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REDUCTION IN THIGH MUSCLE STRENGTH OCCURS CONCURRENTLY, BUT DOES NOT APPEAR TO PRECEDE INCIDENT KNEE PAIN IN WOMEN: DATA FROM THE OSTEOARTHRITIS INITIATIVE COHORT

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Abstract

Objective: To investigate whether muscle strength declines prior to or concurrent with incident knee pain in subjects with and without radiographic knee osteoarthritis (RKO).

Design: Osteoarthritis Initiative participants with incident knee pain (occurrence of infrequent/frequent knee pain during the past 12 months at two consecutive follow-up time points [either years[Y] 3+4 or Y4+5]) were compared to controls (no incident knee pain) with 2-year changes in knee extensor strength during BL→Y2 (prior) and Y2→Y4 (concurrent).

Results: 202 knees (49% women; 40% RKO) displayed incident pain, 439 did not (46% women; 23% RKO). Women with RKO displayed a significantly greater ($p=0.04$) reduction in knee extensor strength concurrent with incident pain compared with controls (mean -17.6 Newton vs $+4.5$ Newton), but men did not. A similar trend was observed in women without RKO - but this was not statistically significant ($p=0.08$). There was no significant relationship with change in extensor strength prior to incident pain ($p=0.43$).

Conclusion: These results suggest that, in women, incident knee pain is accompanied by a concurrent reduction in knee extensor strength, whereas loss in strength does not precede incident knee pain. The findings encourage interventional studies that attempt to attenuate a decline in extensor strength once knee symptoms occur.

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Keywords

thigh muscle strength; osteoarthritis; knee pain; incident pain; strength decline

INTRODUCTION

Knee pain is the most common reason why patients with knee osteoarthritis (KOA) seek medical care¹; it has a substantial impact on the quality of life² and forces patients to modify their daily routines such as stair climbing or simply walking³. Thigh muscle weakness is known to be associated with knee pain, once the latter is consistently present, potentially by mechanisms of insufficient joint stabilization during dynamic activities⁴⁻⁶.

Steidle et al.⁷ reported that the presence of knee pain even in only one limb has been shown to have a “global” impact on thigh muscle strength. Further, the within person between-knee comparison revealed a more than 6% lower quadriceps strength in the painful compared to the painless limb⁷. This was also shown by other cross-sectional studies on the Osteoarthritis Initiative (OAI) with strength differences ranging from 7 to 13% between the painful and painless limbs^{6,8}. However, it is still unclear, whether a decline in extensor muscle strength precedes and/or is associated with the onset of pain, or whether it is a sequelae of the knee being painful and potentially less used. Unraveling the exact time sequence of these relationships is important, as muscle strength is a modifiable risk factor - which has already shown to be capable of improving knee pain^{9,10} - and, hence, an important player in the management of OA additionally to pharmacological treatment¹⁰.

In longitudinal studies, using OAI data, lower thigh muscle strength was reported to increase the risk for symptomatic deterioration and for surgical knee replacement in women, but not in men^{4,11}. Yet, in a study of persistent, i.e. chronic, pain¹², a potential window during which a change in muscle strength may have occurred, may have been missed¹² indicating the importance of focusing on an early stage of the disease.

Studies of the association between muscle strength and incident knee pain have produced somewhat conflicting results: While knee extensor weakness at baseline was significantly associated with combined incident knee symptoms and radiographic KOA in women over the next 30 months in the Multicenter KOA (MOST) cohort¹³, it was not associated with incident knee symptoms assessed independently of radiographic change over this observation interval in the same cohort¹⁴. Notably, no previous study has examined the longitudinal change in thigh muscle strength during a time interval prior to the onset of knee pain. Given large differences in strength between people¹⁵, however, the longitudinal change in muscle strength may be more sensitive in identifying a relationship with incident symptoms than strength measured at only one point in time^{13,14}. The current study therefore aimed to test the hypothesis that a longitudinal decline in thigh muscle strength occurs prior to, or concurrent with, incident knee pain.

METHODS

Participants

For participant selection, we used the OAI database (clinical data releases 0.2.2, 1.2.2, 3.2.2, 5.2.2, and 7.2.2; <http://www.oai-ucsf.edu>; approval by the International review Board of University of California San Francisco, approval number 10-00532). This database comprises 4,796 men and women aged 45–79 years from various socio-economic and ethnic backgrounds. Detailed inclusion/exclusion criteria for this cohort have been described previously¹⁶. Participants encompassed a so-called incident cohort at risk of developing symptomatic KOA (n=3,284), a progression cohort with already established symptomatic KOA at baseline in at least one knee (n=1,390), and a healthy reference cohort without (risk factors for) KOA (n=122)¹⁶.

Of the 9,592 knees (4,796 participants), we excluded those participants without baseline, year 2 or year 4 data on age, body mass and body mass index (BMI) (Figure 1). Other exclusions were missing data on pain frequency (OAI variable KXSX) and ii) pain intensity evaluated by the numeral Rating Scale (NRS; ranging from 0–10 with 10 being the worst pain during the last month) at baseline (BL) as well as at year (Y) 1, Y2, Y3, and Y4 of follow-up (FU); and a missing Kellgren-Lawrence grade reading at Y2, i.e. the last time point at which all selected participants were without knee pain (see below and Figure 1). Finally, knees were required to have complete data on isometric extensor and flexor strength at BL, Y2, and Y4 (Figure 1). The current study conforms to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist).

Definition of incident knee pain

For the definition of incident knee pain, we used the symptom frequency variable (Sx) in the OAI. The symptom frequency question is a knee-specific self-assessment regarding pain, aching or stiffness in or around the knee within the last 12 months – covering the longest period of time of all OAI pain variables. In the current study, incident knee pain knees (cases) were defined as absence of knee pain at Y1 and Y2 (i.e. SX=0), with the development of infrequent (SX=1) or frequent pain (SX=2) at Y3 or Y4 (Figure 2). In order to exclude knees with fluctuating pain, pain (SX1 or 2) was required to persist at least for another year after its first incidence (at Y4 when first occurring at Y3, or at Y5 when first occurring at Y4) (Figure 2). Only one knee per participant was included in the statistical analysis (Figure 1). If both knees qualified as case, the one with the higher pain frequency (SX=2) was selected. In cases of equal pain frequency, the knee with the greater pain severity (i.e. higher NRS) was chosen. In cases of equal Sx and NRS status, the right knee was selected (Figure 1). Control knees were defined as having no pain (SX=0) at all time points (BL, Y1, Y2, Y3, Y4). In participants with one case and one control knee, only the case knee was included (Figure 1).

Measurement of isometric thigh muscle strength

For the evaluation of thigh muscle strength, OAI participants had been seated upright in the “Good Strength Chair” (Metitur Oy, Jyväskylä, Finland) with the thigh and pelvis fixed^{6,8,17} and knee flexed at 60°. The load cell was attached 2cm proximal to the calcaneus. After

three trials of 50% effort for familiarization, the highest value of three trials with 100% effort was recorded as the maximum isometric knee extensor and flexor strength (Newtons) and used for the current study. Please note that strength measurements were only obtained biannually and not at every follow-up visit in the OAI.

Statistical Analysis

As previous studies observed a different relationship between muscle strength and pain in people with and without radiographic KOA¹⁸, participants were stratified for the radiographic status at Y2 (i.e. the KLG), specifically those with definite radiographic KOA (i.e. KLG 2–4) and those without (i.e. KLG 0 and 1). As previous studies observed sex-differences with regard to the association of knee symptoms and thigh muscle strength^{4,5}, analyses were performed for men and women separately. The 2-year change in strength (Newtons) prior to (i.e. from BL→Y2) and concurrent with (i.e. from Y2→Y4) incident knee pain was determined. Longitudinal changes were the primary analytic focus of the current study, whereas a secondary focus was the cross-sectional comparison of knee extensor strength between cases and controls at Y2 (i.e. prior to incident knee pain). ANCOVA analyses were performed using SPSS (SPSS Statistics 22, IBM, Armonk, NY, USA), adjusting for baseline or Y2 age or body mass as covariates. Within-group longitudinal changes in strength were tested for statistical significance (difference from zero) using two-sided, paired t-tests. As knee flexor strength has also been shown to be associated with symptomatic progression of KOA in at least one study⁵, exploratory analyses for knee flexor strength were performed. For exploratory purposes, analyses were repeated using knee extensor and flexor torque/body mass (with age as covariate). Pearson correlation coefficients for 2-year changes in knee extensor strength and 2-year changes in the Physical Activity Scale for the Elderly (PASE) score were calculated.

RESULTS

Demographics

202 knees (49% from women, 40% with radiographic KOA) were included as cases with incident knee pain. Of these, 145 had incident infrequent knee pain (n=99 at Y3 and n=46 at Y4) and 57 incident frequent knee pain (n=34 at Y3, n=23 at Y4). 439 knees (46% from women, 23% with radiographic KOA) qualified as controls. Demographic data for women and men with and without radiographic KOA are shown in Table 1. At Y2, 87 case and 244 control knees were KLG 0 (49% and 47% women), 34 and 93 were KLG 1 (56% and 45%), 55 and 79 were KLG 2 (45% and 46%), 26 and 23 were >KLG2 (46% and 43%).

Incident pain in knees without radiographic KOA

Between baseline and Y2 (prior to incidence), female knees with incident pain displayed an increase in thigh extensor muscle strength (+3.0% 95% confidence interval [CI] [0.3, 5.7%]) that appeared to be statistically significantly greater (p=0.049) than the longitudinal change in knee extensor strength in control knees (−6.7% 95% CI [−9.5, −3.9%]) (Table 2, Figure 3A). The longitudinal change of knee extensor strength in men with incident knee pain, however, did not significantly differ from that observed in the controls (p=0.37) (Table 2, Figure 3B). From Y2 to Y4 (concurrent with incidence), women and men with incident knee

pain tended to show a greater loss in knee extensor strength of -6.8% , 95%CI $(-9.7, -3.9\%)$ and -5.0% , 95%CI $(-7.4, -2.6\%)$ compared to controls with -1.7% 95%CI $(-3.2, -0.2\%)$ and -0.7% 95%CI $(-2.0, 0.6\%)$ (Table 2, Figure 3AB), and although these changes in cases were statistically significantly different from zero, differences between groups were not statistically significantly different from each other. Comparable results were observed for knee extensor torque/body mass in both sexes (Table 2). There were no statistically significant differences between groups in knee flexor strength or torque/body mass at either time period in either sex (Table 2).

Incident pain in knees with radiographic KOA

From BL to Y2, changes in knee extensor strength did not statistically significantly differ between cases and control knees in either sex (Table 3, Figure 3AB). From Y2 to Y4, women with incident knee pain displayed a decline in knee extensor strength that was statistically significantly different from zero (-6.6% 95%CI $[-9.2$ to $-4.0\%]$, $p=0.01$) and was statistically significantly greater ($p=0.04$) than that observed in control knees ($+1.7\%$ 95%CI $[0.1, 3.4\%]$). This was not the case in men, in which the loss was much less: -1.3% $[-3.7$ to $+1.2\%]$, and did not differ significantly from that in control knees ($p=0.85$) (Table 3, Figure 3AB). Comparable results were observed for knee extensor torque/body mass in either sex (Table 3). Again, there were no statistically significant differences between groups in knee flexor strength or torque/body mass at either time period in either sex (Table 3).

In knees with incident knee pain and radiographic knee OA the correlations did not indicate a linear relationship between 2-year changes in knee extensor strength and the PASE score and were $R=-0.09$ (95%CI $[-0.40, 0.25]$, $p=0.61$) in women and $R=+0.30$ (95%CI $[0.00, 0.55]$, $p=0.049$) in men for BL→Y2 and $R=-0.25$ (95%CI $[-0.53, 0.08]$, $p=0.13$) and $R=+0.16$ (95%CI $[-0.14, 0.44]$, $p=0.30$) for Y2→Y4. Comparable small and non-significant correlations were observed for control knees and case knees without radiographic KOA in either stratum ($p=0.09$) (data not shown).

Cross-sectional comparison at Y2

At Y2, i.e. the last follow-up visit at which the participants were without knee pain, we observed no statistically significant differences in knee extensor and flexor strength between case and control knees regardless of the radiographic status; this applied to both women ($p=0.70$) and men ($p=0.21$) (Tables 2 & 3). In men without radiographic KOA knee extensor torque/body mass was 6% lower in cases compared to control knees ($p=0.049$), but this was not the case in women (Table 2).

DISCUSSION

This is the first study to examine longitudinal changes in thigh muscle strength during an observation period prior to incident knee pain. Here we show that, in women with radiographic KOA prior to the onset of pain, a loss of knee extensor strength occurred concurrently with, but not prior to, the incident knee pain observation interval. While similar relationships were observed in knees without radiographic KOA prior to the onset of knee

pain, the differences with control knees failed to reach statistical significance. No such associations were found in men.

With almost 10,000 knees with longitudinal follow-up available from the OAI, we were able to apply very specific inclusion criteria to study a cohort of 202 cases and 439 control knees with and without incident knee pain after a first longitudinal measurement period of muscle strength. The strict definition of incident pain, i.e. pain needed to persist at least one subsequent follow-up visit, enabled us to account for short-lived fluctuations in knee pain¹⁹ and potential personal/emotional factors influencing the perception or reporting of knee pain²⁰. The extended period of time during which pain was evaluated at each time point (i.e., previous 12 months) was paralleled by other measures of pain (over shorter periods) in the OAI (i.e., WOMAC pain during past 7 or 30 days)^{6,21}, and the rather long observation interval potentially allowed (greater) concurrent changes in muscle strength to occur. We also included participants who reported infrequent pain as incident pain cases, as infrequent pain also can have a profound impact on quality of life². Further, analysis only including cases with frequent pain showed comparable results (data not shown). Another strength of the study design is the longitudinal analysis of thigh muscle strength prior to incident knee pain, using each participant as her/his own control, and thus removing potential bias or variability from between-person differences in muscle status and pain (perception)²², which may be influenced by age²³, sex or body mass¹⁵.

A limitation of the current study is the length of the observation periods for muscle strength (2-years), as the onset of pain may have occurred in the early parts of the 2-year window, whereas when the exact change in muscle strength occurred during this period is unknown. The presence of pain at final follow-up may have impaired participants from providing a maximal strength effort due to discomfort. Previous findings suggest that mild knee pain during strength measurements did not affect the relation between thigh muscle strength and knee function²⁴, indicating that strength measurements in the presence of mild knee pain are valid and clinically relevant²⁴. However, in cases with moderate to severe pain the above relation was weakly affected²⁴, and the current findings should be interpreted with caution. However, only 5 participants displayed a WOMAC knee pain score 10 at year 4, making a major impact of pain during the strength measurement unlikely. Also, we were unable to compare longitudinal changes of strength to those of the 122 healthy control OAI participants, as only a small number had strength measurements throughout the clinical follow-up visits (i.e., n=3 at year 4). Extrapolating from natural aging-related muscle strength loss in other longitudinal cohorts of healthy adults (2–3% per annum)²³ the changes observed in the controls of the current study appear to be generally within these ranges (2–5% over 2 years), and within the range extrapolated from a cross-sectional study on OAI participants²¹. In contrast, female knees with incident pain appeared to exceed this normal rate of loss in extensor strength by a factor of ~2, suggesting that there exists a period of much more rapid longitudinal decline in muscle strength around the time when a knee becomes painful.

Previous prospective studies on the relationship between baseline muscle strength deficits and incident knee symptoms are somewhat conflicting, likely reflecting different inclusion criteria with regard to radiographic status/progression and different outcome measures of

pain, i.e. symptomatic knee OA¹³ or mere knee symptoms¹⁴. However, they appear to be in agreement with our findings that declines in muscle strength with incident pain are more pronounced in knees with radiographic change¹³ rather than in those without¹⁴. The current study extends these previous investigations by evaluating longitudinal changes in thigh muscle strength prior to incident knee pain. We are unsure about the reason for the observed gain in muscle strength in female knees prior to incident knee pain, but a similar phenomenon has been previously observed in knees prior to loss in function²⁵. However, although the underlying mechanism underpinning this association is not known, it may represent a regression-to-the-mean phenomenon. Although we cannot identify with certainty, whether during the interval concurrent with incident knee pain, loss in extensor strength precedes or follows the onset of pain, our study provides the first evidence that, in women, loss in strength occurs around the time of incident knee pain, and does not appear to precede the onset of pain by several years. This finding concurs with observations made on a decline in function²⁵.

The current findings suggest that thigh muscle strength may decrease due to pain avoidance²⁶ and perhaps disuse once knee pain is present, rather than being a cause of pain. Gait changes³ (e.g., less knee excursion) and histological changes, such as muscle fiber degeneration and selective loss of type-2 fibers²⁶ have been reported previously in association with pain avoidance²⁷, and in muscle inhibition due to pain²⁸. Yet, this was not reflected in changes in the PASE score – the only measure for patient reported physical activity available for the OAI cohort.

Several training intervention studies have reported the beneficial effects of strengthening exercises on knee symptoms^{10,29,30}. A systematic review including 45 trials found increases in thigh muscle strength of at least 30–40% to be effective to relevantly decrease knee pain²⁹. Interestingly though, lower limb muscle strengthening programs did not appear to reduce the risk of knee pain development in younger athletic and military populations³⁰. These findings suggest that muscle strengthening interventions may be more effective in improving symptoms rather than preventing them.

Our study adds to the growing body of evidence that muscle strength appears to be a more relevant element in knee health in women as compared with men. Muscle weakness previously was shown to increase the risk of symptomatic progression and decline in function⁵ and of surgical knee replacement⁴ in women, but not men. The observed sex-differences may result from the lower thigh muscle strength in women (as also observed in the current study), placing them closer to an (unknown) threshold for concurrent knee pain onset. Alternatively, joints of women may have a greater laxity than men and muscle strength may thus be more relevant for joint stabilization than in men, in whom joint stability may be conveyed by other factors such as the joint capsule and ligaments.

In contrast to knee extensor strength, we did not find any relationship between incident knee pain and prior or concurrent loss of knee flexor strength. In contrast to a previous cross-sectional study identifying knee flexor strength to be an independent determinant of knee function in KOA and to decrease with increasing pain²¹, the current study did not find any evidence that knee flexor strength is associated with incident knee pain. This may be due to

the “anti-gravitational” nature of the extensor muscles and their more direct relationship with joint loading, which may render them more prone to slight “disuse” in context of incident pain.

In conclusion, the current findings suggest that, in women, incident knee pain is accompanied by a decline in isometric knee extensor strength and that more so in the presence of radiographic KOA. However, incident knee pain does not appear to be preceded by a reduction in strength that occurs several months / years before. These findings may indicate that muscle strengthening interventions may be more effective in improving symptoms rather than preventing them. The findings encourage interventional studies that attempt to attenuate a decline in quadriceps strength once knee symptoms occur.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosure of interest

The image and clinical data were acquired by the OAI ([Clinicaltrials.gov](https://clinicaltrials.gov) identification:), a public-private partnership comprised five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institute of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners of the OAI include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institute of Health.

Dr. Eckstein is CEO/CMO and co-owner of Chondrometrics GmbH, and he has provided consulting services to Merck KGaA, Samumed, Tissuegene, Servier, and Roche. He also has received speaker honoraria from Medtronic. Dr. Wirth is part-time employed and is co-owner of Chondrometrics GmbH, and provides consulting services to MerckSerono.

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PAIN INCIDENCE**Participant Selection** **Figure 1. Participant selection**

for cases with knee pain incidence at year 3 or 4 and control knees with no pain throughout the observation period. For the selection process pain frequency (SX), Numeral Rating Scale (NSR), Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) knee pain score, and isometric thigh muscle strength were used. KLG=Kellgren-Lawrence grade.

Figure 2. Study design:

Cases had no knee pain from baseline to year 2 but reported incident knee pain, i.e. frequent or infrequent knee pain, at year 3 or year 4 that needed to persist the subsequent follow-up time point. Controls had no knee pain throughout baseline to year 4.

Figure 3. AB:

2-year % changes (with 95% confidence intervals) in knee extensor strength in women and men without and with established radiographic knee osteoarthritis (OA) in the time prior (baseline [BL] to year 2 [Y2]) and concurrent (Y2 to Y4) to the incidence of knee pain. The asterisks indicate $p < 0.05$ for BL vs Y2 or Y2 vs Y4.

Table 1.

Demographic data (mean±standard deviation) and Kellgren-Lawrence grades (KLGs) at baseline for case knees with incident pain at year 3 or year 4 of follow-up and control knees with no pain incidence in women and men and with/ without radiographic knee osteoarthritis (OA).

	WOMEN		MEN	
	Cases	Controls	Cases	Controls
NO radiographic knee osteoarthritis				
	n=62	n=157	n=59	n=180
Age (years)	63.3 ± 7.8	62.9 ± 8.7	60.9 ± 9.7	62.4 ± 9.4
Body Mass (kg)	71.0 ± 12.4	69.8 ± 13.0	91.7 ± 13.6	85.8 ± 12.2
Body Mass Index (kg/m ²)	26.8 ± 4.2	26.9 ± 4.8	29.3 ± 3.7	27.6 ± 3.6
Radiographic knee osteoarthritis				
	n=37	n=46	n=44	n=56
Age (years)	65.5 ± 7.8	67.1 ± 9.9	61.8 ± 7.3	67.1 ± 8.5
Body Mass (kg)	77.2 ± 14.3	73.6 ± 15.1	94.5 ± 13.4	88.0 ± 16.0
Body Mass Index (kg/m ²)	29.4 ± 5.2	28.3 ± 5.1	30.3 ± 4.5	28.6 ± 4.2

n=participant number, kg=kilogram, m=meter

Table 2.

Women and men without radiographic knee osteoarthritis (OA). Knee extensor and flexor strength and torque/body mass at baseline (BL), year 2 (Y2), and year 4 (Y4) and two-year percent changes in cases with incident pain and controls without incident pain.

	WOMEN			MEN		
	Cases (n=62)	Control (n=157)	p	Cases (n=59)	Controls (n=180)	p
EXTENSOR STRENGTH						
BL	275 (263, 288)	290 (283, 298)		464 (444, 483)	461 (449, 473)	
Y2	283 (271, 296)	280 (274, 287)	0.76	433 (415, 450)	440 (430, 450)	0.21
Y4	264 (253, 275)	276 (269, 282)		411 (393, 429)	437 (427, 446)	
% BL→Y2	+3.0 (0.3, 5.7)	-3.4 (-5.1, -1.7)	0.049	-6.7 (-9.5, -3.9)*	-4.6 (-6.1, -3.2)*	0.37
% Y2→Y4	-6.8 (-9.7, -3.9)*	-1.7 (-3.2, -0.2)	0.08	-5.0 (-7.4, -2.6)*	-0.7 (-2.0, 0.6)	0.11
FLEXOR STRENGTH						
BL	108 (103, 114)	116 (111, 120)		209 (198, 221)	197 (190, 204)	
Y2	105 (100, 111)	107 (103, 110)	0.92	175 (166, 185)	173 (168, 178)	0.90
Y4	99 (94, 104)	101 (98, 105)		171 (162, 181)	160 (156, 165)	
%BL→Y2	-2.9 (-6.5, 0.7)*	-8.0 (-10, -5.7)	0.22	-16 (-20, -12)*	-12 (-14, -9.6)*	0.25
%Y2→Y4	-6.1 (-9.9, -2.2)	-4.9 (-7.3, -2.5)*	0.79	+2.3 (-5.9, 1.4)	-7.5 (-10, -4.9)*	0.27
EXTENSOR TORQUE/BODY MASS						
BL	1.16 (1.10, 1.22)	1.19 (1.16, 1.23)		1.64 (1.57, 1.71)	1.72 (1.67, 1.76)	
Y2	1.18 (1.13, 1.24)	1.16 (1.13, 1.19)	0.62	1.54 (1.47, 1.60)	1.64 (1.61, 1.68)	0.049
Y4	1.10 (1.05, 1.15)	1.14 (1.11, 1.17)		1.45 (1.39, 1.52)	1.63 (1.59, 1.67)	
% BL→Y2	+2.1 (-0.6, 4.8)	-2.8 (-4.6, -1.1)	0.14	-6.1 (-9.0, -3.1)*	-4.3 (-5.7, -2.8)*	0.58
% Y2→Y4	-6.8 (-9.8, -3.7)*	-1.4 (-2.9, 0.2)	0.08	-5.5 (-8.1, -2.9)*	0.9 (-2.1, 0.4)	0.10
FLEXOR TORQUE/BODY MASS						
BL	0.46 (0.43, 0.49)	0.48 (0.46, 0.49)		0.74 (0.70, 0.78)	0.73 (0.71, 0.76)	
Y2	0.44 (0.42, 0.47)	0.44 (0.43, 0.45)	0.87	0.62 (0.59, 0.65)	0.65 (0.63, 0.67)	0.28
Y4	0.41 (0.39, 0.44)	0.42 (0.41, 0.44)		0.60 (0.57, 0.64)	0.60 (0.58, 0.62)	
%BL→Y2	-3.0 (-6.7, 0.8)*	-7.6 (-10, -5.2)	0.30	-16 (-20, -12)*	-12 (-14, -9.5)*	0.32
%Y2→Y4	-6.3 (-10, -2.2)	-4.2 (-6.7, -1.7)	0.66	-2.8 (-6.6, 1.1)	-7.2 (-9.8, -4.7)*	0.34

Extensor & Flexor strength in Newton; Extensor & Flexor torque/body mass in Newton/kilogram

p value for ANCOVA for cases versus controls

* p for BL versus Y2 follow-up and Y2 versus Y4 of follow-up, respectively < 0.05

Table 3.

Women and men with radiographic knee osteoarthritis (OA). Knee extensor and flexor strength and torque/body mass at baseline (BL), year 2 (Y2), and year 4 (Y4) and two-year percent changes in cases with incident pain and controls without incident pain.

	WOMEN			MEN		
	Cases (n=37)	Control (n=46)	p	Cases (n=44)	Controls (n=56)	p
EXTENSOR STRENGTH						
BL	285 (269, 300)	289 (282, 296)		432 (416, 447)	423 (414, 433)	
Y2	266 (251, 281)	261 (255, 266)	0.86	434 (418, 449)	405 (396, 414)	0.98
Y4	249 (236, 261)	265 (259, 271)		428 (412, 444)	396 (388, 405)	
% BL→Y2	-6.5 (-9.8, -3.1)	-9.8 (-12, -8.0)*	0.47	0.4 (-2.0, 2.8)*	-4.4 (-5.9, -2.9)	0.43
% Y2→Y4	-6.6 (-9.2, -4.0)*	+1.7 (0.1, 3.4)	0.04	-1.3 (-3.7, 1.2)	-2.1 (-3.3, -0.9)	0.85
FLEXOR STRENGTH						
BL	114 (107, 121)	109 (105, 113)		192 (182, 202)	175 (169, 180)	
Y2	107 (100, 115)	102 (99, 105)	0.70	169 (160, 178)	156 (151, 161)	0.97
Y4	101 (94, 107)	100 (97, 103)		171 (162, 181)	146 (141, 151)	
%BL→Y2	-6.0 (-10, -1.9)	-6.5 (-9.0, -4.0)	0.91	-12 (-16, -8.0)	-11 (-13, -8.7)	0.85
%Y2→Y4	-5.7 (-8.8, -2.7)	-2.4 (-4.8, -0.1)	0.51	+1.3 (-3.0, 5.5)	-6.2 (-8.3, -4.2)	0.35
EXTENSOR TORQUE/BODY MASS						
BL	1.08 (1.01, 1.15)	1.12 (1.09, 1.15)		1.50 (1.44, 1.56)	1.60 (1.56, 1.64)	
Y2	1.03 (0.95, 1.10)	1.04 (1.01, 1.06)	0.81	1.52 (1.46, 1.59)	1.57 (1.53, 1.61)	0.32
Y4	0.95 (0.90, 1.01)	1.04 (1.02, 1.07)		1.51 (1.44, 1.57)	1.54 (1.50, 1.57)	
% BL→Y2	-5.0 (-8.5, -1.5)	-7.5 (-9.3, -5.7)*	0.70	+1.5 (-0.8, 3.8)	-2.1 (-3.7, -0.5)	0.74
% Y2→Y4	-7.1 (-10, -4.1)	0.7 (-0.8, 2.2)	0.09	-0.9 (-3.1, 1.3)	-2.0 (-3.2, -0.8)	0.97
FLEXOR STRENGTH/BODY MASS						
BL	0.43 (0.40, 0.46)	0.43 (0.41, 0.45)		0.66 (0.63, 0.69)	0.66 (0.64, 0.68)	
Y2	0.41 (0.38, 0.45)	0.41 (0.39, 0.42)	0.99	0.58 (0.55, 0.61)	0.60 (0.58, 0.62)	0.28
Y4	0.39 (0.36, 0.42)	0.39 (0.38, 0.41)		0.59 (0.56, 0.63)	0.57 (0.55, 0.59)	
%BL→Y2	-3.5 (-7.7, 0.8)	-5.5 (8.1, -3.0)	0.77	-12 (-16, -7.3)*	-8.5 (-11, -6.4)*	0.49
%Y2→Y4	-5.7 (-8.5, -3.0)	-3.0 (-5.4, -0.6)	0.68	+2.2 (-2.5, 6.8)	-5.7 (-7.7, -3.7)	0.33

Extensor & Flexor strength in Newton; Extensor & Flexor torque/body mass in Newton/kilogram

p value for ANCOVA for cases versus controls

* p for BL versus Y2 follow-up and Y2 versus Y4 of follow-up, respectively < 0.05