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Composite measures of physical activity and pain associate better with functional assessments than pain alone in knee osteoarthritis

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Compliance with ethical standards

This research was approved by the Institutional Review Board at the DVAHCS. All participants provided written informed consent.

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Abstract

Introduction—Recent research showed that physical activity (PA)–adjusted pain measures were more strongly associated with radiographic osteoarthritis (OA) severity than an unadjusted pain measure. This exploratory study examined whether PA-adjusted pain measures were more closely associated with other key OA-related measures, compared to unadjusted pain scores.

Method—Participants were 122 Veterans (mean age = 61.2 years, 88.5% male) with knee OA. Baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores were adjusted for accelerometer-derived daily: (1) step counts, (2) minutes of any activity, (3) minutes of moderate or greater intensity activity, (4) minutes of light intensity activity, and (5) energy expenditure. Partial correlations, adjusted for age, sex, and body mass index, estimated associations of unadjusted and PA-adjusted WOMAC pain scores with functional assessments (6-minute walk test, 8-foot walk test, chair stand test, satisfaction with physical function), fatigue (Brief Fatigue Inventory), and anxiety/depressive symptoms (single item).

Results—Significant ($p < 0.05$) associations were found in 29 of 36 of models. For the four function-related assessments, step count and energy expenditure–adjusted WOMAC pain scores had stronger associations (partial r s = 0.24–0.48) than WOMAC pain score (partial r s = 0.19–0.25). For fatigue and anxiety/depressive symptoms, WOMAC pain score had stronger, positive associations than most PA-adjusted pain scores. Of the PA-adjusted measures, the strongest associations overall were observed for step count and energy expenditure.

Conclusion—PA-adjusted pain scores may have particular value for OA studies involving functional assessments, whereas unadjusted WOMAC pain scores are more closely associated with psychological symptoms. This has implications for measurement in clinical OA studies.

Trial registration— [NCT01058304](https://clinicaltrials.gov/ct2/show/study/NCT01058304)

Keywords

Measurement; Osteoarthritis; Pain; Physical activity

Introduction

Standard measures of osteoarthritis (OA)-related pain do not account for individuals' physical activity (PA) levels. Yet pain experiences and activity levels are often related, with some individuals reducing activity in an attempt to avoid or minimize pain [1, 2]. However, PA is essential for managing OA, and patients who remain physically active experience better physical function and other outcomes [3-5]. Even among patients with high pain scores, other outcomes may differ between those with higher vs. lower PA levels. Therefore, incorporating PA levels with pain scores may provide a better representation of patients' overall pain experiences and have greater clinical and prognostic value. In addition, consideration of PA levels in the context of pain measurement may have differential importance when studying different types of interventions or risk factors, depending on the expected mechanism of action.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale is routinely used to assess OA-related pain [6]. A recent study found that

adjustment of WOMAC pain scores for PA measures—including step and activity counts—resulted in stronger associations with radiographic knee OA severity, compared with unadjusted WOMAC scores [7]. Those results support the utility of composite pain and PA measures; specifically, composite measures were better able to discriminate between levels of radiographic severity than pain alone. While those data suggest that PA-adjusted pain scores are associated with radiographic OA, it is unknown whether PA-adjusted pain scores are associated with other OA outcomes across different domains. Therefore, the purpose of this secondary analysis was to determine whether PA-adjusted WOMAC pain scores were more strongly associated with key OA-related measures (physical function, fatigue, mental health symptoms) than unadjusted WOMAC pain scores.

Materials and methods

Participants

Participants were a subset of those enrolled in a randomized controlled trial comparing group vs. individual physical therapy for knee OA; details of the study have been published previously [8]. Data for these analyses were collected at baseline, prior to randomization or receipt of any study intervention. Study participants were patients at the Department of Veterans Affairs Healthcare System (DVAHCS) in Durham, NC. All participants had a prior diagnosis of knee OA (ascertained from information in the electronic medical record), joint symptoms on most days of the past month, and no physical therapy for knee OA in the prior 6 months. Among the 320 participants enrolled in the parent trial, 157 were given an accelerometer, as this measurement was added after the parent study was initiated. Among those issued an accelerometer, 17 had insufficient wear time, resulting in 140 participants for this analysis. There were no significant differences between those with and without accelerometer data with respect to sex, body mass index (BMI), or WOMAC pain score. However, those with accelerometer data were older (61.8 vs. 58.7 years; $p < 0.05$) than those without accelerometer data. An additional 18 individuals had missing data on other variables of interest, resulting in a final sample size of $n = 122$. This research was approved by the Institutional Review Board at the DVAHCS. All participants provided written informed consent.

Measures

Accelerometry procedures—At the baseline assessment, participants were given a waist-worn Actigraph GT3X (ActiGraph LLC, Pensacola, FL). Participants were instructed to wear the monitor during waking hours for 7 days and return it by mail using a provided self-addressed, stamped envelope. Accelerometer data were first processed using the non-wear threshold applied by Song and colleagues, which consists of an interval of at least 90 min of zero activity counts that contain no more than 2 total minutes of low (< 100) activity counts [9]. Participants with 4 or more days with 10 h of daytime wear were included [10]. Accelerometer data were scored using Sasaki (2011) and Troiano (2008) processing algorithms [11, 12]. Five daily metrics derived from the accelerometer data included step counts, minutes of light intensity activity, minutes of moderate or greater (moderate+) intensity activity, minutes of any intensity activity, and energy expenditure from activity. In

addition, total daily time spent in any activity (above sedentary threshold) was calculated by summing the time across the various intensities.

Pain and PA-adjusted pain measures—Participants completed the WOMAC pain scale, which includes five items assessing pain during walking, going up or down stairs, standing, sitting or lying down, and at night while in bed [13]. Each item was scored on a Likert scale; the total score range is 0–20, with higher scores indicating worse pain. Following the methods of Lo et al. [7], we calculated PA-adjusted WOMAC scores using each of the six accelerometer-derived PA metrics described above, as follows: $((\text{WOMAC pain} + 1) / \text{PA metric}) \times 10,000$; one exception was that for the moderate or greater intensity activity variable we used a multiplication factor of 1000 due to the very low values. One point was added to WOMAC pain scores to avoid division of zeros, and the 10,000 multiplication factor helped to scale values toward a range of 0–100 for interpretability. For all PA-adjusted WOMAC scores, higher scores indicate a poorer clinical status due to lower PA level and/or greater pain; if two individuals have the same WOMAC pain score, a lower PA metric would result in a higher PA-adjusted pain score or poorer clinical status.

Additional OA-related measures

Six-minute walk test—Participants were instructed to walk on a level surface for a 6-min period, without assistance from another person (assistive devices permitted). Scores were recorded as total feet walked. Participants who were unable to complete the test were given a score of 0. Higher scores, reflective of a greater distance walked, indicate better aerobic and functional capacity [14–16].

Chair stand test—Participants were instructed to complete five sit-to-stands as quickly, and safely, as possible. Time (seconds) was recorded from initiation until participants touched the chair after the fifth repetition. Participants were instructed to fold arms across their chest and position their back against the chair to begin the test. Lower scores, reflective of faster completion, indicate better lower body strength and dynamic balance [14, 17, 18].

Eight-foot walk test—Participants were instructed to walk at their self-selected usual pace, for 8 feet. Scores were measured in seconds. The test was conducted twice, and the average of the two trials was used in analyses. Lower scores reflect faster usual gait speed, a measure of functional capacity that has been associated with a wide range of health-related outcomes [19, 20].

Satisfaction with Physical Function Scale—This validated 5-item questionnaire assesses patients' satisfaction with their ability to complete basic functional tasks that are often affected by lower extremity OA, including stair climbing, walking, doing housework (light and heavy), and lifting and carrying [21]. All items are rated on a 7-point scale ranging from Very Dissatisfied (– 3) to Very Satisfied (+ 3), with a total possible range of – 15 to + 15.

Brief Fatigue Inventory—This 9-item, 11-point rating scale assesses perceived severity of fatigue and the impact of fatigue on daily functioning [22]. Three items measure fatigue

severity from 0 (inferring no fatigue) to 10 (indicating the highest severity possible) in the past 24 h. The next six items measure fatigue impact with daily activities in the past 24 h, including mood, walking ability, work inside and outside the home, relations with others, and enjoyment of life. Response options range from 0 (indicating no interference) to 10 (indicating complete interference). A global fatigue score was calculated by averaging all nine items, with a total possible range of 0–10 and higher scores indicating more fatigue.

Anxiety/depressive symptoms—We used a single item from the EQ-5D that asked participants to select which of the three responses best described their own health state: I am not anxious or depressed, I am moderately anxious or depressed, or I am extremely anxious or depressed [23]. Response options range from 1 (indicating no anxiety or depressive symptoms) to 3 (indicating higher levels of anxiety or depressive symptoms).

Statistical analysis

Descriptive statistics (means and standard deviations (SDs) or proportions, as appropriate), were calculated for demographic characteristics, OA measures, and accelerometer-derived variables. The associations between pain, PA-adjusted pain measures, and OA-related physical performance and psychosocial measures were examined using partial Spearman correlations and associated 95% confidence intervals (CIs), controlling for age, sex, and BMI [24]. In addition, we ran individual multivariable linear regression models for each combination of pain or PA-adjusted pain measure and each other OA-related measure, adjusted for age, sex, and BMI. Results of those regression models confirmed the findings of the partial correlations, so only the partial correlations are presented here for simplicity. All analyses were performed in IBM SPSS Statistics v22.0 and SAS version 9.4 (SAS Institute).

Results

The mean age of this VA-based sample was 61.2 ± 9.2 years, and the majority were male (88%) and non-White (59%, primarily African American). Additional participant characteristics are shown in Table 1. Table 2 shows partial correlations, with associated 95% CIs, between each pain/composite measure and each other OA-related measure, adjusted for age, sex, and BMI. Partial correlations ranged from 0.02 to 0.45. The majority of these associations were statistically significant; exceptions were (1) the unadjusted WOMAC pain score was not significantly associated with the chair stand test, (2) WOMAC-Energy Expenditure was not significantly associated with anxiety and depressive symptoms, and (3) WOMAC-Moderate+Intensity Activity had a significant association only with the 8-foot walk test.

Compared to the unadjusted WOMAC pain score, WOMAC-Step Count had stronger correlations with all measures related to physical function (6-minute walk, chair stands, 8-foot walk, and satisfaction with Physical Function Scale), whereas the unadjusted WOMAC pain score was more strongly associated with Brief Fatigue Inventory and anxiety and depressive symptoms (Table 2). Associations of WOMAC-Energy Expenditure with other OA-related measures were of similar magnitude as those for WOMAC-Step Count; for all measures but anxiety and depressive symptoms, these associations were stronger than those for the unadjusted WOMAC pain score. The WOMAC-All Activity and WOMAC-

Light Intensity composite variables were also more strongly associated with functional assessments than the unadjusted WOMAC pain score, but overall, these correlations were somewhat lower than those for the WOMAC-Step Count and WOMAC-Energy Expenditure composite variables. The WOMAC-Moderate Intensity composite variable had weaker associations with most OA-related measures, compared with the unadjusted WOMAC pain score.

Discussion

This exploratory study found that compared with WOMAC pain scores, PA-adjusted WOMAC pain scores were overall more strongly associated with function measures (6-minute walk, chair stand test, 8-foot walk, self-reported satisfaction with function). PA-adjusted WOMAC pain scores were also significantly associated with measures of fatigue and anxiety/depressive symptoms. However, for the measure of anxiety/depressive symptoms, the unadjusted WOMAC score had the strongest association. For the fatigue measure, associations were similar for unadjusted WOMAC pain and WOMAC pain adjusted for energy expenditure; the remainder of the associations with other PA-adjusted pain measures were lower.

Although these results extend the findings of Lo et al. [7] and offer additional support for the importance of PA-adjusted pain measurement, there was variability regarding which pain or composite measure had the strongest association with a given functional assessment or symptom measures. This suggests that the importance of using a PA-adjusted pain measure may differ based on the intervention or outcome of interest. In particular, the largest differences between correlations for unadjusted and PA-adjusted pain measures were observed for the functional assessments, and this is likely due to the association of physical activity with function. However, it is still notable that the composite measures that considered both pain and PA were more closely associated with function than measurement of pain severity alone. These results suggest that PA-adjusted pain measures may be more sensitive to change in exercise, rehabilitation, or bracing-type interventions that focus on functional outcomes, and this should be examined in future studies.

It is interesting that WOMAC pain adjusted for Moderate+Intensity Activity was not significantly associated with fatigue or anxiety/depressive symptoms, and associations with other measures were weak. This may be due to the relatively limited amount of Moderate+Intensity Activity performed in this sample; these associations may differ in a population with a higher level and/or wider range of Moderate+Intensity Activity. In contrast, WOMAC pain adjusted for light intensity activity was significantly associated with all OA-related measures.

Among the different composite measures examined, PA adjusted for step count and energy expenditure had the strongest associations overall with other OA-related measures. PA adjusted for step count is easiest to obtain. Step counts can be measured via simple pedometers and many commercially available activity trackers, whereas other activity measures we assessed require use of higher level commercial or research grade accelerometers. In addition, step count is a simple metric on which PA counseling can

be based. Lo et al. also found that WOMAC adjusted for step count was better able to discriminate among grades of radiographic knee OA severity than unadjusted WOMAC pain score [7]. Based on these findings and the simplicity of measuring step counts, we recommend that step count-adjusted pain scores should be considered for broader use in OA clinical trials and epidemiologic studies.

We acknowledge some limitations to this study. First, this study was conducted at one site within the DVAHCS, and participants were mostly men, which limits generalizability. Second, analyses were conducted among a sub-sample of the total study, based on availability of accelerometer data. Although those included in the analyses did not differ from those without accelerometer data on most characteristics, those in this sub-sample were somewhat older. Third, only one pain measure (WOMAC) was included, and findings regarding PA-adjusted pain may not generalize to other pain measures. Seventh, we acknowledge that in this cross-sectional study, causality cannot be inferred. Rather, these analyses present some initial data on the potential value of combined pain and PA measures, which need to be further evaluated for predictive ability in longitudinal studies. Relatedly, more research is needed to understand whether differences in unadjusted and PA-adjusted measures are clinically meaningful in terms of their sensitivity to change within longitudinal observational studies and clinical trials.

In summary, this study found that several PA-adjusted WOMAC pain measures (particularly those adjusted for step count and energy expenditure) were more strongly associated with measures of physical function, compared to unadjusted WOMAC pain scores. However, unadjusted WOMAC pain score was more strongly associated with a measure of psychological symptoms. These results suggest that in clinical OA studies, the most appropriate or sensitive symptom measure (pain vs. PA-adjusted pain) may depend on the type of intervention or outcome.

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Key points

- Among patients with osteoarthritis, physical activity–adjusted pain measures (particularly those adjusted for step count and energy expenditure) were more strongly associated with measures of physical function, compared to unadjusted pain scores, whereas unadjusted pain score was more strongly associated with a measure of psychological symptoms.
- In clinical osteoarthritis research, the most appropriate or sensitive symptom measure (pain vs. physical activity–adjusted pain) may depend on the type of intervention or outcome being studied.

Table 1Characteristics of study sample ($N = 122$)

Age, mean (SD), years	61.2 (9.2)
Men, n (%)	108 (88.5)
Non-White race, n (%)	72 (59.0)
With some college education, n (%)	100 (82.0)
WOMAC pain subscale score, mean (SD)	9.0 (3.2)
Duration of self-reported arthritis symptoms, mean years (SD)	12.7 (12.8)
Accelerometer-derived data [*] (daily metrics)	Mean (SD)
Steps (#)	4915 (2679) (range 1040–13,674)
Activity-related energy expenditure (kCal)	434.0 (276.3) (range 95.5–1561.8)
Time spent in all activity (min)	265.3 (95.1) (range 79.6–512.0)
Time spent in moderate + intensity activity (min)	8.4 (12.8) (range 0.1–82.4)
Time spent in light intensity activity (min)	257.1 (87.9) (range 79.1–481.1)
OA-related outcomes	Mean (SD)
6-minute walk distance (feet)	1315.5 (345.7)
Chair stand test time (seconds)	16.2 (7.5)
8-foot walk test (usual pace), time to complete, seconds	0.9 (0.2)
Satisfaction with physical function score	– 0.9 (1.5)
Brief Fatigue Inventory score	3.5 (2.1)
Anxiety/depressive symptoms	1.4 (0.5)

^{*} Overall means across all days

Table 2

Partial Spearman correlations (*r*) and associated 95% CI for each pain/PA-adjusted pain measure with other OA-related function and symptom measures

	WOMAC pain (unadjusted) <i>r</i> (<i>p</i> value) (95% CI)	WOMAC-Step Count <i>r</i> (<i>p</i> value) (95% CI)	WOMAC-Energy Expenditure <i>r</i> (<i>p</i> value) (95% CI)	WOMAC-All Activity <i>r</i> (<i>p</i> value) (95% CI)	WOMAC-Light Intensity Activity <i>r</i> (<i>p</i> value) (95% CI)	WOMAC-Moderate-Intensity Activity <i>r</i> (<i>p</i> value) (95% CI)
6-minute walk distance	-0.19 (0.04) (-0.36, -0.01)	-0.32 (<0.01) (-0.47, -0.14)	-0.31 (<0.01) (-0.47, -0.14)	-0.28 (<0.01) (-0.44, -0.10)	-0.26 (<0.01) (-0.42, -0.08)	-0.17 (0.06) (-0.34, 0.01)
Chair stands (time to complete 5)	0.15 (0.11) (-0.04, 0.32)	0.36 (<0.01) (0.19, 0.51)	0.35 (<0.01) (0.18, 0.50)	0.25 (<0.01) (0.07, 0.42)	0.25 (<0.01) (0.07, 0.41)	0.17 (0.07) (-0.02, 0.34)
8-foot walk time	0.25 (<0.01) (0.07, 0.41)	0.42 (<0.01) (0.26, 0.56)	0.45 (<0.01) (0.29, 0.58)	0.37 (<0.01) (0.20, 0.52)	0.35 (<0.01) (0.18, 0.50)	0.36 (<0.01) (0.19, 0.50)
Satisfaction with function	-0.22 (0.02) (-0.39, -0.04)	-0.26 (<0.01) (-0.42, -0.14)	-0.24 (<0.01) (-0.41, -0.07)	-0.28 (<0.01) (-0.44, -0.10)	-0.27 (<0.01) (-0.43, -0.09)	-0.17 (0.06) (-0.34, 0.01)
Brief Fatigue Inventory	0.25 (<0.01) (0.07, 0.42)	0.21 (0.02) (0.03, 0.38)	0.27 (<0.01) (0.10, 0.43)	0.21 (0.02) (0.03, 0.38)	0.20 (0.03) (0.02, 0.37)	0.03 (0.72) (-0.15, 0.21)
Anxiety and depressive symptoms	0.31 (<0.01) (0.13, 0.46)	0.20 (0.03) (0.02, 0.37)	0.14 (0.13) (-0.04, 0.31)	0.22 (0.02) (0.04, 0.39)	0.22 (0.02) (0.04, 0.38)	-0.02 (0.83) (-0.20, 0.16)

All measures adjusted for age, sex, and BMI. Strongest association for each outcome variable in *italics*. For WOMAC pain, higher scores indicate worse pain. For 6-minute walk and satisfaction with function, higher scores indicate better outcomes. For chair stands, 8-foot walk, Brief Fatigue Inventory, and anxiety and depression measures, higher scores indicate poorer outcomes