicit a slight increase in heart rate, preferred modes of transportation, weekly time allocated to household tasks such as cleaning, cooking and laundry, as well as engagement in activities like brisk walking or ballroom dancing. The cumulative duration of moderate physical activity per week was determined by aggregating reported times spent in work-related, transportation, household and gardening, and leisure activities. Additionally, we conducted rigorous training for objective functional raters, ensuring uniformity in guiding patients through functional tests based on standardised guidelines.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Statistical analyses

All statistical analyses were performed using Stata V.15.1. The normality of continuous variables was assessed through histograms, Q-Q plots, and the Skewness and Kurtosis test. Descriptive statistics included means±SDs for normally distributed data, medians and IQRs for non-normally distributed data, and frequencies with percentages for categorical variables. Based on body fat percentage, patients were stratified into obese group and non-obese group. Statistical comparisons between the obese and non-obese groups were performed using t-tests for normally distributed data, Wilcoxon rank-sum tests for non-normally distributed data and χ^2 tests for categorical variables.

In the multifactor analysis phase, both linear regression and logistic regression models were employed to estimate β-values, capturing the associations of body composition and physical activity with outcomes. In logistics regression, the dependent variable is bilateral knee pain, and the independent variables are BFM, SMI, vigorous activity, moderate activity, walking and sedentary. In linear regression, the dependent variables are WOMAC pain, WOMAC function and FTSST, respectively, and the independent variables are BFM, SMI, vigorous activity, moderate activity, walking and sedentary. We controlled for potential confounding factors in the regression model, but retained confounding factors with important biological plausibility (such as FFM and appendicular lean mass) or altered the estimated coefficients by >10%.[42] To avoid collinearity and to study anthropometric measures specifically, BMI, percentage fat mass, FFM and ASM, mass were not included in the multivariable analyses.[20] The variance inflation factor (VIF) was used to test the collinearity of other measures. As a general guideline, a VIF>4 requires further investigation, and a VIF>10 indicates severe multicollinearity requiring correction.[20] The significance level was set at p<0.05.

RESULTS

Participant characteristics

A total of 178 patients with KOA were recruited for the current study, with a median age of 64 years. More than 82% of subjects were female. Most patients with KOA were less educated, and more than 56.7% of the patients with KOA graduated from middle school or below, 14.0% from high school and <8% held a diploma or higher academic qualifications. Most of the patients with KOA were married (87%). In terms of clinical characteristics, most of the patients with KOA had bilateral knee pain (60.7%). The median WOMAC-P and WOMAC-F scores were 25.0 and 22.1, respectively. The median time taken for the FTSST was 12.4 s. According to China's BMI rating standard, 28.6% of patients with KOA were categorised as obese.[34] Regarding physical activity, the median total time of physical activity per week was 9.5 hours. However, the median time spent in a sedentary position was 21 hours per week. Regarding body composition, 57.9% of patients with KOA were classified as obese based on body fat percentage.[17] More details are shown in table 1.

Differences between obese and non-obese participants

To explore the differences between obese and non-obese patients with KOA grouped based on body fat percentage, we performed an intergroup comparison. The age distribution (mean (SD) 63.4 (8.8) vs 64.7 (7.9), p=0.311), marital status and educational level showed no significant differences between the obese and non-obese groups. However, patients with KOA and obesity were more likely to have bilateral knee pain (p<0.001) and higher WOMAC-P scores (p<0.004) and WOMAC-F scores (p<0.001). Additionally, patients with KOA and obesity had higher BFM (p<0.001) and body fat percentage (p<0.001). Additionally, the total weekly activity time for patients with KOA and obesity was lower than that of their non-obese counterparts (median (IQR) 11.1 (15.0) vs 7.0 (12.9), p<0.001). Specifically, patients with KOA and obesity spent less time in moderate-intensity physical activity (p=0.030) and walking (p=0.010) but spent more time engaged in sedentary behaviour (p=0.004). No significant differences were observed in the distribution of FTSST, fat-free mass, appendicular lean mass and SMI between obese and non-obese patients with KOA. More details are shown in table 2.

Association between body composition, physical activity and outcomes

The associations between body composition, physical activity and outcomes, after adjusted for age and gender in general patients with KOA (n=178), are detailed in table 3. In 178 patients with KOA, BFM was positively associated with bilateral knee pain (β=1.21, 95% CI 0.03 to 0.15), WOMAC-F scores (β=0.28, 95% CI 0.35 to 1.29), WOMAC-P scores (β=0.25, 95% CI 0.23 to 1.22) and FTSST (β=0.19, 95% CI 0.03 to 0.42). SMI demonstrated a weak negative association with WOMAC-F scores (β=–0.27, 95% CI –7.82 to –1.05), and other correlations with outcomes did not reach statistical significance. Additionally, moderate physical activity was negatively associated with bilateral knee pain (β=–0.80, 95% CI –0.10 to –0.01), and walking was negatively associated with WOMAC-F scores (β=–0.16, 95% CI –0.66 to –0.03). Associations between physical activity and WOMAC-P

Table 1 Characteristics of study participants

Characteristic	Patient-reported outcomes (n=178)
Age (years)	64.2 (8.3)
Gender, female, n (%)	146 (82.0)
Marital status, n (%)	
Unmarried	1 (0.6)
Married	155 (87.1)
Divorced	2 (1.1)
Widowed	20 (11.2)
Educational level, n (%)	
Primary school or below	37 (20.8)
Middle school	64 (36.0)
High school	53 (29.8)
Diploma or above	24 (13.5)
Painful joints, n (%)	
Unilateral	70 (39.3)
Bilateral	108 (60.7)
WOMAC pain, median (IQR)	25.0 (25.0)
WOMAC function, median (IQR)	22.1 (29.4)
FTSST, median (IQR)	12.4 (5.6)
BMI, kg/m^2, n (%)	
<28.0	127 (71.4)
≥28.0	51 (28.6)
Body composition, kg	
BFM	23.0 (6.5)
FFM, median (IQR)	42.3 (7.6)
ALM, median (IQR)	22.7 (4.5)
SMI, kg/m^2, median (IQR)	9.0 (1.4)
Per cent of fat mass, %, n (%)	34.0 (7.0)
Non-obese (female <35%, male <25%)	75 (42.1)
Obese (female ≥35%, male ≥25%)	103 (57.9)
Physical activity, hour/week, median (IQR)	
Vigorous activity	0 (0)
Moderate activity	3.5 (10.5)
Walking	3.5 (7.0)
Sedentary	21.0 (7.0)
Total activity	9.5 (17.5)

Values are mean (SD) unless stated otherwise.
ALM, appendicular lean mass; BFM, body fat mass; BMI, body mass index; FFM, fat-free mass; FTSST, Five-Time-Sit-to-Stand Test; SMI, Skeletal Muscle Index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

scores and FTSST were not statistically significant. In summary, the correlation between body fat and bilateral knee pain far exceeds the correlation between moderate physical activity and bilateral knee pain. Only BFM shows a weak correlation with WOMAC-P scores. The correlation of BFM with WOMAC-F scores is greater than that of walking, and the correlation of SMI with WOMAC-F scores is relatively weak.

Regarding patients with KOA and obesity (n=103), the associations between body composition, physical activity and outcomes, adjusted for age and gender, are detailed in table 4. Within this subgroup, SMI was negatively associated with FTSST (β=−0.30, 95% CI −3.94 to −0.00). Although moderate physical activity was negatively associated with bilateral knee pain (β=−0.99, 95% CI −0.13 to −0.00), and sedentary activity was positively associated with WOMAC-F scores (β=0.22, 95% CI 0.15 to 2.21), these associations did not reach statistical significance after adjusting for age and sex. Associations between BFM, SMI and physical activity measures with knee pain and function were not statistically significant. Although SMI exhibited a negative correlation with FTSST, its impact on FTSST was minimal.

DISCUSSION

In this comprehensive investigation, we delved into the intricate relationship between body composition, physical activity and outcomes among 178 patients with KOA. Interestingly, a substantial 57.9% of individuals with KOA were classified as obese based on body fat percentage, a prevalence notably higher than the conventional BMI-defined obesity rate of 28.6%. This observation aligns with the findings of Ericsson *et al*.[43] According to body fat percentage, patients with KOA were stratified into obese and non-obese groups. Unsurprisingly, our findings revealed that individuals with KOA and obesity exhibited heightened knee pain, diminished function, and reduced engagement in moderate-intensity physical activity and walking when compared with their non-obese counterparts. Notably, in 178 patients with KOA, we further found that BFM was positively associated with bilateral knee pain, WOMAC-P scores, WOMAC-F scores and FTSST. Additionally, SMI was negatively associated with WOMAC-F scores. In terms of physical activity, moderate physical activity was negatively associated with bilateral knee pain, and walking was negatively associated with WOMAC-F scores. In the subset of 103 patients with both KOA and obesity, we found that SMI was negatively associated with FTSST.

Our finding that patients with KOA and obesity experienced more pronounced knee pain aligns with findings from relevant studies.[10 44 45] In addition, obese patients exhibited a higher likelihood of experiencing bilateral knee pain, underscoring the detrimental impact of obesity on individuals with KOA. Furthermore, we also found that patients with KOA and obesity had poor self-reported function, which is consistent with related studies. Riebe *et al*[46] documented the association between obesity and functional limitations in the elderly community. A recent study also showed that obesity has detrimental effects on function in overweight and obese older adults.[47]

Table 2 Characteristics of the study participants stratified by the presence of obesity

	Non-obese (n=75)	Obese (n=103)	P value
Age (years)	63.4 (8.8)	64.7 (7.9)	0.311
Gender, female, n (%)	62 (82.7)	84 (81.6)	0.849
Marital status			0.240
Unmarried	1 (1.3)	0 (0)	
Married	64 (85.3)	91 (88.3)	
Divorced	2 (2.7)	0 (0)	
Widowed	8 (10.7)	12 (11.7)	
Educational level			0180
Primary school or below, n (%)	13 (17.3)	24 (23.3)	
Middle school, n (%)	23 (30.7)	41 (39.8)	
High school, n (%)	25 (33.3)	28 (27.2)	
Diploma or above, n (%)	14 (18.7)	10 (9.7)	
Painful joints			0.001*
Unilateral, n (%)	40 (53.3)	30 (29.4)	
Bilateral, n (%)	35 (46.7)	72 (70.6)	
WOMAC pain score, median (IQR)	20.0 (20.0)	30.0 (30.0)	0.004*
WOMAC function score, median (IQR)	17.6 (19.1)	30.9 (30.9)	0.001*
FTSST, median (IQR)	12.2 (5.6)	12.4 (5.7)	0.195
BMI, kg/m^2	23.6 (2.7)	27.8 (2.8)	<0.001*
Body composition, kg			
BFM	17.6 (4.1)	26.9 (4.9)	<0.001*
FFM, median (IQR)	42.2 (10.0)	42.4 (7.3)	0.674
ALM, median (IQR)	22.7 (5.9)	22.7 (4.3)	0.778
SMI, kg/m^2, median (IQR)	8.9 (1.6)	9.0 (1.4)	0.285
Per cent of fat mass, %	28.6 (5.4)	38.0 (5.2)	<0.001*
Physical activity, hour/week, median (IQR)			
Vigorous activity	0 (0)	0 (0)	0.070
Moderate activity	6.0 (13.0)	1.8 (7.0)	0.030*
Walking	4.7 (8.8)	3.0 (7.0)	0.010*
Sedentary	21.0 (7.0)	21.0 (0.0)	0.004*
Total activity	11.1 (15.0)	7.0 (12.9)	<0.001

Values are mean (SD) unless stated otherwise.
*p < 0.05
ALM, appendicular lean mass; BFM, body fat mass; BMI, body mass index; FFM, fat-free mass; FTSST, Five-Time-Sit-to-Stand Test; SMI, Skeletal Muscle Index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Nonetheless, Okyar *et al*[48] have highlighted that an understanding of functional limitations in the elderly requires distinguishing between muscle and fat, cautioning against simplifying the cause solely to obesity defined by BMI or body fat percentage. To comprehensively elucidate the interplay between obesity and function, a more nuanced exploration of body composition, encompassing factors such as muscle mass and fat mass, is warranted.

In 178 patients with KOA, our investigation revealed a positive correlation between BFM and both bilateral knee pain and WOMAC-P scores. This finding is consistent with the existing literature on knee pain,[49] where a baseline increase of one standard deviation (8.7 kg) in total BFM was associated with a 36% heightened risk of increased knee pain over an average of 5.1 years. Our results substantiate the conclusion that BFM may constitute a more pertinent metric for predicting knee pain in patients with KOA.[43] Walsh *et al*[50] in their systematic review identified positive associations between increased BFM and widespread knee pain. Additionally, our investigation revealed positive associations between BFM and WOMAC-F scores, as well as FTSST, aligning with findings in pertinent literature.[51] However, in a subset of 103 patients with KOA and obesity, our analysis did not unveil

Table 3 Association between body composition and physical activity with outcomes (n=178)

	Bilateral knee pain, β (95% CI)		Normalised WOMAC pain, β (95% CI)		Normalised WOMAC function, β (95% CI)		FTSST, β (95% CI)	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Body composition								
BFM	0.87* (0.01 to 0.12)	1.21** (0.03 to 0.15)	0.19* (0.13 to 1.02)	0.25** (0.23 to 1.22)	0.19* (0.12 to 0.99)	0.28*** (0.35 to 1.29)	0.16* (0.01 to 0.36)	0.19* (0.03 to 0.42)
SMI	−0.28 (−0.41 to 0.17)	−0.90 (−0.81 to 0.04)	−0.06 (−3.52 to 1.51)	−0.15 (−6.10 to 1.03)	−0.11 (−4.26 to 0.64)	−0.27* (−7.82 to −1.05)	−0.14 (−1.90 to 0.10)	−0.19 (−2.67 to 0.18)
Physical activity								
Vigorous activity	0.63 (−0.07 to 0.38)	0.75 (−0.05 to 0.42)	−0.11 (−2.44 to 0.37)	−0.09 (−2.31 to 0.51)	−0.08 (−2.17 to 0.57)	−0.06 (−1.90 to 0.78)	−0.08 (−0.87 to 0.25)	−0.07 (−0.84 to 0.29)
Moderate activity	−0.91** (−0.11 to 0.02)	−0.80* (−0.10 to 0.01)	0.00 (−0.39 to 0.39)	0.02 (−0.33 to 0.46)	−0.03 (−0.45 to 0.31)	0.02 (−0.34 to 0.41)	0.09 (−0.06 to 0.25)	0.11 (−0.05 to 0.27)
Walking	0.13 (−0.03 to 0.05)	0.07 (−0.03 to 0.04)	−0.14 (−0.63 to 0.03)	−0.14 (−0.65 to 0.01)	−0.15* (−0.64 to 0.00)	−0.16* (−0.66 to −0.03)	−0.02 (−0.15 to 0.12)	−0.02 (−0.15 to 0.12)
Sedentary	0.27 (−0.04 to 0.10)	0.18 (−0.05 to 0.09)	0.10 (−0.18 to 1.05)	0.09 (−0.26 to 0.99)	0.12 (−0.12 to 1.08)	0.09 (−0.22 to 0.96)	−0.13 (−0.46 to 0.03)	−0.15 (−0.48 to 0.01)
Adj. R-squared			0.072	0.080	0.085	0.135	0.030	0.034
F value			3.303	2.911	3.742	4.444	1.917	1.785
P value	0.005	0.005	0.004	0.005	0.002	0.000	0.081	0.083

Adjusted for baseline age and gender. *P<0.05, **p<0.01, ***p<0.001.
ALM, appendicular lean mass; BFM, body fat mass; FTSST, Five-Time-Sit-to-Stand Test; SMI, Skeletal Muscle Index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4 Association between body composition and physical activity with outcomes in obese patients (n=103)

	Bilateral knee pain, β (95% CI)		Normalised WOMAC pain, β (95% CI)		Normalised WOMAC function, β (95% CI)		FTSST, β (95% CI)	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Body composition								
BFM	−0.25 (−0.12 to 0.07)	0.19 (−0.10 to 0.13)	0.13 (−0.28 to 1.38)	0.15 (−0.31 to 1.55)	0.10 (−0.40 to 1.17)	0.17 (−0.20 to 1.54)	0.12 (−0.13 to 0.46)	0.17 (−0.09 to 0.56)
SMI	0.63 (−0.22 to 0.76)	−0.35 (−0.84 to 0.54)	0.01 (−3.80 to 4.17)	0.00 (−5.55 to 5.60)	0.00 (−3.77 to 3.78)	−0.11 (−7.17 to 3.25)	−0.21 (−2.77 to 0.05)	−0.30* (−3.94 to −0.00)
Physical activity								
Vigorous activity	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	−0.03 (−2.68 to 2.06)	−0.03 (−2.85 to 2.04)	0.01 (−2.15 to 2.35)	0.01 (−2.15 to 2.42)	−0.07 (−1.14 to 0.54)	−0.06 (−1.11 to 0.61)
Moderate activity	−0.99* (−0.13 to 0.00)	−0.97 (−0.13 to 0.00)	−0.10 (−0.88 to 0.32)	−0.09 (−0.88 to 0.34)	−0.12 (−0.91 to 0.22)	−0.10 (−0.86 to 0.28)	0.11 (−0.09 to 0.33)	0.13 (−0.08 to 0.34)
Walking	−0.01 (−0.05 to 0.05)	−0.18 (−0.06 to 0.04)	−0.19 (−0.80 to 0.04)	−0.19 (−0.82 to 0.04)	−0.17 (−0.74 to 0.06)	−0.20 (−0.79 to 0.02)	0.06 (−0.11 to 0.19)	0.05 (−0.12 to 0.18)
Sedentary	0.61 (−0.04 to 0.19)	0.50 (−0.06 to 0.18)	0.16 (−0.20 to 1.97)	0.14 (−0.34 to 1.91)	0.22* (0.15 to 2.21)	0.19 (−0.07 to 2.03)	0.07 (−0.25 to 0.52)	0.05 (−0.30 to 0.50)
Adj. R-squared			0.042	0.029	0.067	0.080	−0.003	−0.013
F value			1.754	1.378	2.218	2.103	0.956	0.832
P value	0.206	0.130	0.117	0.216	0.048	0.043	0.459	0.576

Adjusted for baseline age and gender. *P<0.05.
ALM, appendicular lean mass; BFM, body fat mass; FTSST, Five-Time-Sit-to-Stand Test; SMI, Skeletal Muscle Index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

a significant association between BFM and knee pain or physical function. This absence of association may be attributed to the meticulous control of obesity factors in our study design.

All positive findings can be interpreted through both mechanical and metabolic lenses.[52] Mechanically, the overload of mechanical stress is known to stimulate receptors on cartilage surfaces, triggering various inflammatory pathways. This, in turn, leads to the sensitisation of nociceptors and central nociceptor pathways, ultimately causing pain.[53–55] Additionally, this mechanical overload induces low-grade inflammation in the musculoskeletal system, contributing to reduced muscle strength and impaired physical function.[56 57] From a metabolic perspective, the accumulation of excess adipose tissue has the potential to infiltrate muscles, disrupting energy metabolism in muscle cells. This disruption can result in decreased production of mitochondrial ATP, ultimately impacting skeletal muscle function and leading to decreased physical function.[58 59] Studies have demonstrated that aerobic exercise or a combination of resistance exercises can effectively mitigate skeletal muscle fat infiltration, thereby improving muscle function and overall bodily function.[60]

In 178 patients with KOA, we identified a negative association between SMI and WOMAC-P scores. However, no such negative relationship was observed between SMI and the FTSST. Conversely, in a subgroup analysis of 103 patients with KOA and obesity, we did find a negative association between SMI and FTSST. The impact of muscle on function appears inconsistent, and the underlying mechanisms remain unclear. Jeanmaire *et al*[20] demonstrated that patients with hip or KOA and low muscle mass reported poorer function compared with those with normal body composition. On the contrary, Chao *et al*[21] reported that in the elderly population, muscle mass showed no correlation with gait speed and grip strength. While muscle mass may play a pivotal role in physical function, it may not be the sole determinant of muscle strength. Existing studies suggest that the interplay of muscle function, mass, composition and their interactions collectively contribute to influencing physical function.[61]

In 178 patients with KOA, our investigation into the association between physical activity and KOA outcomes revealed notable findings. Specifically, moderate physical activity exhibited a negative association with bilateral knee pain, and walking demonstrated a negative association with WOMAC-F scores. Robust evidence supports the notion that moderate levels of physical activity are linked to reduced pain and enhanced physical function in adults with KOA.[62] More interestingly, engaging in 1 hour of moderate-to-vigorous physical activity, as opposed to sedentary or light physical activity, was correlated with increased muscle mass, walking speed and grip strength.[63] This positive relationship is thought to stem from physical activity's ability to enhance antioxidant responses, diminish proinflammatory signalling, and stimulate anabolic and mitochondrial biogenic pathways in skeletal muscle.[64] However, intriguingly, our analysis did not reveal a significant association between physical activity and outcomes in patients with KOA and obesity. This lack of association may be attributed to obese individuals harbouring a heightened fear of pain, leading to markedly low levels of physical activity, and consequently, an absence of positive effects in this subgroup of KOA patients.[65] Furthermore, the median time of moderate physical activity in the obese group (1.8 hours, IQR 7.0 hours) fell significantly below the 150–300 min of moderate-intensity physical activity per week recommended.[66]

Our study has several strengths. First, to enhance the precision of obesity classification, we opted to define obesity using body fat percentage rather than relying on a conventional BMI approach. Notably, we observed that the obesity rate defined by body fat percentage was higher than that determined by BMI. Second, for a more nuanced characterisation of patients with KOA and obesity, we categorised individuals into obese and non-obese groups based on body fat percentage, enabling a detailed comparison between these groups. Third, to delve deeper into the intricate relationship between body composition, physical activity and outcomes in patients with KOA, we conducted regression analyses both within the general population and specifically within the obese subgroup.

Our study has certain limitations that should be acknowledged. First, the absence of radiographs prevented us from assessing the severity of KOA according to established criteria like Kellgren-Lawrence, potentially restricting the generalisability of our findings. Despite this limitation, we assert that employing a combination of electronic health record diagnoses, clinician-assessed patient self-reports and current knee pain offers a reasonable strategy for identifying KOA patients within the healthcare system. Second, physical activity data were collected in the form of questionnaires, which may lead to recall bias. Although recall bias is inevitable, in the process of questionnaire collection, we adopted associative recall method to help patients recall last week's physical activities to reduce recall bias. Third, the cross-sectional nature of our study design hinders causal explanations for the observed relationships between variables. Consequently, we recommend future investigations employ high-quality longitudinal studies to delve deeper into the connections between body composition, physical activity, and knee pain and function. To enhance the accuracy of physical activity assessment, we advocate for the incorporation of wearable devices, allowing for a more comprehensive evaluation over a week-long period.

Conclusion

In conclusion, our findings highlight that patients with KOA and obesity exhibit more pronounced knee pain and functional limitations compared with their non-obese counterparts. In the general population of patients with KOA, lower muscle mass and reduced engagement in moderate-intensity to low-intensity physical activity correlate with heightened knee pain and compromised self-reported function. Greater fat mass is linked to exacerbated knee pain and poorer self-reported function. Interestingly, among patients with KOA and obesity, increased muscle mass is associated with improved objective function. As a practical recommendation, we suggest that individuals with KOA, regardless of obesity status, prioritise reducing fat mass and increasing muscle mass. Furthermore, incorporating more moderate-intensity to low-intensity physical activity into their routines may contribute to overall better outcomes in terms of knee pain and physical function.

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REFERENCES

1 Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet* 2019;393:1745–59.
2 Sharma L. Osteoarthritis of the knee. *N Engl J Med* 2021;384:51–9.
3 Yan Y, Lu A, Dou Y, *et al*. Nanomedicines Reprogram Synovial Macrophages by scavenging nitric oxide and silencing Ca9 in Progressive osteoarthritis. *Adv Sci (Weinh)* 2023;10:2207490. 10.1002/advs.202207490 Available: https://onlinelibrary.wiley.com/toc/21983844/10/11
4 Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis: A review. *JAMA* 2021;325:568–78.
5 Liu Q, Wang S, Lin J, *et al*. The burden for knee osteoarthritis among Chinese elderly: estimates from a nationally representative study. *Osteoarthritis Cartilage* 2018;26:1636–42.
6 Riddle DL, Stratford PW. Unilateral vs bilateral symptomatic knee osteoarthritis: associations between pain intensity and function. *Rheumatology (Oxford)* 2013;52:2229–37.
7 Feng B, Zhu W, Bian Y-Y, *et al*. China artificial joint annual data report. *Chin Med J (Engl)* 2020;134:752–3.
8 Bennell KL, Hunter DJ, Paterson KL. Platelet-rich plasma for the management of hip and knee osteoarthritis. *Curr Rheumatol Rep* 2017;19:24.
9 Zhang H, Shao Y, Yao Z, *et al*. Mechanical Overloading promotes Chondrocyte Senescence and osteoarthritis development through downregulating Fbxw7. *Ann Rheum Dis* 2022;81:676–86.
10 Alghadir AH, Khan M. Factors affecting pain and physical functions in patients with knee osteoarthritis: an observational study. *Medicine* 2022;101:e31748.
11 Crowley S, Mickle AM, Wiggins ME, *et al*. Relationships between cognitive screening composite scores and pain intensity and pain disability in adults with/at risk for knee osteoarthritis. *Clin J Pain* 2022;38:470–5.
12 Wilfong JM, Badley EM, Power JD, *et al*. Discordance between self-reported and performance-based function among knee osteoarthritis surgical patients: variations by sex and obesity. *PLoS One* 2020;15:e0236865.
13 Messier SP, Callahan LF, Beavers DP, *et al*. Weight-loss and exercise for communities with arthritis in North Carolina (we-can): design and rationale of a pragmatic, assessor-blinded, randomized controlled trial. *BMC Musculoskelet Disord* 2017;18:91.
14 Batsis JA, Zbehlik AJ, Barre LK, *et al*. Impact of obesity on disability, function, and physical activity: data from the osteoarthritis initiative. *Scand J Rheumatol* 2015;44:495–502.
15 Raud B, Gay C, Guiguet-Auclair C, *et al*. Level of obesity is directly associated with the clinical and functional consequences of knee osteoarthritis. *Sci Rep* 2020;10:3601.
16 Davis HC, Blue MNM, Hirsch KR, *et al*. Body composition is associated with physical performance in individuals with knee osteoarthritis. *J Clin Rheumatol* 2020;26:109–14.
17 Phillips CM, Tierney AC, Perez-Martinez P, *et al*. Obesity and body fat classification in the metabolic syndrome: impact on Cardiometabolic risk Metabotype. *Obesity* 2013;21. 10.1002/oby.20263 Available: https://onlinelibrary.wiley.com/toc/1930739x/21/1
18 Ertürk C, Altay MA, Sert C, *et al*. The body composition of patients with knee osteoarthritis: relationship with clinical parameters and radiographic severity. *Aging Clin Exp Res* 2015;27:673–9.
19 Kyle UG, Bosaeus I, De Lorenzo AD, *et al*. Bioelectrical impedance analysis--part I: review of principles and methods. *Clin Nutr* 2004;23:1226–43.
20 Jeanmaire C, Mazières B, Verrouil E, *et al*. Body composition and clinical symptoms in patients with hip or knee osteoarthritis: results from the KHOALA cohort. *Semin Arthritis Rheum* 2018;47:797–804.
21 Chao Y-P, Chen W-L, Peng T-C, *et al*. Examining the association between muscle mass, muscle function, and fat indexes in an elderly population. *Nutrition* 2021;83:S0899-9007(20)30354-3.
22 Hangming Z, Yixin H, Zheng L, *et al*. Association between body composition and symptomatic knee osteoarthritis in the elderly. *Chin J Clin Healthc* 2021;24:652–5.
23 Zhang X, Pan X, Deng L, *et al*. Relationship between knee muscle strength and fat/muscle mass in elderly women with knee osteoarthritis based on dual-energy X-ray Absorptiometry. *IJERPH* 2020;17:573.
24 Wellsandt E, Golightly Y. Exercise in the management of knee and hip osteoarthritis. *Curr Opin Rheumatol* 2018;30:151–9.
25 Gay C, Chabaud A, Guilley E, *et al*. Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis. *Ann Phys Rehabil Med* 2016;59:174–83.
26 Zampogna B, Papalia R, Papalia GF, *et al*. The role of physical activity as conservative treatment for hip and knee osteoarthritis in older people: A systematic review and meta-analysis. *J Clin Med* 2020;9:1167.
27 Riley RD, Ensor J, Snell KIE, *et al*. Calculating the sample size required for developing a clinical prediction model. *BMJ* 2020;368:m441.
28 Xiaojia T, Rugeng Z, Meng Z, *et al*. Prevaience of knee osteoarthritis in the middle-aged and elderly in China: a meta-analysis. *Chinese Journal of Tissue Engineering Research* 2018;22:650–6.
29 Allen KD, Woolson S, Hoenig HM, *et al*. Stepped exercise program for patients with knee osteoarthritis. *Ann Intern Med* 2021;174:298–307.
30 Weimann A, Fischer M, Oberänder N, *et al*. Willing to go the extra mile: prospective evaluation of an intensified non-surgical treatment for patients with morbid obesity. *Clin Nutr* 2019;38:1773–81.
31 Widhalm HK, Seemann R, Hamboeck M, *et al*. Osteoarthritis in Morbidly obese children and adolescents, an age-matched controlled study. *Knee Surg Sports Traumatol Arthrosc* 2016;24:644–52.
32 Ricci MA, De Vuono S, Scavizzi M, *et al*. Facing morbid obesity: how to approach it. *Angiology* 2016;67:391–7.
33 Csuka M, McCarty DJ. Simple method for measurement of lower extremity muscle strength. *Am J Med* 1985;78:77–81.
34 Zeng Q, Li N, Pan X-F, *et al*. Clinical management and treatment of obesity in China. *Lancet Diab Endocrinol* 2021;9:393–405.
35 Lin C-L, Yu N-C, Wu H-C, *et al*. Association of body composition with type 2 diabetes: A retrospective chart review study. *Int J Environ Res Public Health* 2021;18:4421.

36 Cheng KY-K, Chow SK-H, Hung VW-Y, *et al*. Diagnosis of Sarcopenia by evaluating Skeletal muscle mass by adjusted Bioimpedance analysis validated with Dual-Energy X-Ray Absorptiometry. *J Cachexia Sarcopenia Muscle* 2021;12:2163–73.
37 Macfarlane DJ, Lee CCY, Ho EYK, *et al*. Reliability and validity of the Chinese version of IPAQ [short]. *J Sci Med Sport* 2007;10:45–51.
38 Craig CL, Marshall AL, Sj??str??m M, *et al*. International physical activity questionnaire: 12-country Reliability and validity. *Medicine & Science in Sports & Exercise* 2003;35:1381–95.
39 Lee PH, Yu Y, McDowell I, *et al*. Performance of the International physical activity questionnaire (short form) in subgroups of the Hong Kong Chinese population. *Int J Behav Nutr Phys Act* 2011;8:81.
40 Gay C, Guiguet-Auclair C, Mourgues C, *et al*. Physical activity level and association with behavioral factors in knee osteoarthritis. *Ann Phys Rehabil Med* 2019;62:14–20.
41 Mengyu F, Jun L, Pingping H. Chinese guidelines for data processing and analysis concerning the International physical activity questionnaire. *Chin J Epidemiol* 2014;35:961–4.
42 Greenland S. Modeling and variable selection in epidemiologic analysis. *Am J Public Health* 1989;79:340–9.
43 Ericsson YB, McGuigan FE, Akesson KE. Knee pain in young adult Women- associations with muscle strength, body composition and physical activity. *BMC Musculoskelet Disord* 2021;22:715.
44 Riddle DL, Stratford PW. Body weight changes and corresponding changes in pain and function in persons with symptomatic knee osteoarthritis: a cohort study. *Arthritis Care Res (Hoboken)* 2013;65:15–22. 10.1002/acr.21692 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/65/1
45 Gomes-Neto M, Araujo AD, Junqueira IDA, *et al*. Comparative study of functional capacity and quality of life among obese and non-obese elderly people with knee osteoarthritis. *Rev Bras Reumatol Engl Ed* 2016;56:126–30.
46 Riebe D, Blissmer BJ, Greaney ML, *et al*. The relationship between obesity, physical activity, and physical function in older adults. *J Aging Health* 2009;21:1159–78.
47 Rogers NT, Power C, Pinto Pereira SM. Birthweight, lifetime obesity and physical functioning in mid-adulthood: a nationwide birth cohort study. *Int J Epidemiol* 2020;49:657–65.
48 Okyar Baş A-O, Balcı C-O. Comment on: the relationship between Multimorbidity, obesity, and functional impairment in older adults. *J Am Geriatr Soc* 2022;70:2173–4.
49 Jin X, Ding C, Wang X, *et al*. Longitudinal associations between Adiposity and change in knee pain: Tasmanian older adult cohort study. *Semin Arthritis Rheum* 2016;45:564–9.
50 Walsh TP, Arnold JB, Evans AM, *et al*. The association between body fat and musculoskeletal pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord* 2018;19:233.
51 Wada O, Kurita N, Kamitani T, *et al*. Implications of evaluating leg muscle mass and fat mass separately for quadriceps strength in knee osteoarthritis: the SPSS-OK study. *Clin Rheumatol* 2020;39:1655–61.
52 Chen L, Zheng JJY, Li G, *et al*. Pathogenesis and clinical management of obesity-related knee osteoarthritis: impact of mechanical loading. *J Orthop Translat* 2020;24:66–75.
53 Wang T, He C. Pro-inflammatory Cytokines: the link between obesity and osteoarthritis. *Cytokine Growth Factor Rev* 2018;44:38–50.
54 Francisco V, Ruiz-Fernández C, Pino J, *et al*. Adipokines: linking metabolic syndrome, the immune system, and Arthritic diseases. *Biochem Pharmacol* 2019;165:196–206.
55 Fang T, Zhou X, Jin M, *et al*. Molecular mechanisms of mechanical load-induced osteoarthritis. *Int Orthop* 2021;45:1661:1125–36.:.
56 Francisco V, Pérez T, Pino J, *et al*. Biomechanics, obesity, and osteoarthritis. The role of Adipokines: when the levee breaks. *J Orthop Res* 2018;36:594–604.
57 Zapata-Linares N, Eymard F, Berenbaum F, *et al*. Role of Adipose tissues in osteoarthritis. *Curr Opin Rheumatol* 2021;33:84–93.
58 Kim M, Oh JH, Won CW. Sex-specific differences in lower body fat distribution and association with physical performance among healthy community-dwelling older adults: A pilot study. *IJERPH* 2022;19:4201.
59 Meng T, Antony B, Venn A, *et al*. Association of body composition, physical activity and physical performance with knee cartilage thickness and bone area in young adults. *Rheumatology (Oxford)* 2020;59:1607–16.
60 Tuñón-Suárez M, Reyes-Ponce A, Godoy-Órdenes R, *et al*. Exercise training to decrease ectopic Intermuscular Adipose tissue in individuals with chronic diseases: A systematic review and meta-analysis. *Phys Ther* 2021;101:pzab162.
61 Krishnasamy P, Hall M, Robbins SR. The role of skeletal muscle in the pathophysiology and management of knee osteoarthritis. *Rheumatology (Oxford)* 2018;57:iv124.
62 Whitaker KM, Pettee Gabriel K, Laddu D, *et al*. Bidirectional associations of accelerometer measured sedentary behavior and physical activity with knee pain, stiffness, and physical function: the CARDIA study. *Prev Med Rep* 2021;22:101348.
63 Sánchez-Sánchez JL, Mañas A, García-García FJ, *et al*. Sedentary behaviour, physical activity, and Sarcopenia among older adults in the TSHA: Isotemporal substitution model. *J Cachexia Sarcopenia Muscle* 2019;10:188–98.
64 El Assar M, Álvarez-Bustos A, Sosa P, *et al*. Effect of physical activity/exercise on oxidative stress and inflammation in muscle and vascular aging. *Int J Mol Sci* 2022;23:8713.
65 Lawford BJ, Bennell KL, Allison K, *et al*. Challenges with strengthening exercises for individuals with knee osteoarthritis and comorbid obesity: A qualitative study with patients and physical therapists. *Arthritis Care & Research* 2022;74:113–25. 10.1002/acr.24439 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/74/1
66 Bull FC, Al-Ansari SS, Biddle S, *et al*. World health organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020;54:1451–62.