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ASSOCIATION OF KNEE PAIN WITH A REDUCTION IN THIGH MUSCLE STRENGTH – A CROSS-SECTIONAL ANALYSIS INCLUDING 4553 OSTEOARTHRITIS INITIATIVE PARTICIPANTS

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Abstract

Objective—To cross-sectionally determine the quantitative relationship of age-adjusted, sex-specific isometric knee extensor and flexor strength to patient-reported knee pain.

Methods—Difference of thigh muscle strength by age, and that of age-adjusted strength per unit increase on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) knee pain scale, was estimated from linear regression analysis of 4553 Osteoarthritis Initiative participants (58% women). Strata encompassing the minimal clinically important difference (MCID) in knee pain were compared to evaluate a potentially non-linear relationship between WOMAC pain levels and muscle strength.

Results—In Osteoarthritis Initiative participants without pain, the age-related difference in isometric knee extensor strength was −9.0%/−8.2% (women/men) per decade, and that of flexor strength was −11%/−6.9%. Differences in age-adjusted strength values for each unit of WOMAC pain (1/20) amounted to −1.9%/−1.6% for extensor and −2.5%/−1.7% for flexor strength. Differences in torque/weight for each unit of WOMAC pain ranged from −3.3 to − 2.1%. There was no indication of a non-linear relationship between pain and strength across the range of observed WOMAC values, and similar results were observed in women and men.

Conclusion—Each increase by 1/20 units in WOMAC pain was associated with a ~2% lower age-adjusted isometric extensor and flexor strength in either sex. As a reduction in muscle strength is known to prospectively increase symptoms in knee osteoarthritis and as pain appears to reduce

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Author's Contribution
All authors have made substantial contributions to: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Disclosure of interest
Felix Eckstein is CEO and is co-owner of Chondrometrics GmbH, a company providing MR image analysis services. He provides consulting services to MerckSerono, Novartis, Sanofi Aventis, and Abbot. Wolfgang Wirth is part-time employed and is co-owner of Chondrometrics GmbH, and provides consulting services to MerckSerono. Anja Ruhdorfer has no conflicting interests.

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Keywords

thigh muscle strength; WOMAC knee pain score; minimal clinically important difference; knee osteoarthritis

INTRODUCTION

Muscle strength is highly adaptive to the external/internal environment, e.g. to immobilization[1] or training[2–4]. Thigh muscle strength was found to be substantially reduced in osteoarthritic knees[5–7] and to be strongly related to knee function[8]. Muscle strength, hence, represents an important target for the treatment of disability in the elderly[9], and training interventions have been observed to beneficially affect knee pain and function in patients with knee osteoarthritis (KOA)[10–16]. In a previous study we showed that knees with moderate to severe levels of knee pain (Western Ontario and McMasters Universities Osteoarthritis Index [WOMAC]≥5 [on a 0–20 Likert scale]) displayed significantly lower isometric thigh muscle strength than painless knees, independent of their radiographic KOA status(Kellgren-Lawrence grade [KLG])[5]. Yet, despite the evidence of a relationship between impaired thigh muscle status in KOA and knee pain[5,6,10], the quantitative magnitude of the difference in thigh strength per unit (or the minimal clinically important difference [MCID]) across the spectrum of observed WOMAC pain units is currently unknown. Further, it is unclear, whether the relationship between pain and difference in muscle strength is linear across the spectrum of pain levels, and whether this relationship is similar between men and women. To address the above questions, age has to be taken into account as a confounder of the interaction between pain and muscle strength, as muscle strength decreases with age, independent of pain[17–20].

The aim of the current study therefore was to analyze the difference of directly age-adjusted knee extensor and flexor strength per unit on the WOMAC knee pain scale, and per strata comprising MCIDs in knee pain across a wide spectrum of WOMAC pain scores. Specifically, we examined whether the relationship between pain and strength is linear across the WOMAC scale, and whether this pain-strength-association differs between men and women.

METHODS

Participants

Participants were drawn from the Osteoarthritis Initiative (OAI) database (clinical data releases 0.2.2; 1.2.2), which includes 4796 participants aged 45–79 years, with various socioeconomic backgrounds[21,22]. Based on risk factor profile and radiographic and symptomatic osteoarthritis status at enrollment, participants were assigned to either the healthy reference cohort without risk factors of KOA (n=122), the incidence cohort at risk of developing symptomatic KOA (n=3284), or the progression cohort with established symptomatic KOA at the time of enrollment (n=1390)[8,21,22]. Detailed in- and exclusion criteria for the OAI and the current study have been described previously[8].

All participants of the entire OAI cohort without missing demographic data (n=4), WOMAC knee pain scores (n=4) and/or WOMAC function scores (n=23), and isometric knee extensor and flexor strength (n=581) were included (one limb per participant)[8]. Since some participants were enrolled before the strength measurement device was applied in the study, we also included those with complete data (of the above measures), who had thigh strength measured at the year 1 follow-up visit (219 women/129 men) instead of the baseline measurements. Hence, 4553 participants (2651 women/1902 men) were available for the analysis.

Of these 4553 participants, all participants without any knee pain (WOMAC=0) and without any signs of radiographic KOA (KLG=0) were used to analyze the relationship between age and strength by regression analysis, separately in women and men. The radiographic status was evaluated on fixed-flexion X-rays[23] in central KLG readings (versions 0.7 for n=3934 and 1.7 for n=338 participants)[24].

Measurement of isometric thigh muscle strength

Amongst the two limbs per OAI participant, the strength data from the dominant limb were used (OAI question: “With which leg do you kick a ball”). When participants considered both limbs as equal (n=65) or when such information was not available (n=38), the right limb was used.

For the maximum isometric knee extensor and flexor strength measurements, the “Good Strength Chair” (Metitur Oy, Jyvaskyla, Finland) was used[6,8,25]. Participants were seated upright, with pelvis and thigh fixated by straps and the knee flexed at 60°. The load cell was positioned at a consistent anatomical position 2cm proximal to the calcaneus. To get familiarized with the measurement procedure, the participants performed two practice trials at 50% effort, before three measurements with maximum voluntary isometric contraction, i.e. 100% effort, were recorded (in Newton [N]). The maximum value of these three trials was used for the analysis.

Torque was used, to normalize strength with the most appropriate scaling to body weight[26]. To calculate knee extensor and flexor torque (moment), leg length measurements of the OAI database were used. These were available for the right legs (only) in 4518 participants (58% women) and were also used for the left-dominant participants, assuming symmetry in limb length.

Assessment of self-reported knee pain

For assessment of the patient-reported pain status, the WOMAC knee pain score was used. The scale ranges from 0–20 (0=no pain)[27,28]. This subscale of the total WOMAC score comprises five questions (Likert scale), each rated from 0–4, where 4 units represent extreme pain. In the OAI, the questions ask for knee-specific, i.e. side-specific, pain when walking, climbing or going down stairs, lying in bed, sitting or lying down, and when standing, within the past seven days. During a rehabilitation intervention, an MCID of 2 units for the WOMAC knee pain score has been previously reported by Angst et al.[29].

Assessment of comorbidities and depression

For assessment of the presence of comorbidities, the Modified Charlson Comorbidity Index was used[30,31]. This score provides the only documentation of existing comorbidities such as previous heart attack, oncologic pathologies or asthma, for the OAI database as described previously[32]. For assessment of depression, the Center for Epidemiologic Studies Depression Scale (CES-D) Score[33] from the OAI database was used. Participants rated their feelings such as having appetite, feeling depressed, restless, fearful, lonely, happy, sad, hopeful for the future, having crying spells, etc. (20 questions) for the past week from 1 (=rarely or none of the time; <1day) to 4 (=most or all of the time; 5–7days). Both scores were available for 4460 participants (58% women) for the analysis of strength and for 4429 participants (58% women) for the analysis of torque/body weight.

Statistical Analysis

Given previous reports on sex differences in strength between men and women[5,34], analyses were performed for men and women separately. Further, analyses were repeated for torque (isometric strength*lever arm of leg length in meter) with normalization to body weight (torque/weight; Newton-meter/kilogram) to account for inter-personal variations and the influence of weight on strength. All analyses were performed using SPSS 22 (IBM Corp., Armonk, NY) and Microsoft Excel 2010 (Redmond, WA).

To estimate the difference in strength per age decade, only participants without knee pain (WOMAC 0) and without radiographic KOA (KLG 0) were included. Linear regression models with age (independent variable), and extensor and flexor strength (dependent variable), were used. The slope coefficient of the regression equation (equation 1) represented the difference in strength per annum, which was then used as the basis for directly adjusting the observed values for age. We calculated the difference per decade by multiplying this slope coefficient with the factor 10. Because 45 was the youngest age for OAI inclusion[21,22], this was considered the starting point to relate the difference per decade to (equation 2). By entering 45 in the regression equation, we calculated the strength at age 45 (equation 3). For the direct age-adjustment, we used the slope coefficient calculated in the previous analysis (equation 1). We calculated the theoretical strength of every participant at the mean age of the cohort (61.4 years) using the age-difference to the mean and the actual strength (equation 4).

After direct age-adjustment, linear regression models were used to calculate the difference in thigh muscle strength (torque/body weight) (dependent variable), per unit increase in the WOMAC knee pain score (independent variable). Slope coefficients of the regression equations (equation 5) represented the difference in strength per unit increase in WOMAC knee pain. To compare the association between men and women, the slopes of the regression models were compared based on the standard error of the slopes. Additional linear regression models were used with strength (torque/body weight) as dependent and WOMAC knee pain score, the Modified Charlson Comorbidity Index, and the CES-D as independent variables. Analyses were repeated with exclusion of all participants with strength measurements at year 1 of follow-up.

EQUATIONS USED

$$\text{strength (age)} = y\ \text{intercept} + \text{slope coefficient} * \text{age} \quad (1)$$

$$\%\ \text{Strength decline per decade} = \frac{\text{slope coefficient} * 10}{\text{strength}\,(45)} * 100 \quad (2)$$

$$\text{Strength}\,(45) = y\ \text{intercept} + \text{slope coefficient} * 45 \quad (3)$$

$$\text{Strength}\,(61.4) = \text{Strength} + \text{slope coefficient} * (\text{participant age} - 61.4) \quad (4)$$

$$\text{Strength}\,(WOMAC) = y\ \text{intercept} + \text{slope coefficient} * WOMAC \quad (5)$$

Since the MCID for the WOMAC knee pain score has been reported to be 2 units[29], participants were divided into strata encompassing 2 WOMAC knee pain units each (0; 1–2; 3–4; 5–6; 7–8; 9–10; 11–12; >12) across the observed WOMAC spectrum to evaluate non-linearity in the dose-response relationship of pain and muscle strength. These strata were compared to the stratum with painless participants (WOMAC=0) and to the next lower WOMAC stratum (1–2 vs 0; 3–4 vs 1–2, etc.). Because only few participants had knee pain worse than WOMAC=12, these participants were combined to one stratum. As a measure of the between-group effect size, Cohen's d was calculated[8]. To relate the relevance of a difference in strength (torque/body weight) to the MCID in knee pain, the mean of the %-differences in strength (torque/body weight) between participants being 2 WOMAC units apart (0 vs 2, 1 vs 3, up to 11 vs 13) was calculated.

For exploratory purposes the R^2 for the simple linear regression model with strength (torque/body weight), i.e. dependent variable, and WOMAC knee pain score, the Modified Charlson Comorbidity Index, and the CES-D, i.e. independent variables, were calculated to estimate how much of the variability in strength and torque/body weight is explained by them.

RESULTS

Demographics and age-adjustment of thigh muscle strength

Of the 2651/1902 women/men studied, 33%/37% were KLG0, 17%/17% KLG1, 29%/23% KLG2, 12%/14% KLG3, and 2%/4% KLG4. For 7% and 5% of the women and men, KLG data was not available. The age was 61.4±9.2 years (mean ±standard deviation [SD]) and the body mass index (BMI) was 28.7±4.8 kg/m^2 (Table 1). Demographic data for all WOMAC strata are displayed in Table 1. Women and men in higher WOMAC strata tended to be heavier, but also younger, than those without any pain (WOMAC=0).

798 participants (426 women/372 men) without knee pain and without radiographic KOA were included. The 426 women were 60.7±9.0 years old and had a BMI of 26.2±4.7 kg/m^2 (68.3±13.2 kg body weight). The 372 men were 59.0±9.4 years old and had a BMI of 27.6±3.7 kg/m^2 (86.1±13.2 kg body weight).

Extensor muscle strength was found to be 9.0%/8.2% lower per decade relative to 354N/530N at 45 years of age in the pain-free limbs of women/men (R^2=0.11/R^2=0.09; $p<0.0001$ in both sexes) (Figure 1). Flexor muscle strength was found to be 10.8%/6.9% lower (R^2=0.09/R^2=0.03; $p<0.0001$ in both sexes) relative to 146N/217N. Extensor and flexor torque/body weight in women/men were 6.4%/6.7% (R^2=0.04/R^2=0.06) (Figure 1) and 8.0%/8.2% (R^2=0.03/R^2=0.04) lower per decade, respectively.

Relationship between age-adjusted thigh muscle strength and self-reported knee pain

For example, when calculating the difference in strength, the regression equation for WOMAC knee pain versus extensor strength was Y=300.619−5.859x. Hence, the difference of extensor strength/unit of the WOMAC knee pain score, i.e. the slope, was −5.859N. The value of −5.859N was divided by the y-intercept=300.619N(*100) to extract the −1.9% difference (−5.9N; R^2=0.053) in directly age-adjusted isometric extensor strength per unit WOMAC knee pain in women, and the −1.6% strength difference (−7.4N; R^2=0.029) in men (y-intercept: 452.333, slope coefficient: −7.365) (Figure 2). The difference in directly age-adjusted flexor strength was −2.5% (−3.0N; R^2=0.048) in women and −1.7% (−3.3N; R^2=0.017) in men. For directly age-adjusted extensor torque/body weight (Figure 2) and flexor torque/body weight, differences amounted to 2.7% (R^2=0.092) and 3.3% lower strength (R^2=0.077) in women and 2.1% (R^2=0.044) and 2.2% (R^2=0.026) lower strength in men, respectively.

The differences in extensor strength (y-intercept: 300.962, slope coefficient: −5,695 in women; y-intercept: 459.091, slope coefficient: −7.075 in men) and flexor strength as well as torque/body weight remained largely unchanged (ranging from 1.5 to 3.1%) after adjusting for the Modified Charlson Comorbidity Index and the CES-D and in participants with baseline strength measurements only (data not shown).

A clear trend was observed for participants in strata with more severe pain to exhibit lower extensor and flexor strength (torque/body weight), in women and men. Women without knee pain (WOMAC=0) had an extensor strength of 300±86N (304±81N after age-adjustment) and men an extensor strength of 459±130N (458±124N) (Tables 2&3). Women and men in the stratum with the strongest pain (WOMAC>12) had a 24% and 19% lower extensor strength compared to those with WOMAC=0 (Tables 2&3). The observed %-differences in strength (torque/body weight) for each pain stratum vs the painfree (WOMAC=0) knees did not suggest that the relationship between pain and thigh strength was non-linear, i.e. the differences in strength between strata were similar across the entire range of WOMAC pain values (Table 2&3). The differences in strength and torque/body weight appeared somewhat greater in women than in men (Tables 2&3), but the slopes of the regression models relating strength to pain did not statistically differ between sexes ($p \geq 0.17$).

The MCID of the WOMAC knee pain score across all 2-unit WOMAC score comparisons related to a 3.7% lower extensor strength and 4.7% lower extensor torque/body weight in women and to a 3.1% and 3.6% lower strength and torque/body weight in men, respectively. For flexor strength and torque/body weight %-differences were −4.6% and −5.1% in women and −2.6% and −2.9% in men.

The effect of comorbidities and depression on age-adjusted thigh muscle strength

In the linear regression model in men the Modified Charlson Comorbidity Index, but not the CES-D score, had a significant independent effect on knee extensor and flexor strength ($p=0.005$ and 0.03) additionally to the WOMAC knee pain score ($p<0.0001$). With the WOMAC knee pain score as the only independent variable in the linear regression model, R^2 was 0.031 for extensor and 0.017 for flexor strength and with all three scores added into the model, R^2 was 0.036 and 0.021. In women, however, neither the Modified Charlson Comorbidity Index nor the CES-D significantly explained any variability (0%) in extensor or flexor strength ($p \geq 0.07$).

When extensor and flexor torque/body weight were the dependent variables, the Modified Charlson Comorbidity Index, but not the CES-D, had a significant, independent effect on torque/body weight in men ($p \leq 0.007$) and in women ($p<0.0001$). With the WOMAC knee pain score as the only independent variable in the linear regression model R^2 was 0.092 for extensor and $R^2=0.074$ for flexor torque/body weight in women and $R^2=0.046$ and $R^2=0.027$ in men and when all three scores were added into the model, R^2 was 0.098 for extensor and $R^2=0.079$ for flexor torque/body weight in women and $R^2=0.056$ and $R^2=0.033$ in men.

DISCUSSION

To our knowledge, this is the first study to explore the dose-response relationship between knee pain and sex-specific, age-adjusted thigh muscle strength across a large range of WOMAC knee pain scores. In the OAI cohort, we found age-related differences in women/men without knee pain or radiographic KOA in extensor strength to be 9%/8% lower, and those in flexor strength to be 11%/7% lower/decade, when related to 45 years (i.e. youngest age for OAI enrollment). These differences were accounted for when exploring the impact of pain on (directly age-adjusted) muscle strength. We found an increase of 1 unit on the WOMAC knee pain scale to be associated with a 2–3% lower knee extensor and flexor strength and torque/body weight in both women and men. As an estimate of an MCID in strength, a 3–5% lower strength (torque/body weight) was related to the MCID in pain. Across WOMAC knee pain strata of 2 units (=MCID[29]), there was no evidence for a non-linear dose-response relationship between WOMAC knee pain and thigh muscle strength in either sex.

A limitation of the current study is its cross-sectional approach that precluded an evaluation of longitudinal changes within subjects, and the impact of longitudinal changes in WOMAC pain on that of thigh muscle strength. However, although the current study is limited to a cross-sectional setting, it permits the analysis of an age-related difference in strength over an extensive period of time, since the age-range of the participants included in this very large cohort covered a range of 34 years (45 to 79 years). The current findings lack a comparison with a healthy reference cohort, as only 26 of 122 healthy OAI participants had baseline strength measurements. Therefore, age-related adjustments in strength were estimated in those with risk factors for, but without established symptomatic or radiographic KOA, with the estimated percent rates of changes for women and men being in line with previous literature[35]. It is of note that, despite their statistical significance, the strength of the relationship (R^2 values), for instance between age and muscle strength, was relatively low. Therefore, the findings should not be generalized at an individual level.

Using age as covariate would have offered the advantage that the statistical model accounts for each individual’s age and, hence, each individual’s strength at the respective age. However, this might also have introduced interactions between pain and aging into the model (slope of the regression equation). We therefore used a subcohort with no knee pain and radiographic changes (WOMAC=0, KLG=0) to circumvent such potential influences. Further, directly adjusting strength to the mean of the cohort, allowed the calculations of differences in directly age-adjusted strength values across MCID strata.

A strength of our study design was that it enabled us to assess the pain-related reduction in age-adjusted strength in a very large cohort at risk of or with established KOA (comprising all KLGs), and across a wide range of WOMAC knee pain scores. The WOMAC knee pain score is a thoroughly validated[27,28] and extensively applied tool for assessing patient-reported pain with a well-defined MCID[29]. An additional advantage was the knee-specific application of the questionnaire for the OAI. For the linear regression models, the WOMAC knee pain score was treated as continuous variable. However, for the question of the linearity of the pain-strength-relationship the MCID, although originally established as a measure to follow-up participants over time, provided a means to estimate a difference in strength in the context of a validated and relevant difference in knee pain.

Another limitation of the current study is the use of isometric strength. Compared to isometric strength, isokinetic strength might have the advantage of a potentially stronger correlation to lower leg function[36] which, in turn, is largely determined by knee pain[8] as WOMAC knee pain and WOMAC function scores are highly correlated (R=0.85 in women; R=0.78 in men) in the OAI cohort[8]. Hence, isokinetic training was shown to be more effective for strength and pain improvement than isometric training[37]. However, isometric strength measurements are robust – especially when using more than one trial[38] – and easy to apply in a large cohort such as the OAI[22]. Knee pain during an actual isokinetic strength measurement may be affected by the angular velocity[39] and decreases strength measures[40], whereas for isometric strength it was suggested that knee pain does not significantly affect the actual measurement[41].

For the current study, we did account for the influence of weight[42] on thigh muscle strength as well as on knee pain[43] by normalizing torque to body weight. Torque was used for this purpose to attain the most appropriate scaling with body weight (mass) with Newton-meter:body weight as 1:1[26,44]. In the OAI, no data on muscle mass was acquired to directly normalize strength to the actual mass of the muscles. However, the overall body mass might be the better surrogate for interpersonal differences as it may also take into account obesity[26], which in turn favors knee pain[45]. Therefore, the actual body mass may also be more important in view of functional limitations, which are mainly driven by knee pain[8], as it allows a better estimate of the work the muscles have to exert[26]. Unfortunately, the distance between the axis of rotation and the application of force was not available from the OAI database, but the distance between the transducer and the knee joint line was available and was used for this analysis. Yet, we assume that both distances are highly related and that therefore the correlations are not affected, albeit absolute values may differ for both measurements. Further, similar results were observed for actual strength measures and torque/body weight. Hence, this consistency between both measures, i.e. actual force (N) and torque/body weight (Nm/kg), suggests that both ways provide an appropriate tool to evaluate pain-strength-relations.

We did not adjust for KLG in the analyses, as we previously[5] found the association of knee pain with strength to be independent of the radiographic disease stage (KLG). However, we did adjust for potential confounders of knee pain and strength, i.e. depression[46] and comorbidities[47], but they only explained a minimal portion, if any, of the variability in strength and torque/body weight. The CES-D appeared to have no additional effect, when we also adjusted for comorbidities. This might reflect the high proportion of participants with low scores and a potential inter-relation between comorbidities with depression[48] and also knee pain.

Knee flexor strength was also included in the current analysis, as hamstring strengthening has proven to have additional beneficial effects on the WOMAC knee pain score compared to quadriceps strengthening alone[13,16]. Thus, the observed 2–3% lower flexor strength and torque/body weight per increase of one WOMAC knee pain unit supports previous findings on the importance of flexor strength in context of knee pain in either sex[13,16].

Knee pain and thigh muscle strength are significantly associated with each other. Previous literature has suggested that a reduction in thigh muscle strength may cause knee pain[49]. However, there also is evidence that knee pain causes a reduction in thigh muscle strength[50], with the quantification of specific pain levels across the entire WOMAC range on thigh muscle strength representing the scope of the current study. The current findings suggest that the association of knee pain with thigh muscle strength does not differ between sexes, and that these relations do not appear to be non-linear. This emphasizes that adequate pain treatment is important across the entire range of knee pain levels, with the aim of maintaining muscle strength and of breaking a vicious circle of increasing pain and declining muscle strength and knee function[8]. However, neither men nor women reached the maximum pain score of 20 (1 man with WOMAC=16 and 2 men with WOMAC=15; 1 woman with WOMAC=19 and 2 women with WOMAC=18 as the highest scores). There were only a few participants within the stratum >12 units on the WOMAC knee pain scale and, hence, strength (torque) might plateau when approaching the end of the WOMAC knee pain scale which appears hard to reach even in a large cohort. Our findings of lower strength in the presence of knee pain are in line with previous literature focusing on OAI participants with moderate/severe levels of knee pain in a cross-sectional study design[5,6]: A between-knee, within-person study reported an 8% lower isometric knee extensor strength in painful knees (mean WOMAC= 4.4) versus contra-lateral painless knees (mean WOMAC=0.6). Further, in our previous study, participants with WOMAC≥5 had 11–17% lower knee extensor strength and 9–21% lower flexor strength compared to painless (WOMAC=0) women and men[5]. Hence, the current study extends these findings and suggests that mild levels of knee pain are also associated with lower thigh muscle strength, and that the association between pain and age-adjusted strength does not appear to be non-linear across the spectrum of WOMAC pain scores. However, longitudinal studies are needed for confirmation of these findings.

In conclusion, an approximately 2% lower directly age-adjusted isometric extensor and flexor strength and an approximately 2–3% lower torque/body weight is related to each 1-unit increase on the WOMAC knee pain scale, both in men and women. Comparing WOMAC pain strata across the full observed spectrum did not indicate that the difference in directly age-adjusted isometric muscle strength is non-linear. As a reduction in muscle strength is known to prospectively increase symptoms in KOA and as pain appears to reduce thigh muscle strength, adequate therapy of pain and muscle strength is required in knee OA patients to avoid a vicious circle of self-sustaining clinical deterioration.

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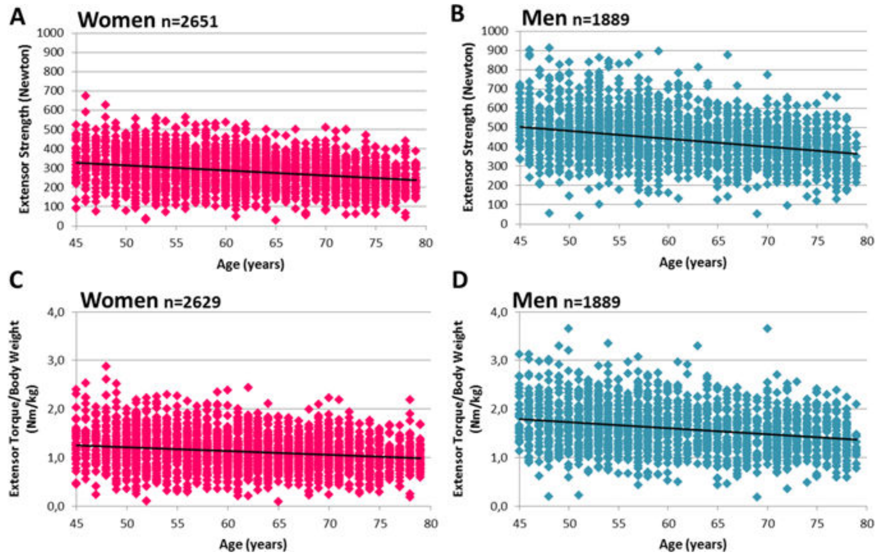

Figure 1.

Scatterplots showing the association between age (X axis) and knee extensor strength (Y axis) for in women **(A)** and in men **(B)** and that between age and isometric knee extensor torque per body weight in women **(C)** and men **(D)**.

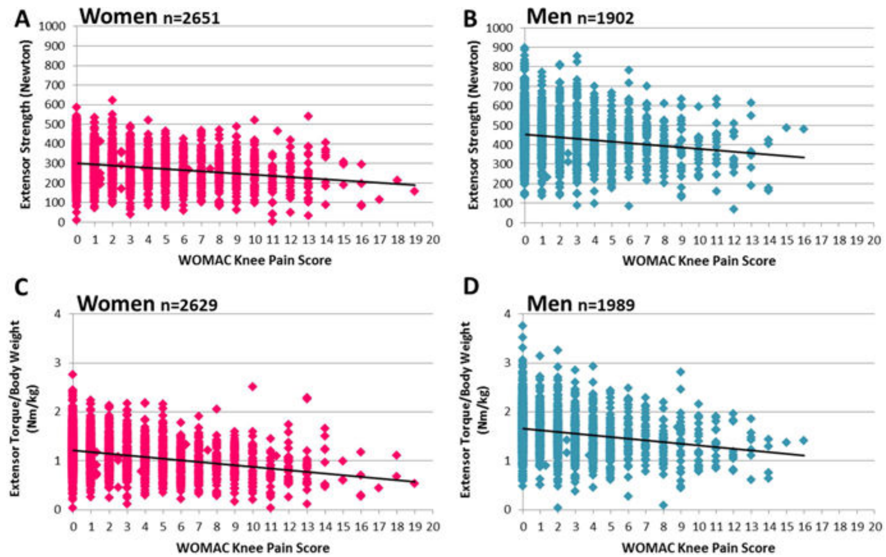

Figure 2.

Scatterplots showing the association between the Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) knee pain score (range 0–20; 20=worst pain; X axis) and age-adjusted knee extensor strength (Y axis) in women **(A)** and in men **(B)** and that of age-adjusted isometric knee extensor torque per body weight in women **(C)** and men **(D)**.

Table 1

Demographic data for women and men for each WOMAC knee pain stratum.

	n	Age years	BMI kg/m^2	Body Height cm	Body Weight kg
WOMEN					
All	2651	61.7 ± 8.9	28.5 ± 5.2	162.2 ± 6.3	75.1 ± 14.6
WOMAC 0	1018	62.4 ± 9.0	27.4 ± 4.9	162.0 ± 6.3	72.0 ± 14.0
WOMAC 1–2	624	61.1 ± 8.8	28.2 ± 4.9	162.4 ± 6.3	74.3 ± 13.8
WOMAC 3–4	379	61.6 ± 8.6	28.7 ± 5.0	162.3 ± 6.5	75.6 ± 14.3
WOMAC 5–6	252	61.2 ± 9.3	29.6 ± 5.1	162.0 ± 6.1	77.9 ± 14.8
WOMAC 7–8	158	62.6 ± 8.9	30.2 ± 4.9	162.2 ± 6.1	79.5 ± 13.5
WOMAC 9–10	113	59.5 ± 8.5	31.7 ± 5.7	162.1 ± 6.9	83.4 ± 16.2
WOMAC 11–12	64	59.5 ± 7.8	31.1 ± 6.0	162.6 ± 6.3	82.2 ± 15.7
WOMAC >12	43	59.9 ± 9.8	32.8 ± 6.2	164.7 ± 7.1	88.5 ± 16.0
MEN					
All	1902	61.1 ± 9.5	28.9 ± 4.1	176.6 ± 8.1	90.1 ± 14.5
WOMAC 0	851	61.2 ± 9.6	28.4 ± 3.9	176.7 ± 6.7	88.7 ± 13.7
WOMAC 1–2	450	61.4 ± 9.4	28.6 ± 4.0	176.8 ± 6.8	89.3 ± 13.9
WOMAC 3–4	284	61.3 ± 9.6	29.2 ± 4.0	176.7 ± 7.5	91.3 ± 14.1
WOMAC 5–6	155	60.3 ± 9.1	29.9 ± 4.4	176.3 ± 6.9	93.1 ± 16.0
WOMAC 7–8	73	60.2 ± 9.2	30.9 ± 4.9	176.3 ± 8.0	96.3 ± 17.5
WOMAC 9–10	50	59.5 ± 9.3	29.9 ± 4.7	175.5 ± 8.7	92.0 ± 15.8
WOMAC 11–12	26	59.0 ± 10.5	30.3 ± 5.0	174.8 ± 6.0	92.8 ± 17.7
WOMAC >12	13	59.5 ± 7.0	32.0 ± 4.2	181.2 ± 5.5	105 ± 15.6

Demographic data for time point of strength measurement, i.e. n=4205 at baseline and n=348 at year 1 follow-up; n=participant number; BMI=body mass index; kg/m^2= kilogram per meter^2; cm=centimeter;

Table 2

Women: Strength and torque/body weight (age-adjusted values in brackets) in WOMAC strata, with percent differences to WOMAC 0 and to the next lower WOMAC stratum.

WOMAC Pain Strata		**%Diff vs WOMAC =0‡**	**Cohen d‡**		**%Diff vs next WOMAC$^{\Delta,‡}$**			**%Diff vs WOMAC =0‡**	**Cohen d‡**	**%Diff vs next WOMAC$^{\Delta,‡}$**
	Extensor Strength					**Flexor Strength**				
0	300±86	(304±81)	ref.	ref.		118±46	(119±44)	ref.	ref.	
1–2	291±89	(290±85)	−4.4	−0.16	−4.4	116±47	(115±45)	−3.6	−0.10	−3.6
3–4	273±85	(273±81)	−9.9	−0.37	−5.8	108±47	(108±46)	−9.5	−0.26	−6.2
5–6	268±85	(267±83)	−12.0	−0.45	−2.4	101±45	(100±44)	−15.9	−0.44	−7.1
7–8	253±88	(256±87)	−15.6	−0.58	−4.0	98±46	(99±44)	−16.8	−0.46	−1.0
9–10	266±89	(260±89)	−14.4	−0.36	+1.4	100±42	(97±44)	−19.0	−0.31	−2.7
11–12	228±88	(222±90)	−26.9	−1.00	−14.7	75±47	(72±46)	−39.7	−1.08	−25.5
>12	235±105	(230±107)	−24.2	−0.89	+3.8	87±56	(84±58)	−29.4	−0.80	+17.0
	Extensor Torque/BW					**Flexor Torque/BW**				
0	1.22±0.4	(1.23±0.4)	ref.	ref.		0.48±0.2	(0.48±0.2)	ref.	ref.	
1–2	1.15±0.4	(1.15±0.4)	−6.3	−0.22	−6.3	0.46±0.2	(0.46±0.2)	−5.4	−0.14	−5.4
3–4	1.06±0.4	(1.06±0.3)	−13.3	−0.46	−7.5	0.42±0.2	(0.42±0.2)	−13.0	−0.33	−8.1
5–6	1.01±0.3	(1.01±0.3)	−17.8	−0.61	−5.2	0.38±0.2	(0.38±0.2)	−21.1	−0.54	−9.3
7–8	0.94±0.3	(0.94±0.3)	−23.0	−0.79	−6.3	0.36±0.2	(0.36±0.2)	−24.5	−0.63	−4.3
9–10	0.95±0.4	(0.93±0.3)	−24.0	−0.66	−1.3	0.35±0.1	(0.35±0.2)	−28.2	−0.52	−4.9
11–12	0.84±0.3	(0.82±0.3)	−33.1	−1.13	−12.0	0.27±0.2	(0.27±0.1)	−44.9	−1.15	−23.3
>12	0.85±0.5	(0.84±0.5)	−31.5	−1.06	+2.5	0.31±0.2	(0.30±0.2)	−37.0	−0.93	+14.4

Mean±standard deviation; %Diff=percent difference; WOMAC=WOMAC knee pain score; ref=reference; BW= body weight;

$^{\Delta}$compared to the next lower WOMAC stratum (1–2 vs 0; 3–4 vs 1–2; 5–6 vs 3–4,…);

‡calculated using age-adjusted strength values

Table 3

Men: Strength and torque/body weight (age-adjusted values in brackets) in WOMAC strata, with percent differences to WOMAC 0 and to the next lower WOMAC stratum.

WOMAC Pain Strata			%Diff vs WOMAC =0‡	Cohen d‡	%Diff vs next WOMAC$^{\Delta,‡}$			%Diff vs WOMAC =0‡	Cohen d‡	%Diff vs next WOMAC$^{\Delta,‡}$
	Extensor Strength					**Flexor Strength**				
0	459±130	(458±124)	ref.	ref.		192±77	(192±76)	ref.	ref.	
1–2	431±123	(431±116)	−5.9	−0.22	−5.9	177±74	(177±72)	−7.8	−0.20	−7.8
3–4	423±129	(423±121)	−7.7	−0.29	−1.9	175±72	(175±69)	−8.6	−0.22	−0.9
5–6	416±123	(412±115)	−10.2	−0.38	−2.6	183±75	(181±72)	−5.6	−0.14	+3.3
7–8	415±117	(410±114)	−10.5	−0.39	−0.4	159±73	(157±72)	−18.2	−0.46	−13.3
9–10	385±121	(377±117)	−17.8	−0.66	−8.1	159±68	(156±66)	−18.8	−0.48	−0.7
11–12	386±125	(375±129)	−18.1	−0.67	−0.5	156±62	(152±64)	−20.8	−0.53	−2.4
>12	380±128	(371±143)	−19.0	−0.70	−1.0	165±68	(162±73)	−15.6	−0.40	+6.5
	Extensor Torque/BW					**Flexor Torque/BW**				
0	1.68±0.5	(1.68±0.5)	ref.	ref.		0.70±0.3	(0.70±0.3)	ref.	ref.	
1–2	1.58±0.5	(1.58±0.5)	−5.7	−0.21	−5.7	0.65±0.3	(0.65±0.3)	−7.5	−0.20	−7.5
3–4	1.50±0.5	(1.50±0.4)	−10.5	−0.39	−5.1	0.62±0.3	(0.62±0.2)	−11.2	−0.30	−4.0
5–6	1.46±0.4	(1.45±0.4)	−13.7	−0.50	−3.6	0.63±0.2	(0.63±0.2)	−10.3	−0.27	+1.1
7–8	1.43±0.4	(1.41±0.4)	−15.7	−0.58	−2.3	0.55±0.2	(0.54±0.2)	−22.3	−0.58	−13.3
9–10	1.38±0.5	(1.36±0.5)	−18.8	−0.68	−3.7	0.57±0.3	(0.56±0.2)	−19.6	−0.51	+3.5
11–12	1.41±0.4	(1.37±0.4)	−18.1	−0.66	+0.8	0.57±0.2	(0.55±0.2)	−21.5	−0.56	−2.4
>12	1.27±0.3	(1.24±0.4)	−25.8	−0.94	−9.3	0.55±0.2	(0.54±0.2)	−23.2	−0.60	−2.1

Mean±standard deviation; %Diff=percent difference; WOMAC=WOMAC knee pain score; ref=reference; BW= body weight;

$^{\Delta}$compared to the next lower WOMAC stratum (1–2 vs 0; 3–4 vs 1–2; 5–6 vs 3–4,…)

‡calculated using age-adjusted strength values