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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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SUMMARY

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 (OAI) 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 OAI 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 (KOA) and as pain appears to reduce thigh muscle strength, adequate therapy of pain and muscle strength is required in KOA patients to avoid a vicious circle of self-sustaining clinical deterioration.
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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].

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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 socio-economic 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 2 cm 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 to 20 (0 = no pain)[27,28]. This subscale of the total WOMAC score comprises five questions (Likert scale), each rated from 0 to 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 7 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; <1 day) to 4 (=most or all of the time; 5–7 days). 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 (Eq. (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 (Eq. (2)). By entering 45 in the regression equation, we calculated the strength at age 45 (Eq. (3)).

For the direct age-adjustment, we used the slope coefficient calculated in the previous analysis (Eq. (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 (Eq. (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 (Eq. (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

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