SciForschen
Open HUB for Scientific Research

(ISSN 2380-5528)

Obesity: Open Access

Research article Volume: 1.3 Open Access

Assessment of Knee Pain in Obese and Non-Obese Individuals Diagnosed with Osteoarthritis of the Knee Before and After Performance-Based Tests: A Pilot Study

Kamary Coriolano[1]*, Alice Aiken[1], Caroline Pukall[2] and Mark Harrison[3]

[1]*School of Rehabilitation Therapy, Queens University, Canada*
[2]*Department of Psychology, Queens University, Canada*
[3]*Department of Orthopaedic Surgery, Queens University, Canada*

***Corresponding author:** Kamary Coriolano, School of Rehabilitation Therapy, Queens University, Canada, **E-mail:** kamary.coriolano@gmail.com

Received date: 15 July 2015; **Accepted date:** 5 Nov 2015; **Published date:** 10 Nov 2015.

Citation: Coriolano K, Aiken A, Pukall C, Harrison M (2015) Assessment of Knee Pain in Obese and Non-Obese Individuals Diagnosed with Osteoarthritis of the Knee Before and After Performance-Based Tests: A Pilot Study. Obes Open Access 1(3): doi http://dx.doi.org/10.16966/2380-5528.111

Copyright: © 2015 Coriolano K, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: 1) To examine whether self-reported pain, measured with the Western Ontario McMaster University Osteoarthritis Index pain subscale and Visual Analog Scale, of individuals diagnosed with knee Osteoarthritis would change after performance-based tests were completed; irrespective of their body weight and Body Mass Index. 2) To assess whether self-reported pain before and after performance-based tests differs between obese and non-obese individuals and whether both VAS and WOMAC scales of pain would demonstrate similar changes from before to after the completion of performance-based tests in obese and non-obese individuals with knee OA. 3) To observe whether depressive symptoms and BMI explain the variance of self-reported pain before and after performance based tests.

Methods: This pilot study included 31 participants diagnosed with radiographic knee osteoarthritis by an orthopedic surgeon using the Kellgren-Lawrence Scale. The sample was divided in two groups of obese individuals with knee Osteoarthritis and non-obese individuals with knee osteoarthritis. Two self-reported measures, the Western Ontario McMaster University Osteoarthritis Index and Visual Analog Scale assessed knee pain before and after performance-based tests in these two groups of individuals. Depressive symptom was obtained with Back depression questionnaire II.

Results: The Visual Analog Scale ratings showed a significant increase in pain in both groups, but the Western Ontario McMaster University Osteoarthritis Index pain subscale only captured a significant increase in the obese osteoarthritis group. A significant proportion of variance in pain before and after functional activities was explained by depressive symptoms and obesity, with higher levels of depression and obesity predicting worse reports of pain.

Conclusion: The Visual Analog Scale pain rating may be a better tool for assessing knee pain of obese and non-obese individuals diagnosed with knee osteoarthritis. Furthermore, symptoms of depression might predict increase in knee pain and disability in obese individuals.

Keywords: Obesity; Knee pain; Osteoarthritis; Depression

Introduction

Osteoarthritis (OA) is a significant cause of joint pain and disability in elderly individuals [1] and joint pain is unquestionably one of the most debilitating aspects of OA [2,3]. OA is heterogeneous and characterized by progressive cartilage loss, deterioration of subchondral bone, osteophyte formation and synovial inflammation, resulting in joint pain. Whilst the disease progression may cause pain and increase disability, approximately 50% of persons with structural change consistent with OA are asymptomatic [4]. Therefore, the nature of knee pain and its causes seem to vary among individuals diagnosed with knee OA [1,5].

In general, radiological information is used during a clinical consultation to identify the severity level of knee OA [4,6]. However, the confirmation of radiological OA is not necessarily an indication of symptomatic knee OA [7]. Symptomatic knee OA, which is clinically more important, requires consistent limitation in activities of daily living and presence of joint pain on most of the days of the previous month [4,8]. Some clinical and epidemiological studies have reported several cases of people with structural change, based on radiological information, who indicate mild or no pain [1,4,9], whereas others with higher levels of joint pain may not have severe radiographic indices of OA [10]. Therefore, radiographic imaging of the knee OA seems to be an invaluable tool for the assessment and diagnosis of disease severity [11], but not joint pain. Joint pain due to knee OA is interpreted as a unique and subjective experience lived by the individual [12]; therefore, self-reported tools developed to assess pain are important for both research and clinical use [13].

The Western Ontario McMaster University Osteoarthritis Index (WOMAC) is a validated questionnaire used to assess self-reported disability in individuals with knee OA [14,15]. It has been used extensively in clinical trials with individuals with knee OA [16,17]. Although the WOMAC also yields a total score in addition to the subscale scores, subscale scores have been reported in the literature independently of the total score [18]. The WOMAC pain subscale has been consistently used to assess pain, and change in pain—particularly at its chronic stage [4]- in individuals with knee OA [19]. However, self-reported pain may show different results if captured at the moment of its occurrence [20]. Pain intensity can also be assessed using a visual analog scale (VAS) during a clinical evaluation or right after a functional test that triggers pain [21,22]. The VAS is a validated pain measurement tool that has been used to assess pain levels of individuals with knee OA [13]. Given the use of both of these measures in knee OA [22] and that they may capture the experience of pain differently [20,23], it may be appropriate to use both generic (VAS) and specific (WOMAC) tools [22] and observe whether one measure would capture the experience of pain better than the other.

Copyright: © 2015 Coriolano K, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Moreover, considering the current increase of obese individuals in our population [24], obesity may have a substantial effect on self-reported pain, particularly for those diagnosed with knee OA. Excessive body weight is an important factor that contributes to increased pain in individuals with knee OA [25]. A recent study suggested that for every kilogram gained, WOMAC pain scores went up by 1.9 points on a 500-point scale, the WOMAC stiffness scores worsened by 1.4 points (on a 200 point scale), and the WOMAC function scores increased by 6.1 points (on a 1,700 point scale) [2]. It is likely that obese and non-obese individuals with symptomatic knee OA are somehow exposed to similar daily physical tasks, such as stair climbing, walking, and standing from a sitting position; however, it is not known whether self-reported pain experienced by obese individual with knee OA before and after performance-based tests would be similar to those who are also diagnosed with knee OA, but are not obese.

Another factor that seems to influence self-reported pain is depressive symptoms [26]. A previous study [27] that observed the relationship between depressive symptoms and knee pain indicated that the presence of depressive symptoms limits the ability to associate knee pain complaints to radiographic OA. In other words, the correlation between knee pain and OA severity was likely weakened by depressive symptoms [27]. Other studies have emphasized the psychological and social burdens of knee OA, caused by pain and disability [3,28].

The incidence of depressive symptoms seems to be a common issue in individuals diagnosed with chronic knee OA [3,26]. Likewise, obesity is a primary modifiable risk factor for knee OA [25] and is closely linked to depressive symptoms [29]. However, a few studies have indicated that both Body Mass Index (BMI) and depressive symptoms are associated with knee pain [30].

This is a pilot study, all analyses conducted for this paper were primary analyses and its objectives were threefold: 1) To examine whether self-reported pain, measured with the WOMAC pain subscale and VAS, of individuals diagnosed with knee OA would change after performance-based tests were completed; irrespective of their weight and BMI. 2) To assess whether self-reported pain before and after performance-based tests differs between obese and non-obese individuals and whether both VAS and WOMAC scales of pain would demonstrate similar changes from before to after the completion of performance-based tests in obese and non-obese individuals with knee OA. 3) To observe whether depressive symptoms and BMI explain the variance of self-reported pain before and after performance based tests.

Methods

Ethical approval was obtained from the Health Science Research Ethics Board (HSREB) of Queen's University. Patients were recruited from the orthopedic surgical case load of one participating orthopedic surgeon at Kingston General Hospital, Kingston, Ontario, Canada. Recruitment and data collection started in May, 2013 and was completed in October 2013. Patients were identified as potential participants for the study by the surgeon during an initial consultation. Those who showed moderate to severe radiological knee OA using the Kellgren-Lawrence Scale [31] and who were symptomatic (knee pain on most of the days of the previous month) [4] were subsequently contacted by a research associate who described the study procedures and invited them to participate in the study once informed consent was obtained.

This pilot study population was a sample of convenience and 50 patients were invited to participate but only 31 were eligible to participate. Of the 19 participants, 12 could not participate because they were not eligible according to our exclusion criteria. The other 7 participants were from rural areas or from further locations outside of Kingston, therefore, transportation was an issue and these 7 individuals could not participate.

All 31 participants between the ages of 50 and 80 years with knee OA were able to tolerate moderate activity for 60 to 90 minutes. Additionally, they were free from severe comorbidities that would prevent them from participating in the study, such as unstable angina and/or heart disease, uncontrolled blood pressure (systolic pressure >140 mmHg, diastolic pressure >90 mmHg) and non-knee OA related mobility restrictions (neurological and musculoskeletal). All 31 participants were eligible for the study and they were scheduled for an initial assessment conducted in a university laboratory.

Upon arrival at the laboratory, participants were given a letter of information and consent form. If they agreed to participate, their demographic data including height and weight was obtained. Depression was assessed using the Beck Depression Inventory-II (BDI-II). Pain was assessed before (Time 1) and after (Time 2) performance-based tests (i.e., 6 Minute Walk Test [6MWT], Timed Up and Go [TUG] test, stair climbing test) using the Western Ontario McMaster University Index Osteoarthritis for pain (WOMAC pain) and a VAS.

Outcome measures

Self-report measures: Pain was assessed before and after performance-based tests using two measurements: The first was a VAS. The VAS is a measurement tool that indicates the amount of a pain an individual experiences measured across a continuum of values [32]. The scoring range was measured from 0 (no pain) to 10 (highest pain level). The participants were asked to grade the amount of pain they experienced by indicating it on a horizontal line between 0 and 10. The VAS was used to record participants' perceived level of pain before and after all performed-based tests were completed. The VAS has been validated for pain [33] and has been used in previous studies of joint replacement patients [32,34]. The second pain measurement was the Likert scale version of the WOMAC subscale for pain, which asks about pain experienced over the past 72 hours [2]. This subscale consists of 5 items on a scale of 0 (none) to 4 (extreme) with a total score ranging from 0 to 20. Higher scores indicate greater levels of pain.

Baseline covariates variables

The BDI-II is a commonly used measure to assess depressive symptoms, and the latest revised version from the original BDI format [35] is a 21-item test presented in multiple choice format, which measures the presence and degree of depression in adults [35]. The BDI-II is widely used as a screening instrument of depression mood for clinical research [36]. The BDI-II evaluates 21 symptoms of depression, 15 of which cover emotions, four cover behavioural changes, and six cover somatic symptoms. The items cover sadness, pessimism, past failure, self-dislike, self-criticism, suicidal thoughts or wishes, crying, agitation, loss of interest, indecisiveness, worthlessness, loss of energy, changes in sleeping patterns, irritability, changes in appetite, difficulty concentrating, tiredness or fatigue, and loss of interest in sex [37]. Each answer is scored on a scale of 0–3. A total score of 0–9 indicates no depression, 10–18 indicates mild-moderate depression, 19–29 indicates moderate-severe depression and 30–63 indicates severe depression [37].

Imaging examination: The Kellgren and Lawrence (KL) radiographic scale method of radiographic examination [31] was used to score the severity of knee OA. KL is the earliest and by far the most commonly used global scale that gives an overall score of OA severity ranging from zero to four [31,38]. The confirmation of several features were graded as an evidence of OA: grade 0, no radiographic findings of OA; grade 1, possible osteophytes and doubtful narrowing of joint space; grade 2, definite osteophytes and narrowing of joint space; grade 3, moderate multiple osteophytes and definite narrowing of joint space; and grade 4, large osteophytes and marked narrowing of joint space [31]. Both

tibiofemoral compartments of the knee were assessed using a standard set of radiographs for reference [31].

Performance-based tests and physiological test: Three performance-based tests of physical functioning and one physiological test were obtained during a single testing session. The functional tests consisted of the Six Minute Walking Test (6MWT), Timed Up and Go Test (TUG), and the modified Margaria stair climbing test [39]. Peak of oxygen consumption (VO_2 peak), based on a nomogram previously used [40,41] for calculation of upper body aerobic power with an arm ergometer, was the physiological test used.

The 6MWT is generally conducted in an enclosed, quiet corridor on a 25-meter track delineated by two lines marked on the floor [42]. Patients were instructed to walk from one line to the other, covering as much ground as possible in six minutes. Individuals were told that they could rest if they became too short of breath or tired, but to continue walking when they were able to do so. To calculate the walking distance, a metre wheel was used to measure the additional steps of any incomplete lap (in meters). The procedure for the TUG requires documenting the time, in seconds, that an individual takes to rise from a standard armchair, walk 3 meters, turn, walk back to the chair and sit down [43]. The participants were allowed to use any assistive devices that they would normally use for walking, to make them feel safe and comfortable during the test. Prior to testing, the subjects were warned that there would be two test trials and then they were instructed about the basic sequence of the test as follows: "When I say, 'go', you will stand up pushing from the arm of the chair, walk to the mark (line) on the floor, turn around, walk back to the chair and sit down. I will be timing you using a stopwatch." The subjects were allowed to rest, as much as they needed, between each trial. The average of these two trials was used as the final score. A shorter time taken to complete the task indicates a lower risk for falling and greater functional status.

Lower limb mechanical power output was assessed by a stair climbing test. This test is a modified version from the original test proposed by Margaria et al. [44] and has been previously validated in obese individuals [45,46]. Participants were asked to climb one step at time, at the highest speed possible. Even though they were allowed to use railings, they were encouraged to use them only if they felt it was extremely necessary. A staircase of 13 steps covering a total vertical distance of 2.0 meters was used. The final climbing time of the participants was obtained with a stop watch. The average mechanical power (W) can be calculated by multiplying body mass (BM), gravity (g) and vertical distance (h) and dividing its outcome by time (t).

The arm ergometry test was used to predict the VO_2 peak in participants with knee OA. The participants were asked to pedal at a frequency of 70 revolutions per minute (rpm) against a constant workload of 21 Watts (125 kg/min) for females and 42 Watts (250 kg/min) for males. The workload was adjusted and maintained using the weights from the arm ergometer [41,47]. To predict VO_2 peak using an arm cycling submaximal test, the subjects should achieve a continuous steady state heart rate either equal to or above 110 beats per minute (bpm) during the last 30 seconds of submaximal test [41]. Heart rate was monitored constantly using a chest strap heart rate monitor and a digital watch set (Polar Electro, Inc Woodbury, NY) during the test. The test's length of time was four minutes and pulse rate was recorded every 10 seconds during the last 30 seconds, between the third and fourth minutes. If the difference between the lowest and the highest pulse rate, recorded in the last 30 seconds of exercising, did not exceed 5 bpm, a steady state heart rate was considered to be present [40,41]. The average HR, from the steady state, was used to find a corresponding VO_2 peak (L.min) on the nomogram. Further to that, VO_2 peak was calculated in ml/kg/min based on the nomogram's equation: *VO_2 peak (L.min) × 1000 / Body Weight (BW)*. All of the participants reached at least 110 bpm or more; consequently, a new test was not needed. However, if their heart rates had not reached at least 110 bpm during the last 30 seconds of testing, the workload would have been increased by 21 W (125 kg/min) and a new test would have been initiated.

Data analysis – statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21 (SPSS 21) and Microsoft Excel 2010. The alpha (α) level was set at $p<0.05$. Results are presented as mean ± standard deviation (SD) unless otherwise specified. Normality test was used before statistical analysis to assure whether the age distribution of the group and their level of pain for VAS and WOMAC prior performance based tests were normally distributed. Participants' age and pain levels before performance based tests were normally distributed as demonstrated by Shapiro-Wilk test. Furthermore, homogeneity tests for variance and multicollinearity test were performed were carried out to assure that groups of data had a similar variance and that there was no evidence of strong multicollinearity among the independent variables. In order to test our first hypothesis that self-reported pain would be higher after performance-based tests, two paired t-tests were conducted. In order to test our second hypothesis that obese individuals with knee OA would score higher on pain measures than non-obese individuals, and that the VAS pain, rather than the WOMAC pain, would capture change in pain from Time 1 to Time 2 for both groups of individuals with knee OA, we conducted a repeated measures ANOVA that examined whether the obese OA group had higher scores on the WOMAC pain subscale and the VAS as compared to the non-obese OA group. In order to test our third hypothesis that the proportion of variance of self-reported pain, explained by depressive symptoms and BMI would increase after performance-based tests, we conducted four stepwise regression analyses *before* (Time 1) and *after* (Time 2) the completion of performance-based tests.

Results

Manipulation checks and group composition analyses

Of the 31 participants diagnosed with knee OA, 15 were considered obese (BMI ≥ 30 kg/m^2) and 16 were non-obese. Specifically, of the 16 non-obese participants, 9 were overweight (BMI=25–29.9 kg/m^2) and 7 were healthy weight (BMI=18.5–24.9 kg/m^2). A one-way ANOVA between overweight and healthy weight participants with knee OA demonstrated that they did not differ significantly on any demographic or main variables of interest, including radiographic examination findings (p's>.05). Likewise, a chi-square analysis did not reveal any significant difference in gender (p>.05) between the overweight and healthy weight groups or when compared between healthy weight, overweight and obese individuals (p>.05). Therefore, we combined the overweight and healthy weight groups into one group: the non-obese OA group. Radiographic examination was obtained from all 31 participants diagnosed with knee OA. A one-way ANOVA between the obese OA and non-obese OA groups was conducted to examine whether knee OA severity was significantly different between these two groups. The analysis indicated no significant differences between-groups on knee OA severity at baseline (p>.05) (Table 1).

Further analyses between obese OA and non-obese OA groups indicated that body weight ($F(1, 29)=24.4$; $p \leq .0001$) and BMI ($F(1, 29)=28.8$; $p \leq .0001$) and that BDI-II ($F(1, 29) = 38.6$; $p \leq .0001$) were significantly different between groups (Table 1). The three performance-based tests (stair climbing, 6MWT, and TUG) and the VO_2 peak (physiological test) were also compared between obese OA and non-obese OA groups. Analyses indicated that results from the stairs climbing test ($F(1, 29)=21.3$; $p \leq .0001$), 6MWT ($F(1, 29)=30.5$; $p \leq .0001$), TUG ($F(1, 29)=18.4$; $p \leq .0001$) and the VO_2 peak ($F(1, 29)=30.5$; $p \leq .0001$) were significantly different between groups (Table 1).

Sub-groups		Gender		Pearson Chi-Square		
BMI levels		Man	Woman	Value	df	p-value
Non- obese OA (Healthy weight Overweight)		8 (50%)	8 (50%)	3.32[a]	2	0.19
Obese		3 (20%)	12 (80%)			
Baseline information/Group		Mean (SD)	Minimum	Maximum	F	P-value
Age	Obese OA	65.9 (8.3)	50	80	3.3	0.80
	Non-obese OA	70.6 (5.9)	62	81		
BMI	Obese OA	39.0 (8.4)	29.3	62.1	24.4	0.000
	Non-obese OA	27.0 (2.6)	23.4	28.4		
Body Weight	Obese OA	104.3 (19)	70	143.7	28.8	0.000
	Non-obese OA	76.8 (11.2)	62	82		
X-Ray (KL)	Obese OA	3.3 (0.97)	2.0	4.0	.056	0.48
	Non-obese OA	3.3 (0.8)	2.0	4.0		
BDI-II	Obese OA	18 (5.5)	11	27	38.6	0.000
	Non-obese OA	6.7 (4.5)	0	15		
Stair Climbing	Obese OA	171.5 (66.1)	79.95	344.00	30.5	0.000
	Non-obese OA	328 (114.6)	170.00	579.75		
VO_2 Peak	Obese OA	15.6 (5.3)	8.36	28.47	18.4	0.000
	Non-obese OA	27.6 (6.6)	14.28	36.56		
TUG	Obese OA	11.0 (2.8)	6.65	18.94	21.3	0.000
	Non-obese OA	7.7 (1.2)	5.17	9.32		
6 Minute Walk	Obese OA	270.2 (109.4)	75.0	425.0	30.5	0.000
	Non-obese OA	447.7 (65.6)	325.0	555.0		

Table 1: (SD) Standard deviation; x –Ray (Kellgren – Lawrence or KL); Age (yrs.); BMI (kg/m^2); Body Weight (Kg); BDI-II: Beck Depression Inventory – Higher score=more depression; Stair Climbing - Lower limb mechanical power- Watts (W); Six Minute Walking Test (6MWT) – meters (m); Timed Up and Go Test (TUG) – seconds (s); Peak of oxygen consumption (VO_2 peak) – (ml.kg/min). Obese OA (N=15) and Non-obese OA (N=16) All significant values between groups were (p<0.05). Pearson Chi-square value was 3.32a. *a=indicates that at least 3 cells (50.0%) have expected count less than or equal to 5. The minimum expected count is 2.48*. Results were under the expected count and therefore, no significant different was observe between man and woman at different levels of BMI.

The paired t-test examined whether the WOMAC pain subscale score and the VAS ratings of all 31 participants changed from before (Time 1) to after (Time 2) performance-based tests (Figure 1). Results indicated that the WOMAC pain subscale score changed significantly (t (30)=-2.68; p=.012) by increasing from Time 1 (mean=8.3, SD=3.2) to Time 2 (mean=9.7, SD=4.6). The VAS ratings also increased significantly (t (30)=-9.21; p ≤ .0001) from Time 1 (mean=2.9, SD=1.5) to Time 2 (mean=4.0, SD=1.4) (Figure 1).

In order to further assess the distribution of pain before and after performance based tests of all 31 participants two boxplots, one for the VAS pain scores and another one for the WOMAC pains scores, were developed (Figures 2 and 3). The graphics illustrate that participants' pain scores were well behaved and there were no ceiling effects observed from before and after performance tests. The top bars or whiskers are the top 25% of all pain scores and the lower bars the bottom 25%. The actual shaded portion of the box represents the interquartile range or the middle 50% of all pain scores while the middle line represents the median score.

The second set of repeated measures ANOVA examined whether the obese OA group had higher scores on the WOMAC pain subscale (Figure 4) and the VAS (Figure 5) as compared to the non-obese OA group from before (Time 1) to after (Time 2) performance-based tests. The results indicated that the WOMAC pain score (F (1, 29)=24; p<.0001) was significantly different between groups, with the obese OA group demonstrating higher WOMAC pain subscale scores (mean=11.5) as compared with the non-obese OA group (mean WOMAC pain subscale score=6.6). The WOMAC mean difference = 4.8, standard error (SE)=.997 and 95% CI [2.83, 6.91]. The within-groups factor examined whether the mean scores of each group changed after performance-based tests were completed and it indicated that only the obese OA group significantly increased from Time 1 to Time 2 when pain was measured with the WOMAC pain subscale (means=9.8 and 13.3; F (1, 29)=12; p=.002).

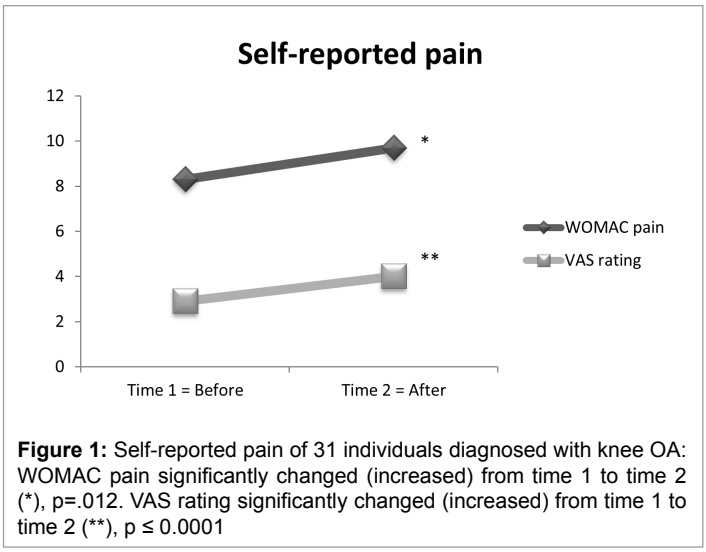

Figure 1: Self-reported pain of 31 individuals diagnosed with knee OA: WOMAC pain significantly changed (increased) from time 1 to time 2 (*), p=.012. VAS rating significantly changed (increased) from time 1 to time 2 (**), p ≤ 0.0001

No change was observed on the WOMAC pain subscale score for the non-obese OA group (Figure 4).

With regard to VAS, results indicated that the VAS pain (F (1, 29)=29; p<.0001) was significantly different between groups, with the obese OA group demonstrating higher VAS ratings (mean=4.5) as compared with the non-obese OA group (mean VAS rating=2.5). The VAS mean difference=2.0, SE=.374 and 95% CI [1.24, 2.77]. The within-group factor for the VAS ratings indicated that the obese OA group (means=3.9 and 5.1; F (1, 14)=76; p<.0001) and the non-obese OA group (means=1.9 and 3.1; F (1, 15)=28; p<.0001) significantly increased after performance-based tests were completed (Figure 5).

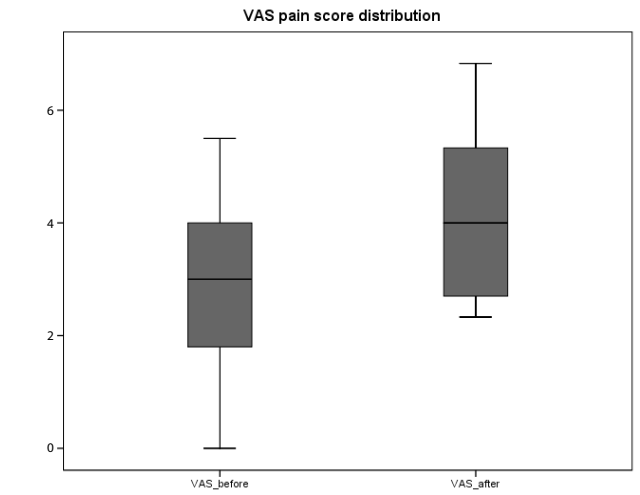

Figure 2: Self-reported pain of 31 individuals diagnosed with knee OA: VAS pain before performance based tests showed the lower / first quartile or Q1 (25% of population are below this value)=1.8, the median / second quartile or Q2 (50% of population are below this value = median of samples)=3.0 and upper / third quartile or Q3 (75% of population are below this value)=4.0. The top 25% score was 5.5 while the bottom 25% 0.0. VAS pain after performance tests showed Q1=2.6, Q2=4.0 and Q3=5.3. The top 25% score was 6.8 and the bottom 25% score was 2.3.

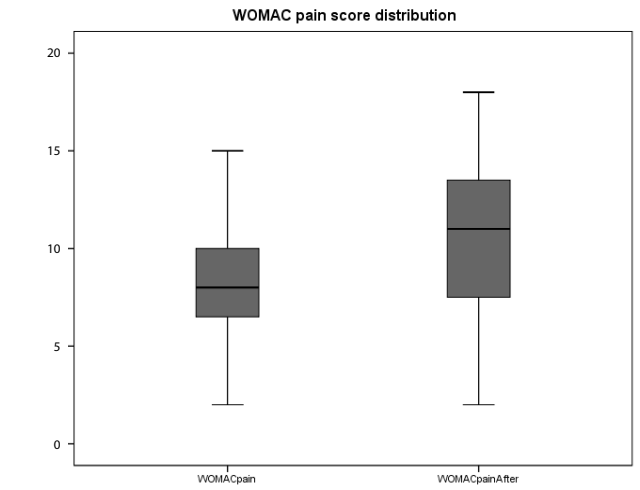

Figure 3: Self-reported pain of 31 individuals diagnosed with knee OA: WOMAC pain before performance based tests showed Q1=6.0, Q2=8.0 and Q3=10.0. The top 25% score was 15.0 while the bottom 25% 2.0. WOMAC pain after performance tests showed Q1=7.0, Q2=11.0 and Q3=14.0. The top 25% score was 18.0 and the bottom 25% score was 2.0.

A four stepwise regression analyses was performed *before* (Time 1) and *after* (Time 2) the completion of performance-based tests. Prior to the analyses, we ensured that there was no evidence of strong multicollinearity among the independent variables (all Pearson correlation coefficients (r) were <0.80) [48]. At Time 1, the stepwise regression analysis indicated that depressive symptoms alone explained a significant proportion of variance of the WOMAC pain, R^2=27%, F (1, 29)=10.8; p=.003. Likewise, at Time 2 depressive symptoms alone also explained a significant proportion of variance of the WOMAC pain, R^2=35.7%, F (1, 29)=16; p<.0001; however, a higher proportion of variance explained was observed at Time 2 compared to Time 1. For the VAS ratings, the stepwise regression analysis at Time 1 indicated that depressive symptoms and BMI explained

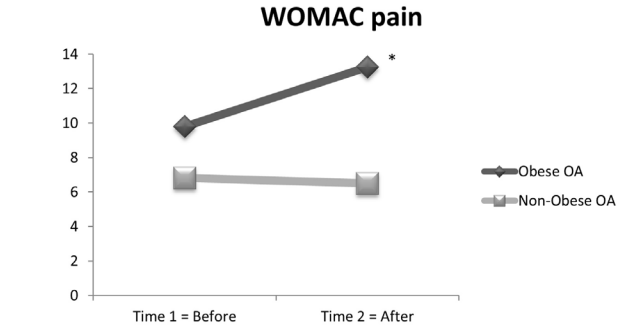

Figure 4: WOMAC pain: 15 obese OA and 16 non-obese OA: Between groups: the obese OA group demonstrated significantly higher WOMAC pain than the non-obese OA group p ≤ 0.0001. Within groups: WOMAC pain significantly change from time 1 to time 2, but only in the obese OA group; (*), p=.002

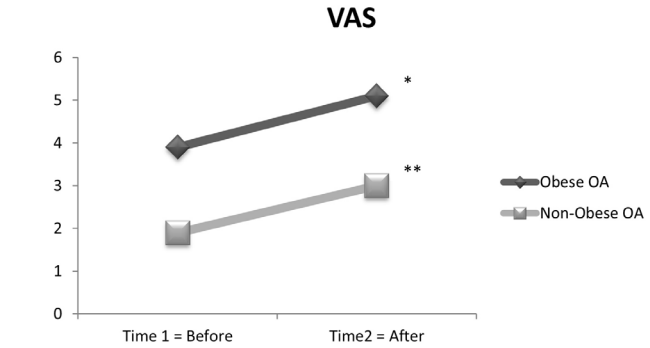

Figure 5: VAS: 15 obese OA and 16 non-obese OA: Between groups: the obese OA group demonstrated significantly higher VAS than the non-obese OA group p ≤ 0.0001. Within group: VAS significantly change from time 1 to time 2 for both groups; obese OA (*), p ≤ 0.0001 and non-obese OA (**), p ≤ 0.0001.

a significant proportion of variance of the VAS ratings, R^2=46.7%, F (1, 29)=12.3; p<.0001, and that at Time 2, both depressive symptoms and BMI also explained a significant proportion of variance of the VAS ratings, R^2=52.6%, F (1, 29)=15.5; p<.0001, with a higher proportion of variance explained observed at Time 2 compared to Time 1. Findings from the WOMAC pain subscale suggested that depressive symptoms alone explained a significant proportion of variance of the WOMAC pain subscale scores, and that after performance-based tests the proportion of variance increased from 27% to 35.7%. Consequently depressive symptoms alone accounted for 35.7% of variance of the WOMAC pain subscale score after completion of performance-based tests. On the other hand, the results from the VAS ratings indicated that both depressive symptoms and BMI explained a significant proportion of variance of the VAS ratings, and that after performance-based tests the proportion of variance increased from 46.7% to 52.6%. Therefore, depressive symptoms and BMI accounted for 52.6% of variance of VAS ratings after completion of performance-based tests.

Discussion

Results demonstrated that both self-report pain scores, measured with the WOMAC pain subscale and VAS ratings, and were significantly higher *after* as compared to before the completion of performance-based tests. This pattern of results suggests that both self-report pain measurements, when possible, should be administered to individuals with OA *after*

performance-based tests (Figure 1) because it captures participants' experience of pain in real time. When the sample was divided into obese and non-obese individuals with OA, we observed that the obese group demonstrated significantly higher levels of self-reported pain. The VAS ratings captured a significant increase in pain in both groups from Time 1 to Time 2. The WOMAC pain subscale, on the other hand, only captured change in the obese OA group after completion of performance-based tests. Further analyses indicated that depressive symptoms and BMI explained a significant proportion of variance in VAS ratings, but that depressive symptoms alone explained a significant proportion of variance in the WOMAC pain subscale scores. Moreover, the proportion of variance explained by both self-report pain measurements was higher after completion of performance-based tests.

Increase in self-reported pain after performance-based tests in individuals with knee OA

Previous studies have indicated that performance-based tests are highly associated with knee pain and therefore performance-based tests may influence self-reported pain ratings [21,49]. Self-reported pain ratings can be obtained at rest, during functional tests or immediately after a test [13,21]. However, we suggest that in general, individuals diagnosed with chronic symptomatic knee OA will likely not report pain levels as accurately when recalling the pain, as compared to when reporting on pain levels in real-time; that is, when they find themselves exposed to a situation in which pain is triggered, as observed in our results.

Even though the WOMAC pain score and the VAS ratings are reliable tools to measure pain in individuals with knee OA [22], the way in which the pain experience is captured by each measurement may influence its final outcome [20]. The WOMAC is generally obtained before or a few minutes after the completion of performance-based tests [50]. While the VAS rating can be obtained before performance-based tests, it is typically obtained during or right after performance-based tests in clinical assessments [21,22]. Taking into consideration that knee pain during a performance-based test could be a "momentary physical experience," it seems logical to capture the experience of pain when it occurs, as measured with the VAS rating, rather than few minutes later (as measured with the WOMAC pain subscale), when some of that physical experience had receded. However, our results indicated that scores on both self-reported pain measures significantly increased after performance-based tests. These findings suggest that capturing knee pain immediately after performance-based tests with the VAS rating, or a few minutes later with the WOMAC pain subscale did not affect the final outcome (Figure 1). Nevertheless, we suggest that both self-report pain measures, when possible, should be administered to individuals with OA after performance-based tests as they capture participants' experience of pain in real time.

Change in self-reported pain in obese and non-obese individuals after performance-based tests

When examining our full sample of 31 individuals with knee OA, we observed that after performance-based tests both the WOMAC pain subscale score and the VAS rating significantly increased. However, when we compared our sample between obese and non-obese individuals with knee OA, differences emerged. First, results indicated that obese individuals with knee OA scored higher on both the WOMAC pain subscale and VAS measures than non-obese individuals. Second, findings suggested that after performance-based tests, only the obese OA group had a significant increase in knee pain when pain was assessed with the WOMAC pain subscale (Figure 4). On the other hand, both groups had a significant increase in knee pain when pain was measured with the VAS (Figure 5).

Previous studies have indicated that obesity is a risk factor for progression of knee OA by decreasing function and increasing pain [25,51]. A meta-analysis of previous weight loss studies suggested that at least 10% of body weight loss is needed to have a considerable clinical effect on pain and physical function [52]. According to Felson et al. [53], if obese men lost enough weight to fit into the overweight category and that if overweight men lost enough weight to be within the reference BMI range of <25 kg/m^2, symptoms in knee OA would drop about 21.4%. In women with the same condition, their drop would be even more, by about 33%. Moreover, being obese increases the load placed on the knee joints, which increases joint stress and pain during walking activities [54]. This pattern of findings support our results that obese individuals tend to experience higher levels of pain compared to non-obese individuals with knee OA.

There is consistent evidence demonstrating that the WOMAC subscales of pain and physical function are more influenced by the ability to perform activity than by the patients' experience of pain and their perception of difficulty to perform daily activities [55,56]. Therefore, because the non-obese individuals with OA were capable of performing functional activities significantly better with significantly less pain than those in the obese OA group (as we observed in our study, see Table 1), we did not expect significant changes on the WOMAC pain subscale for the non-obese OA group. Moreover, a previous study indicated that the WOMAC pain subscale may capture more than just knee pain, suggesting that the WOMAC pain could be influenced by the presence of fatigue, depression and back pain [57]. The authors indicated that WOMAC scores, including the pain subscale score, should be interpreted with caution. Furthermore, psychological factors should be considered when rheumatic diseases are assessed [57]. Based on our findings, the VAS pain rating seems to be more accurate than the WOMAC pain subscale score when pain is assessed during or right after functional activities [50]. Therefore, we suggest that the VAS pain rating may be a better tool for assessing knee pain of symptomatic individuals diagnosed with knee OA during or right after performance-based tests, because it captures the pain at the moment of it occurrence.

The link between depressive symptoms and obesity to explain pain in individuals with knee OA

Excessive body weight and depressive symptoms are commonly observed in individuals diagnosed with knee OA compared to the general population [26,58], and are both positively associated with pain and activity limitations [59,60]. Our results indicated that depressive symptoms alone explained a significant proportion of variance of self-reported pain before (R^2=27%, p=.003) and after (R^2=35%, p<.0001) performance-based tests, as measured by the WOMAC pain subscale. However, when we assessed knee pain using the VAS, both depressive symptoms and BMI explained a significant proportion of the variance in self-reported pain, and the results obtained before (R^2=46.7%, p<.0001) and after (R^2=52.6%, p<.0001) performance-based tests were higher than the ones obtained when knee pain was assessed with the WOMAC pain subscale. Even though the VAS rating revealed a higher proportion of variance explained by depressive symptoms and BMI compared to the WOMAC pain subscale score, these results do not necessarily mean that the findings from the WOMAC pain subscale are not important. The WOMAC pain subscale is widely used in research and clinical settings [23,26,61] and based on our results, its use was not limited to detecting change in pain in obese individuals.

A recent study found that pain due to OA strongly predicted future fatigue and disability (both short and long term), and that fatigue and disability in turn predicted future depressive symptoms [3]. Therefore, persons living longer with the burden of knee OA, particularly those who are obese, may report depressive symptoms and thus the potential occurrence of a pain-depression cycle should be recognized from a clinical point of view. Moreover, previous studies in individuals with

knee OA observed the effect of weight loss on depression, quality of life and functional activity [3,20,23,52]. These studies indicated that after a significant body weight loss, quality of life, depression and functional capacity may improve. One particular study examined the relationship between depression and functional status of overweight and obese patients with knee OA. They found that levels of depression were significantly associated with WOMAC subscale scores: function ($r=0.54$; $p<0.001$), stiffness ($r=0.26$; $p=0.004$) and pain ($r=0.43$; $p<0.001$) [20]. They also indicated that obese individuals with moderate to high depressive symptoms had a higher WOMAC pain score and demonstrated poorer performance in functional tests compared to obese individuals without depressive symptoms [20].

Similar to our findings, our obese OA group, who reported depressive symptoms, also had high WOMAC pain scores before and after performance-based tests (Figure 4). Moreover, our obese OA groups also performed significantly ($p \leq 0.0001$) worse in functional test compared to our non-obese OA group. Together these studies established an important link between depression and obesity to explain pain and disability, suggesting that treatment of depression and successful weight loss management may improve knee pain and function [52,62]. Moreover, from a clinical perspective, by knowing that the relationship between depressive symptoms and pain in obese individuals with knee OA worsen after performance based tests we may imply that obese patients under conservative treatment for knee OA are expected to be more discouraged and withdraw treatments sooner. Consequently, obese patients with knee OA may benefit from conservative physical treatments if physical treatment is provided in association with psychological therapy for depression.

Limitations, Future Directions, and Conclusions

During some stages of our study we encountered some limitations such as lack of funds to intensify recruiting and consequently increase sample size. We also had difficulty recruiting patients within a BMI category of 18.5-24.9 kg/m^2. Finally, some patients refused to participate because they live in rural areas and rely on family for transportation. As a consequence we completed the study with a small sample size. Therefore, some results were not adjusted for confounding variables and this is another limitation of our study as adjustment for these variables may cause your significant findings to become insignificant. However, as a pilot study where results are normally or only expected to be shown in descriptive way, we obtained important findings of significant impact and relevance to the clinical setting. Future studies should include a larger sample size with a longitudinal design. This type of study would provide additional information about long-term changes in pain and disability in individuals with knee OA. Further investigations should focus on treatment for depression and weight loss therapy and try determining whether a combination of treatments is more effective than treating obesity or depressive symptoms individually. Future research should also measure the impact of reduction in depressive symptoms and body weight on physical health and well-being of individuals with knee OA before and after total knee replacement surgery.

In conclusion, we observed that individuals diagnosed with knee OA show higher levels of knee pain measured with the WOMAC pain subscale and VAS rating after performance-based tests. Therefore, assessment of pain, when possible, should be administered to individuals with OA after performance-based tests. Moreover, when the sample was divided into obese and non-obese individuals with OA, the WOMAC pain subscale did not capture change in pain in non-obese individuals. Therefore, the VAS pain rating may be a better tool for assessing knee pain of obese and non-obese individuals diagnosed with knee OA during or right after performance-based tests, because it captures the pain at the moment of its occurrence. In addition, clinicians should encourage obese patients with knee OA to lose weight and those who are not obese to maintain a healthy weight. Finally, depressive symptoms are also predictive of increased pain particularly after functional activities, with higher levels of depression predicting worse reports of pain. Consequently, clinicians should be aware of signs of depression as a potential predictor of decrease in functional activities in individuals with knee OA, especially those who are obese. Therefore, treatment of depression and a successful weight loss management may be necessary to improve the lifestyle of some individuals with knee OA.

References

1. Cubukcu D, Sarsan A, Alkan H (2012) Relationships between Pain, Function and Radiographic Findings in Osteoarthritis of the Knee: A Cross-Sectional Study. Arthritis 2012: 984060.
2. Tanamas SK, Wluka AE, Davies-Tuck M, Wang Y, Strauss BJ, et al. (2013) Association of weight gain with incident knee pain, stiffness, and functional difficulties: a longitudinal study. Arthritis Care Res (Hoboken) 65: 34-43.
3. Hawker GA, Gignac MA, Badley E, Davis AM, French MR, et al. (2011) A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. Arthritis Care Res (Hoboken) 63: 1382-1390.
4. Hunter DJ, Guermazi A, Roemer F, Zhang Y, Neogi T (2013) Structural correlates of pain in joints with osteoarthritis. Osteoarthritis Cartilage 21: 1170-1178.
5. Neogi T, Felson D, Niu J, Nevitt M, Lewis CE, et al. (2009) Association between radiographic features of knee osteoarthritis and pain: results from two cohort studies. BMJ 339: b2844.
6. Derek T, Cooke V, Kelly BP, Harrison L, Mohamed G, et al. (1999) Radiographic grading for knee osteoarthritis. A revised scheme that relates to alignment and deformity. J Rheumatol 26: 641-644.
7. Creamer P, Lethbridge-Cejku M, Hochberg MC (1999) Determinants of pain severity in knee osteoarthritis: effect of demographic and psychosocial variables using 3 pain measures. J Rheumatol 26: 1785-1792.
8. Hunter DJ (2013) Osteoarthritis. Rheumatic Diseases Clinics 39: xv-xviii.
9. Creamer P, Lethbridge-Cejku M, Hochberg MC (2000) Factors associated with functional impairment in symptomatic knee osteoarthritis. Rheumatology (Oxford) 39: 490-496.
10. Hannan MT, Felson DT, Pincus T (2000) Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 27: 1513-1517.
11. Shamir L, Ling SM, Scott WW Jr, Bos A, Orlov N, et al. (2009) Knee x-ray image analysis method for automated detection of osteoarthritis. IEEE Trans Biomed Eng 56: 407-415.
12. Maly MR, Krupa T (2007) Personal experience of living with knee osteoarthritis among older adults. Disabil Rehabil 29: 1423-1433.
13. Hawker GA, Mian S, Kendzerska T, French M (2011) Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res (Hoboken) 63: S240-S252.
14. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW (1988) Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 15: 1833-1840.

15. Jinks C, Jordan K, Croft P (2002) Measuring the population impact of knee pain and disability with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Pain 100: 55-64.

16. Messier SP, Legault C, Mihalko S, Miller GD, Loeser RF, et al. (2009) The Intensive Diet and Exercise for Arthritis (IDEA) trial: design and rationale. BMC Musculoskelet Disord 10: 93.

17. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, Devita P, et al. (2013) Strength Training for Arthritis Trial (START): design and rationale. BMC Musculoskelet Disord 14: 208.

18. Angst F, Ewert T, Lehmann S, Aeschlimann A, Stucki G (2005) The factor subdimensions of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) help to specify hip and knee osteoarthritis. a prospective evaluation and validation study. J Rheumatol 32: 1324-1330.

19. Stratford PW, Kennedy DM (2004) Does parallel item content on WOMAC's pain and function subscales limit its ability to detect change in functional status? BMC Musculoskelet Disord 5: 17.

20. Possley D, Budiman-Mak E, O'Connell S, Jelinek C, Collins EG (2009) Relationship between depression and functional measures in overweight and obese persons with osteoarthritis of the knee. J Rehabil Res Dev 46: 1091-1098.

21. Stratford PW, Kennedy DM, Woodhouse LJ (2006) Performance measures provide assessments of pain and function in people with advanced osteoarthritis of the hip or knee. Phys Ther 86: 1489-1496.

22. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, et al. (2008) Assessment of pain. Br J Anaesth 101: 17-24.

23. Coriolano K, Aiken A, Harrison M, Pukall C, Brouwer B, et al. (2013) Changes in Knee Pain, Perceived Need for Surgery, Physical Function and Quality of Life after Dietary Weight Loss in Obese Women Diagnosed with Knee Osteoarthritis. J Obes Weight Loss Ther 3: 2-6.

24. Bombardier C, Hawker G, Mosher D (2013) The Impact of Arthritis in Canada: Today and Over the Next 30 Years. Toronto: Arthritis Alliance of Canada 1-52.

25. Messier SP (2010) Diet and exercise for obese adults with knee osteoarthritis. Clin Geriatr Med 26: 461-477.

26. Lin EH (2008) Depression and osteoarthritis. Am J Med 121: S16-S19.

27. Pereira D, Severo M, Barros H, Branco J, Santos RA, et al. (2013) The effect of depressive symptoms on the association between radiographic osteoarthritis and knee pain: a cross-sectional study. BMC Musculoskelet Disord 14: 214.

28. Holla JF, van der Leeden M, Knol DL, Roorda LD, van der Esch M, et al. (2013) The association of body-mass index and depressed mood with knee pain and activity limitations in knee osteoarthritis: results from the Amsterdam osteoarthritis cohort. BMC Musculoskelet Disord 14: 296.

29. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, et al. (2010) Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 67: 220-229.

30. Enohumah KO, Imarengiaye CO (2008) Pain in Osteoarthrtis. African Journal of Biomedical Research 11: 119-128.

31. Kellgren JH, Lawrence JS (1957) Radiological assessment of osteo-arthrosis. Ann Rheum Dis 16: 494-502.

32. Dıraçoglu D, Baskent A, Yagci I, Ozcakar L, Aydin R (2009) Isokinetic Strength Measured in Early Knee Osteoarthritis. Acta Reumatol Port 34: 72-77.

33. Finch E, Brooks D, Stratford PW, Mayo NE (2002) Numeric pain rating scale (NPRS). In: Finch E (ed) Physical Rehabilitation outcome. A guide to enhance clinical decision making. 2th edition, BC Decker Inc 180-181.

34. Marks R (2007) Physical and psychological correlates of disability among a cohort of individuals with knee osteoarthritis. Can J Aging 26: 367-377.

35. Grothe KB, Dutton GR, Jones GN, Bodenlos J, Ancona M, et al. (2005) Validation of the Beck Depression Inventory-II in a low-income African American sample of medical outpatients. Psychol Assess 17: 110-114.

36. Ozcakir S, Raif SL, Sivrioglu K, Kucukcakir N (2011) Relationship between radiological severity and clinical and psychological factors in knee osteoarthritis. Clin Rheumatol 30: 1521-1526.

37. Beck AT, Ward H, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. Arch Gen Psychiatry 1961: 561-571.

38. Song IH, Song EK, Seo HY, Lee KB, Yim JH, et al. (2012) Patellofemoral alignment and anterior knee pain after closing- and opening-wedge valgus high tibial osteotomy. Arthroscopy 28: 1087-1093.

39. Margaria R (1966) Assessment of physical activity in oxidative and anaerobic maximal exercise. Int Z Angew Physiol 22: 115-124.

40. Walker R, Powers S, Stuart MK (1986) Peak oxygen uptake in arm ergometry: effects of testing protocol. Br J Sports Med 20: 25-26.

41. Helgerud J, Oiestad BE, Hoff J (2005) A monogram for calculation of upper body aerobic power from heart rate during submaximal arm cycling work. Journal of Applied Physiology.

42. Beriault K, Carpentier AC, Gagnon C, Menard J, Baillargeon JP, et al. (2009) Reproducibility of the 6-minute walk test in obese adults. Int J Sports Med 30: 725-727.

43. Podsiadlo D, Richardson S (1991) The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 39: 142-148.

44. Margaria R (1966) Assessment of physical activity in oxidative and anaerobic maximal exercise. Fed Proc 25: 1409-1414.

45. Lafortuna CL, Fumagalli E, Vangeli V, Sartorio A (2002) Lower limb alactic anaerobic power output assessed with different techniques in morbid obesity. J Endocrinol Invest 25: 134-141.

46. Sartorio A, Fontana P, Trecate L, Lafortuna CL (2003) Short-term changes of fatigability and muscle performance in severe obese patients after an integrated body mass reduction program. Diabetes Nutr Metab 16: 88-93.

47. Brooks GA, Fahey TD, White TP (1996) Exercise Testing and Prescription. In: Beauparlant S, Holmes M, Dondrea C (eds) Exercise Physiology: Human Bioenergetics and its application. 2nd edition, Mountain View, Ca: Mayfield Publisher Company 581-582.

48. Field A (2005) Discovering Statistics using SPSS. Sage Publication Ltd, London.

49. Maly MR, Costigan PA, Olney SJ (2006) Determinants of self-report outcome measures in people with knee osteoarthritis. Arch Phys Med Rehabil 87: 96-104.

50. Juhl C, Lund H, Roos EM, Zhang W, Christensen R (2012) A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. Arthritis 2012: 136245.

51. Felson DT (1996) Does excess weight cause osteoarthritis and, if so, why? Ann Rheum Dis 55: 668-670.

52. Christensen R, Bartels EM, Astrup A, Bliddal H (2007) Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. Ann Rheum Dis 66: 433-439.

53. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF (1988) Obesity and knee osteoarthritis. The Framingham Study. Ann Intern Med 109: 18-24.

54. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ (2004) The effect of body weight on progression of knee osteoarthritis is dependent on alignment. Arthritis Rheum 50: 3904-3909.

55. Kennedy D, Stratford PW, Pagura SM (2003) Exploring the Factorial Validity and Clinical Interpretability of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Physiotherapy Canada 55: 160-165.

56. Guermazi M, Poiraudeau S, Yahia M, Mezganni M, Fermanian J, et al. (2004) Translation, adaptation and validation of the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) for an Arab population: the Sfax modified WOMAC. Osteoarthritis Cartilage 12: 459-468.

57. Wolfe F (1999) Determinants of WOMAC function, pain and stiffness scores: evidence for the role of low back pain, symptom counts, fatigue and depression in osteoarthritis, rheumatoid arthritis and fibromyalgia. Rheumatology (Oxford) 38: 355-361.

58. Axford J, Butt A, Heron C, Hammond J, Morgan J, et al. (2010) Prevalence of anxiety and depression in osteoarthritis: use of the Hospital Anxiety and Depression Scale as a screening tool. Clin Rheumatol 29: 1277-1283.

59. Dekker J, van Dijk GM, Veenhof C (2009) Risk factors for functional decline in osteoarthritis of the hip or knee. Curr Opin Rheumatol 21: 520-524.

60. van Dijk GM, Veenhof C, Schellevis F, Hulsmans H, Bakker JP, et al. (2008) Comorbidity, limitations in activities and pain in patients with osteoarthritis of the hip or knee. BMC Musculoskelet Disord 9: 95.

61. Axford J, Heron C, Ross F, Victor CR (2008) Management of knee osteoarthritis in primary care: pain and depression are the major obstacles. J Psychosom Res 64: 461-467.

62. Hawker GA, Gignac MA, Badley E, Davis AM, French MR, et al. (2011) A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. Arthritis Care Res (Hoboken) 63: 1382-1390.