Predictors of walking capacity in obese adults with knee osteoarthritis

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ABSTRACT

Introduction: Knee osteoarthritis (KOA) has a considerable prevalence in obese individuals and recommendations of weight loss for KOA management are gaining greater importance. Exercise is recommended to interrupt the cycle obesity-KOA-pain-inactivity, where walking is the most common exercise pattern recommended for obese individuals who initiate a weight loss exercise program. Thus this study aimed to analyse the factors which can affect the walking capacity in obese adults with symptomatic KOA.

Methods: 48 obese adults (age=55±7years; BMI=35±5 Kg/m^2) with clinical and radiological KOA completed self-reported questionnaires (Knee Injury and Osteoarthritis Outcome Score, Brief Pain Inventory and Beck Depression Inventory), physical function tests (Six Minutes Walking Test-6MWT, chair sit and reach-CSRT, five repetition sit-to-stand test-FRSTST, handgrip strength-HST, isokinetic knee strength) and body composition was determined.

Results: The best model (F= 41.485; p<.001) explained 73% of the 6MWT's variance, where fat mass of the most painful limb, knee pain severity and lower limb strength were the strongest predictors of the 6MWT.

Conclusion: Despite the importance of lower limb fat mass and strength, pain was the only variable that appeared as a predictor of 6MWT in the three tested models. The existence of knee pain affects the capacity to walk or to perform weight bearing exercises and consequently the exercise's adherence, compromising the objective of body composition improvement. Thus, authors suggest that, additionally to the lower limb strengthening, knee pain should be screened, controlled and acknowledged for exercise prescription. This study is inserted in the PICO Project (Clinical trial: NCT01832545).

Keywords: Walking capacity; Knee osteoarthritis; Knee pain; Obesity; 6MWT

INTRODUCTION

Knee osteoarthritis (KOA) is highly prevalent in obese individuals[1] and with the increasing obesity and aging rate of the world population[2], the expectations are that the prevalence of KOA will increase too. Among the KOA risk factors (age, obesity, occupation, lower limb muscle weakness, previous knee injury and misalignment) only obesity, occupation and strength are considered modifiable factors[1,3,4]. In the predictive model presented by Zhang et al.[5], six risk factors were related to KOA incidence (age, sex, body mass index (BMI), occupation, family history and knee injury) and four risk factors were related to KOA progression (age, sex, knee injury and sports). Regarding BMI, a value above 30 kg/m^2 implies a greater risk of KOA incidence, mainly for bilateral occurrence[6].

The majority of patients with KOA do not meet the recommended levels of physical activity[7], leading to weight gain and obesity[8]; the increased mechanical load and knee muscle weakness related to obesity, exacerbates mechanical pain and may aggravate the disease, providing a general loss of functionality and subsequent inactivity. The combination of obesity and KOA creates a vicious cycle of pain, physical activity reduction, loss of functionality, disease progression and, again, accentuation of sedentary behavior[9]. These cycles can be worsened with depressive symptoms, which are frequently associated with obesity and KOA symptoms[10], whereby each can trigger and influence one another, further compromising the quality of life[4].

In addition to local effects due to increased joint

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loading, obesity has systemic metabolic effects in KOA[11] caused by the higher concentrations of inflammatory markers (such as TNF-α and leptin[12] that are predominantly secreted by adipose tissue)[13]. Beyond the fact of leptin increases the synthesis of TNF-β, a stimulator of osteophyte formation[14], the consequent result of low-grade inflammation plays a pathophysiological role in OA because it can affect muscle function, lower the individual's pain threshold, and affect chondrocyte homeostasis, leading directly to cartilage matrix degradation[12,15]. Thus, weight loss and body composition improvement is gaining increasing importance for KOA prevention and management[3, 4, 13, 16].

For a general weight loss program, with an exercise and behaviour intervention lasting 3-6 months, the recommended reduction of initial body mass is between 5-10%[17]. In cases of KOA, a decrease in BMI close to 10% is suggested to have a beneficial impact on cartilage matrix degeneration[17]. Messier et al.[16] reported that a weight reduction of 1 kg could mean a 4-fold decrease in knee load per step, with a 1.4% reduction in knee abduction moment. Due to the high number of steps taken daily, this reduction can be considered clinically significant and may assist with pain reduction eventually stimulating an increase in physical activity.

Walking is one of the most important functions of the human being and is an essential capacity for autonomy and for maintaining an independent lifestyle[18]. The aerobic capacity and walking ability in different populations have been evaluated using the Six Minutes Walking Test (6MWT), and reference values related to obesity and KOA have been published[5,19-22]. Capodaglio et al.[23] showed that the distance walked in the 6MWT by obese adult individuals significantly correlated to age, gender and BMI, proposing a reference equation where these variables explained 48% of variance of the walked distance. It has been found that the walking distance of obese individuals is significantly less than that of their lean counterparts[20,22,23]. Additionally, individuals suffering from KOA adapt variations in gait biomechanics to avoid mechanical pain, compensating with dynamic balance which compromises gait efficacy[20].

In general, the walking capacity can be affected by age, sex, excess weight, fat free mass, cognitive limitations, lower limb strength, musculoskeletal and cardiovascular disorders, psychological factors, mobility and amount of weekly physical activity[24-27]. It is the most common weight bearing exercise recommended for obese individuals when initiating their weight loss exercise program. However, the muscle weakness, the existence of knee pain and other KOA symptoms could be a constraint for their physical performance, compromising exercise motivation and adherence, especially if symptoms of depression are also present[10, 22].

Although the factors that may affect walking capacity are well-known, in the case of obese individuals with KOA, there may be other factors that compromise their ability to walk and that should be considered in the prescription of exercises. Thus, to provide a better understanding on this subject, the present study aimed to analyse the factors than can affect the walking capacity in obese adults with symptomatic KOA.

METHODS

This study was integrated in the PICO project (Intervention Program Against Osteoarthritis) and approved by the Ethical Committee of the Faculty of Human Kinetics, University of Lisbon. The PICO project took place in Oeiras, Lisbon District, in our faculty campus, being that the physical tests and questionnaires were applied by exercise physiologists in our lab and intervention sessions was done in the auditorium and in the pool. More detailed information can be found in the study protocol previously published[28]. Trial registered number is NCT01832545.

PARTICIPANTS

The recruitment and selection process was performed according to the eligibility criteria previously defined in the PICO project[28]: 40 ≤ age ≤ 65 years, BMI≥28.0 Kg/m2, unilateral or bilateral KOA (radiographic and clinical ACR criteria), knee pain, a sedentary lifestyle, being independent with mobility capacity, and reading and writing knowledge. All eligible individuals who contacted the study secretariat went through the same selection process, namely, a telephone-based pre–selection stage followed by a face to face interview and completion of the Knee Osteoarthritis Pre-Screening questionnaire (KOPS)[29]. Volunteers who fulfilled the ACR clinical criteria[30] were referred to the radiological examination and the final diagnosis was provided by a rheumatologist. The final sample included 48 individuals (55±7 years), 35 females and 13 males with KOA, 71% of the sample was comprised of participants between 40-59 years of age, while 29% fell between 60--65 years of age. Only 25% of total individuals were in retirement. Regarding the educational status, 81% of the participants reported having completed 9th grade, while 46% completed some college.

PROCEDURES

KOA symptoms were assessed by the Portuguese version of the Knee Injury and Osteoarthritis Outcome Score (KOOS)[31] and by Brief Pain Inventory (BPI) – short version[32]; mental health was assessed by Beck Depression Inventory (BDI-II)[33]. The Portuguese version of the short form of the International Physical Activity Questionnaire (IPAQ) was used to assess the amount of physical activity in which each participant engaged per week[34], where results is presented as metabolic equivalent (METs). Questionnaires was applied along the two physical testing days, with random order and were filled by self-report and confirmed in an interview by the exercise physiologist.

The physical function tests included the Six Minutes Walking Test (6MWT), Chair Sit and Reach test (CSR),[35], the Five-Repetition Sit-To-Stand Test (FRSTST)[21] and the Handgrip Strength Test (HST)[36]. Direct measurement of knee strength was assessed by isokinetic and isometric tests of both knee joints using a dynamometer Biodex System III (Biodex Medical Inc., Shirley, NY, U.S.A.)[28]. Lower Limbs were classified as most painful knee (MPK) and less painful knee (LPK).

Whole body, trunk and lower limb fat mass (FM%), strongly associated with KOA[13], were assessed using a Dual-energy X-ray Absorptiometry scanner-DXA (QDR 4500A, fan-beam densitometer, software version 8.21; Hologic, Waltham, USA)[13]. Anthropometric measurements (body mass, stature and waist and hip circumferences) were collected according to the International Society for the Advancement of Kinanthropometry (ISAK) procedures[37]. The intra-observer technical error for circumferences in the pilot study was 0.3. Body mass index was calculated as mass (measured in kilograms by a standard calibrated scale) divided by height squared (measured in meters).

STATISTICAL ANALYSIS

Descriptive analyses for the total sample were performed and the correlations between variables were provided using the Pearson Correlation Coefficient interpreted as strong (r≥0.7), moderate (0.5< r<0.7) and weak (0.3< r<0.5).

Regarding the underlying model assumptions, the independence of predictors, the normality and homoscedasticity were tested. In a first step, the variables with higher association or correlation with 6MWT and less correlated between themselves were selected as candidate predictors. The set of candidate predictors comprised the variables sex, age, KOOS Other Symptoms, BPI pain severity, BDI score, FRSTST, extension isokinetic peak torque (extPKTQ), BMI, waist-to-hip ratio and lower limb fat mass. In case of occurrence of bilateral KOA, measures of the most painful knee were used for statistical analyses. The stepwise method was used for the variable selection purpose, considering the criterion Probability of F-to-enter ≤.05 and Probability of F-to-remove>=.10.

Statistical analysis was performed using IBM SPSS Statistics 20.0 and MedCalc Statistical Software (MedCalc Software, Mariakerke, Belgium). Statistical significance was set at p<.05 (2-tailed) for all analyses.

RESULTS

Mean with standard deviation (SD), range and 95% confidence interval (CI) of main outcomes for the whole sample are given in Table I. The KOOS dimensions with poorest scores were Sport/rec and Quality of Life (QOL). The means of the BPI results, measured over the previous 24 hours, were below 5 on a 0-10 scale in each dimension, where the Pain Severity dimension registered a mean score for the worst pain of 4.5±2.5, for the least pain of 2.6±2.3, and the mean pain on the testing day was 2.9±2.1. Among the seven items of Pain Interference dimension, the lowest scores were found for walking ability (3.9±3.0) and normal working (3.9±2.5).

Concerning depression, although BDI scores showed a wide range, the 95% CI for the entire sample was [9.0,14.7], where the lower limit represents a minimal (0–13) and the upper limit a mild depression classification (14–19) (Table I).

The absolute value, of knee strength, of the most and less painful knee, corresponding to the relative results reported in Table I, were 86±34 Nm (PkTQ extMPK) and 105±41 Nm (PkTQ extLPK) for knee isokinetic extension, and 48±22 Nm (PkTQ flexMPK) and 54±22 Nm (PkTQ flexLPK) for knee isokinetic flexion. The absolute values for isometric knee extension strength were 131±47 Nm (MPK) and 154±58 Nm (LPK).

The mean waist–to-hip ratio across all participants was greater than 0.90 (Table I), classifying the sample as abdominal obesity, according to the World Health Organization[38]. With respect to BMI, the total fat mass

TABLE III. DESCRIPTIVE ANALYSIS OF MAIN OUTCOMES OF TOTAL SAMPLE

	n=48	Mean	SD	Range	95% CI
KOOS	Pain	47.7	16.5	10-89	[42.9,52.5]
	Symptoms	50.7	20.6	11-96	[44.7,56.7]
	Sport/rec	29.4	18.9	0-80	[23.9,34.8]
	ADL	53.9	20.5	24-99	[47.9,59.8]
	QOL	36.1	19.0	0-81	[30.6,41.6]
BPI	Severity	3.6	1.9	0-7.8	[3.0,4.1]
	Interference	3.3	2.3	0-7.3	[2.6,3.9]
BDI	Depression score	11.9	9.7	1-41	[9.0,14.7]
Physical function	6MWT (m)	549	81	330-698	[525,573]
	Handgrip (Kg)	29.6	9.8	10-50	[26.7,32.4]
	FRSTST (s)	11.0	2.7	6-18	[10.2,11.7]
	CSRMPK (cm)	-6.3	10.7	-29.5-14	[-9.4,-3.2]
Knee Strength tests (N-M/Kg)	Isometric PeakTorque MPK	1.44	0.47	0.54-2.59	[1.30,1.58]
	Isometric PeakTorque LPK	1.68	0.53	0.80-2.67	[1.53,1.83]
	Isokinetic PeakTorque extension MPK	0.94	0.34	0.22-1.82	[0.84,1.04]
	Isokinetic PeakTorque extensionLPK	1.15	0.39	0.48-2.05	[1.04,1.26]
	Isokinetic PeakTorque flexion MPK	0.52	0.22	0.09-1.18	[0.46,0.59]
	Isokinetic PeakTorque flexion LPK	0.60	0.23	0.12-1.07	[0.53,0.66]
Body composition	Weight (Kg)	90.8	13.9	67.4-127.8	[86.8,94.9]
	BMI (Kg/m2)	35.0	5.0	29.2-50.7	[33.6,36.4]
	Waist-to-Hip Ratio	0.9	0.1	0.7-1.1	[0.87,0.92]
	Total Fat Mass (%)	34.3	10.0	48.5-61.0	[37.4,42.1]
	Trunk Fat Mass (%)	39.9	6.8	21.2-50.4	[37.9,41.9]
IPAQ	Physical activity (MET /week)	871	714	0-3996	[664,1078]
	Sitting time (min/ week)	2258	808	810-4200	[2023,2492]

Abbreviations: KOOS, Knee injury and Osteoarthritis Outcome Score; BPI, Brief Pain Inventory; BDI, Beck Depression Inventory; 6MWT,Six Minutes Walking Test; FRSTST, Five Repetitions Sit to Stand Test; CSR, Chair Sit and Reach; MPK, Most Painful Knee; LPK,Less Painful Knee; BMI, Body Mass Index; IPAQ, International Physical Activity Questionnaire

and the trunk fat mass, as well as the mean results and CI reinforced the obesity classification of the majority of participants in this study.

The mean waist–to-hip ratio across all participants was greater than 0.90 (Table I), classifying the sample as abdominal obesity, according to the World Health Organization[38]. With respect to BMI, the total fat mass and the trunk fat mass, as well as the mean results and 95% CI reinforced the obesity classification of the majority of participants in this study.

In relation to the initial level of physical activity, although the weekly mean METS of physical activity reported by the total sample was classified as a moderate level, none of the individuals were participating in any structured or supervised exercise program and some participants indicated not having any type of physical activity equal to or greater than 10 min (low level). The reported sitting time per week corresponded to a mean of 5.4 hours per day, and some participants reported being in a seated position up to 10 hours per day.

PREDICTIVE MODELS

Prior to performing linear regression analyses to identify predictive factors of 6MWT, correlation analyses were conducted to gain a better understanding of how KOA symptoms and quality of life (measured by KOOS, BPI, BDI) and physical fitness outcomes (strength, flexibility and body composition) are associated with the 6MWT results. Pearson product-moment correlation coefficients are shown in Table II. Regarding KOOS dimensions, only the Sport/Rec showed no significant correlation with 6MWT, while Other Symptoms and ADL had a weak and moderate correlation, respectively. Furthermore, BPI pain scores had

TABLE II. PEARSON PRODUCT-MOMENT CORRELATIONS AND 2-TAILED P-VALUE BETWEEN 6MWT AND KOOS, BPI, BDI, IPAQ AND BODY COMPOSITION

	Variables	6MWT	
		R Pearson	p-value
KOOS	Pain	.352	.014*
	Symptoms	.528	<.001***
	ADL	.452	.001**
	Sport/Rec	.175	.233
	QOL	.358	.013*
BPI	Pain Severity	-.625	<.001***
	Pain Interference	-.524	<.001***
BDI	Depression	-.435	.002**
Physical Function	Handgrip test	.770	<.001***
	FRSTST	-.387	.007**
	CSRTMPK	.018	.902
Knee Strength tests	Isometric PeakTorque MPK	.505	<.001***
	Isometric PeakTorque LPK	.574	<.001***
	Isokinetic PeakTorque extension MPK	.513	<.001***
	Isokinetic PeakTorque extension LPK	.542	<.001***
	Isokinetic PeakTorque flexion MPK	.655	<.001***
	Isokinetic PeakTorque flexion LPK	.572	<.001***
Body composition and morphology	BMI	-.408	.004**
	Waist-to-Hip ratio	.399	.005**
	Total Fat Mass	-.526	<.001***
	Trunk Fat Mass	-.643	<.001***
	Lower limb Fat Mass MPK	-.760	<.001***
	Lower limb Fat Mass LPK	-.769	<.001***
IPAQ	Physical activity	.179	.223
	Sitting time	-.039	.795

Abbreviations: KOOS: Knee injury and Osteoarthritis Outcome Score; BPI: Brief Pain Inventory; BDI: Beck Depression Inventory; 6MWT,Six Minutes Walking Test; FRSTST: Five Repetitions Sit to Stand Test; CSR: Chair Sit and Reach; MPK: Most Painful Knee; LPK,Less Painful Knee; BMI: Body Mass Index; IPAQ: International Physical Activity Questionnaire.
*p<0.05, **p<0.01, ***p <0.001

a stronger correlation with 6MWT than the KOOS Pain dimension.

Mental health, represented by BDI, had a moderate and significant correlation (p<.001) with the 6MWT. Of the physical function and strength tests, the handgrip test was strongly correlated with the 6MWT while the isokinetic knee extension and flexion and isometric knee extension showed a moderate correlation with the 6MWT. With respect to body composition, lower limb fat mass was strongly and inversely correlated with the 6MWT. All other body composition variables had moderate correlations with 6MWT, while the waist-to-hip ratio had a weak and positive correlation. The 6MWT showed no significant correlation with the IPAQ outcomes. Predictors for the 6MWT in obese adults with KOA were found using stepwise linear regression (Table III).

The first model (F= 41.485; p<.001), explained 73% of the variance in 6MWT. Despite having tested all variables, only the %Fat mass of the most painful knee, BPI pain severity (BPI severity) and FRSTST remained significant (Table III). The equation of model 1 is as follows:

6MWT (m) = 849.676 – (4.883↔Lower Limb FM%) – (17.270↔BPI Sev) – (5.606 ↔ FRSTT)

TABLE III. MULTIPLE REGRESSION MODELS OF PREDICTIVE VARIABLES FOR 6MWT

Model	Adj. R2	F	Predictor Variables	B	SE B	β	p
Model 1	.725	41.49					
			Constant		849.68	32.38	<.001***
			%FM_ MPK	-4.39	0.73	-.537	<.001***
			BPI pain severity	-17.27	3.58	-.407	<.001***
			FRSTST	-5.61	2.51	-.182	.030*
Model 2	.649	29.99					
			Constant	649.81	36.16		<.001***
			Sex	92.37	18.58	.510	<.001***
			BPI pain severity	-14.05	4.20	-.336	.002**
			FRSTST	-6.88	2.71	-.225	.015*
Model 3	.607	37.26					
			Constant	572.29	20.48		<.001***
			Sex	101.64	19.29	.561	<.001***
			BPI pain severity	-14.16	4.45	-.339	.003**

Abbreviations: FM: fat mass; BPI: Brief Pain Inventory; 6MWT: ix Minutes Walking Test; FRSTST: Five Repetitions Sit to Stand Test; CSR: Chair Sit and Reach; MPK: Most Painful Knee; LPK: Less Painful Knee.
*p<.05: **p<.01: ***p<.001

The second model (Table III), which did not consider the outcomes from the scanner and dynamometer (fat mass and isokinetic strength), was significant and explained 65% of the variance of 6MWT (F= 29.989; p<.001), revealing Sex, BPI severity and FRSTST as a predictive factors. The equation of second model is as follow:

6MWT (m) = 649.797 + (92.367 ↔ Sex) – (14.048 ↔ BPI Sev) – (6.878 ↔ FRSTST)

sex = 1, for male and sex = 0, for female.

The third model was tested considering the same candidate predictors as those used in model 2, but without inclusion of the lower limb strength assessed by FRSTST, a physical test that would not be convenient to perform in a clinical context. The third model was also significant (F= 37.262; p<.001) and explained 61% of the variance. In this model two variables predicted 6MWT, Sex and BPI severity. The equation of this third model is as follow:

6MWT (m) = 572.292 + (101.641↔Sex) – (14.162↔BPI Severity)

sex = 1 for male and sex = 0, for female.

DISCUSSION

The difficulty in finding other studies that applied a broad battery of tests with similar sample population, compromised the development of this discussion. However this reinforce the pertinence of this study. The analysis of the three models presented (Table III) provides important information regarding the walking capacity in obese individuals with KOA. In addition to the walking distance of obese individuals being significantly smaller compared to lean individuals[20, 23] there is an association with the functional limitations imposed by KOA symptoms, leading to the adoption of different gait patterns to ensure maintenance of balance and to avoid mechanical pain, thereby compromising gait efficacy[20] and decreasing gait speed.

Capodaglio and coworkers[23] showed that the 6MWT in obese individuals was significantly correlated with age, gender and BMI, and proposed a reference equation where these variables could explain 48% of the walked distance: 6MWTm= 894.2177 – [2.0700 ↔ age (yrs)] – (51.4489 ↔ gender) – [5.1663 ↔ BMI (Kg/m^2)]. Our results are in accordance with this study and show a significant correlation between 6MWT and body composition, body morphology and OA symptoms. However, the model of Capodaglio[23] included age as a predictive factor for 6MWT and in our models, age was not significant, possibly due the fact that our sample included adults rather than older persons. This suggests that the effects of aging lost importance in adults sample, where other variables became more important. The advantage of using data from the present study to evaluate the predictors for 6MWT was the ability to test models with a broad variety of dimensions, from physical fitness and mental health to KOA symptoms and health-related quality of life.

Regarding knee strength, deficits in quadriceps activation can moderate the relationship between knee strength and physical function,[39] and this is considered in the literature as a significant predictor for the 6MWT performance[40]. Curiously, despite the correlations that were found between strength tests and 6MWT, the FRSTST remained significant and, instead of the knee strength tests, was included in Models 1 and 2. A possible explanation is that walking long distances require more resistance than maximal strength. Therefore, although both maximal isometric and isokinetic strength (extension and flexion) were associated with walking distance, only the functional strength obtained by the FRSTST was a predictor of walking ability in models 1 and 2. Also, participants did not reveal considerable knee muscle weakness, and this could explain the observation that knee strength outcomes did not show relevant results in the three models presented. In addition, we did not perform eccentric strength tests, an important component for physical function activities.

Although the variables selected for testing are becoming increasingly simple and accessible, the knee pain obtained from BPI severity is a relevant predictor for the 6MWT in each of the three models. It was expected that the fat mass included in Model 1 would be substituted with the BMI when the variables from DXA scanner became unavailable for Model 2 and 3, but this was not observed, and Models 2 and 3 did not reveal BMI or other body morphology as predictors for 6MWT.

The advantage of this study in comparison with others was the possibility to test objective measures in combination with sex, age and self-reported outcomes from questionnaires. The analysis of predictors for the 6MWT indicated that knee pain is a limitation for obese individuals initiating an exercise program that includes weight bearing activities, and should be considered at the onset. Although it seems obvious, the importance of a frequent knee pain assessment should be reinforced for exercise professionals who works with obese individuals in weight control programs, in order to guarantee an adequate exercise prescription. Exercise mode and volume should be adapted according knee pain intensity, otherwise it becomes a constraint for meeting exercise program goals, compromising the adherence of participants.

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