Chapter 3

Elevated c-reactive protein is associated with lower increase in knee muscle strength in patients with knee osteoarthritis: A 2 year follow up study in the AMS-OA cohort

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Abstract

Objective. To examine the associations of elevated serum c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) with change in muscle strength in patients with established knee osteoarthritis (OA), over two years.

Methods. Data from 186 patients with knee OA were gathered at baseline and at two-years follow up. CRP (mg/l) and ESR (mm/l) were measured in serum from patients' blood. Strength of quadriceps and hamstrings muscles was assessed using an isokinetic dynamometer. The association of inflammatory markers with change in knee muscle strength was analysed using uni- and multivariate linear regression models.

Results. Patients with elevated CRP values at both baseline and two-years follow up exhibited a lower increase in knee muscle strength over two years (β= -0.22; p=0.01) compared with the group with not elevated levels at both times of assessment. The association persisted after adjustment for relevant confounders. Elevated ESR values at both times of assessment were not significantly associated with change in knee muscle strength (β=-0.05; p=0.49).

Conclusion. Our results indicate that elevated CRP values are related to a lower gain in muscle strength over time in patients with established knee OA. Although the mechanism to explain this relationship is not fully elucidated, these results suggest inflammation as a relevant factor influencing muscle strength in this group of patients.

Introduction

In patients with knee osteoarthritis (OA) lower muscle strength is associated with disease progression and activity limitations (1-3). Lower muscle strength in this group of patients is determined by several factors, including pain, avoidance of activities and aging (4;5). More recently evidence from cross-sectional studies has suggested that inflammation is an additional factor influencing muscle strength in patients with knee OA (6;7).

A low grade of inflammation has been reported (8-10) in patients with OA, and slight or moderate elevations of inflammatory markers such as c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) have been described (8;11-15). Recently two cross-sectional studies have found an association between elevated inflammatory markers and lower muscle strength in patients with knee OA (6;7). Although the mechanism has not been fully clarified, the association between elevated levels of inflammatory markers and muscle strength might be explained by the catabolic effect of inflammatory markers on muscle tissue (16). Elevated levels of inflammatory markers might also contribute to reducing the muscle's regenerative potential, probably through lowering protein synthesis rates (17). Longitudinal studies analysing the association of long-term inflammation with changes in muscle strength in patients with OA are needed in order to better understand the influence of inflammation on muscle strength. We hypothesized that if in patients with knee OA inflammatory markers (i.e. CRP, ESR) are elevated at both baseline and two-years follow up, this will be associated with a lower change or decrease in muscle strength compared with patients who do not have elevated levels at both assessments.

Patients and Methods

Subjects

One hundred and eighty six participants from the Amsterdam Osteoarthritis (AMS-OA) cohort (127 females, 59 males) with unilateral or bilateral diagnosis of knee OA according to the American College of Rheumatology (ACR) [18] were included in this study (2009-2011). The AMS-OA is a cohort of patients with OA of the knee and/or hip (18;19), who have been referred to an outpatient rehabilitation centre (Reade, Centre for Rehabilitation and Rheumatology; Amsterdam, the Netherlands) (6). Participants were assessed by rheumatologists, radiologists and rehabilitation physicians. Rheumatoid

arthritis or any other form of inflammatory arthritis (i.e., crystal arthropathy, septic arthritis, spondyloarthropathy) were considered exclusion criteria. Total knee replacement during the follow up period was considered an additional exclusion criterion. Demographic, clinical, radiographic, psychosocial, and biomechanical factors related to OA were assessed at both baseline and at two-years follow up. Patients from the AMS-OA cohort who had completed two years since the baseline measurements were invited to the follow up assessment (2011-2013) (Figure 1). Only patients who completed the assessment at both times were included in the study. All the participants provided written inform consent according to the declaration of Helsinki. The study was approved by the Reade Institutional Review Board.

Measures

Inflammatory Markers. Inflammatory markers were measured in serum from patients' blood samples at baseline and at two-years follow up. CRP (mg/l) was processed immunoturbidimetrically using CRPLX test kits (20;21) and the Roche Cobas-6000 analyser. ESR values were determined by the standard Westergren method (22). In this method, EDTA (ethylenediaminetetraacetic acid) anticoagulated blood samples were pre-diluted with saline solution and aspirated into the Westergren pipette graduated from 0-200 mm. The rate at which red blood cells sedimented in 1 hour was measured and reported in mm/h.

Muscle strength. Knee muscle strength was assessed using an isokinetic dynamometer (EnKnee, Enraf-Nonius, Rotterdam, Netherlands) at baseline and at two-years follow up (23). An initial practice attempt was used for the patients to get familiar with the required movements. The patients performed three maximal test repetitions to measure the isokinetic strength of the quadriceps and hamstrings for each knee, at 60°/second. Mean quadriceps and hamstring muscle strength per leg was calculated (Nm), and divided by the patient's weight (kg) (6;24). This measure (in Nm/kg) has shown an excellent intrarater reliability (ICC 0.93) in knee OA patients (25). Average muscle strength of both legs was used if both knees have OA, otherwise muscle strength of the knee with OA was incorporated in the analyses.

Potential confounders. Demographic data (i.e., age and gender) were recorded. Information related to comorbidities was collected with the Cumulative Illness Rating

Scale (CIRS) (26). This instrument gathers information related to 13 body systems, scoring from 0 (none) to 4 (extremely severe) according to the severity of the condition. The number of diseases on which the patients scored a severity of 2 or higher was calculated. NSAID use was dichotomized (yes, no). Body Mass Index (BMI) was calculated as body mass in kilograms divided by height in meters squared (kg/m^2). Kellgren & Lawrence (KL) scores of the knee were used to assess the radiographic severity of the disease (27). The frequency at which the subjects usually performed physical activity ≥30 minutes during the week (28) was assessed only at two-years follow up. The potential confounder effect of changes in comorbidities score, NSAID use, BMI index (29) and KL score over the follow up period, as well as the information available about physical activity were considered in the analyses.

The pain subscale of the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire was included as potential confounder in the models. The WOMAC questionnaire has five items related to pain, two related to stiffness and seventeen items related to activity limitations (30). Each item can be scored from 0 to 4. Higher scores represent worse outcome. The WOMAC stiffness and activity limitations subscales, as well as information related to physical therapy treatment were not included in the models but were used to further describe the study population (Table 1). A validated Dutch version of WOMAC was used in this study (31). Additionally, at two-years follow up the patients were asked if they had received physiotherapy treatment during the past two years.

Statistical analysis

Descriptive statistics were used to characterize the study population at baseline and at two-years follow up. Percentages were used for categorical variables, medians (inter-quartile ranges (IQRs)) and means (standard deviations (SDs)) for continuous variables. McNemar tests and Paired t-tests were used to analyse the differences in the distribution of the variables at baseline and at two-years follow up (Table 1).

We dichotomized the original CRP and ESR values (6) at baseline and at two-years follow up. CRP was codified as 0 if levels in serum were low to intermediate (≤3mg/l) and 1 if levels were elevated (>3mg/l). This cut-off level was chosen according to previous studies in patients with OA (11;32). ESR was codified following

the classification criteria of low to normal rate 0 (<20mm/h) and elevated rate 1 (≥20mm/h) (19). As previously described [6], overall inflammatory markers (i.e., CRP and ESR) were categorized in 4 subgroups as follows: a) the values in serum were low to intermediate/normal at both times of measurement, b) high values at baseline and decreased at two-years follow up, c) low to intermediate/normal baseline values and increased at two-years follow up, and d) the values were elevated at baseline and at follow up. Change in muscle strength was calculated as the difference between follow up and baseline muscle strength (Nm/kg).

The association of inflammatory markers (CRP and ESR) as independent factors (subgroups described above) and change in muscle strength (Nm/kg) as dependent factor was analysed using linear regression models. The group of patients with not elevated inflammatory markers at both baseline and at follow up was used as reference. First, regression analyses were used to analyse the association of CRP and ESR with change in muscle strength adjusting for baseline muscle strength (crude models). Second, multivariable regression models adding one relevant confounding variable at a time (i.e., age; gender; change in comorbidities, change in NSAID use, change in BMI, change in WOMAC pain, level of physical activity) were analyzed (Table 2). Statistical significance was accepted at p-values < 0.05. All analyses were performed using SPSS software, version 18.0 (SPSS, Chicago, IL).

Results

Participants. A total of 268 patients with knee OA who completed the baseline were invited to participate in the follow up evaluation. Eight percent of the patients (n=21) were excluded from the study due to total knee replacement. From the eligible subjects who met the inclusion criteria at follow up (n=247), 25% (n=61) declined the invitation for various reasons. Figure 1 shows the participants flow during the study. There were no significant differences in baseline characteristics between the groups of patients who were and were not part of the two-years follow up assessment (data no shown).

Descriptives. Demographic and clinical characteristic data of patients who participated at baseline and at two-years follow up (n=186) are shown in Table 1. Sixty eight percent of the study group (n=127) were women. Mean ± SD age at baseline was 61.2 ± 7.3 years. The median (IQR) of CRP and ESR in the group was 2mg/l (1, 4) and

9mm/h (5, 15) at baseline and 2mg/l (1, 3) and 7mm/h (4, 12) at two-years follow up, respectively. Sixty four percent of the study population (n=117) had not elevated CRP at both baseline and at two-years follow up, 11% (n=20) had elevated CRP values at baseline and not elevated at follow up, 9% (n=16) had not elevated CRP values at baseline and elevated levels at follow up, and 16% (n=29) of the study population had elevated CRP levels at both times of measurement. Seventy five percent (n=140) of the patients had not elevated ESR values at both baseline and at follow up, 10% (n=18) had elevated ESR values at baseline and not elevated at follow up, 5% (n=9) had not elevated ESR values at baseline and elevated levels at follow up, 9% (n=16) of the study group had elevated levels of ESR at both times of assessment. Information on CRP and ESR were missing at one point of assessment in 4 and 3 patients respectively.

There was an overall 19% increase in mean knee muscle strength in the study group at follow up, mean±SD (0.09±0.2Nm/kg) ($p<0.001$). Patients with not elevated levels of CRP at both baseline and follow up had a mean muscle strength increase of 27% at two-years follow up, mean±SD (0.10±0.3Nm/kg) ($p<0.001$); patients with elevated CRP levels at both times of assessment showed a no significant increase in mean muscle strength of only 4%, mean±SD (0.02±0.2Nm/kg) ($p=0.59$). In patients with only one knee affected with OA, there was no significant difference in knee muscle strength change over two years between the knee with OA and the one without the disease ($p=0.19$) (data not shown).

Associations of inflammatory markers (CRP and ESR) with muscle strength changes. Tables 2 and 3 show the associations of the CRP and ESR (subgroups) with muscle strength change using the group of not elevated inflammatory markers at both baseline and at follow up as reference. Elevated CRP values at both baseline and two-years follow up (crude beta -0.17; $p=0.02$), but not ESR (crude beta -0.11; $p=0.16$), were significantly associated with a lower increase in muscle strength after two years compared with the reference group. In the multivariable regression models one relevant confounding variable was added at a time (Table 2 and 3). In the fully adjusted model, elevated levels of CRP at both times of assessment (beta -0.21; $p=0.01$), but not ESR (beta -0.07; $p=0.38$), were still associated with lower gains in muscle strength, compared with the reference group, after adjustment for baseline muscle strength, age, gender, change in comorbidities, change in NSAID use, change in BMI, change in

WOMAC pain, Kellgren/Lawrence score change and level of physical activity. The coefficients of the full model were not affected once number of knees affected with OA was incorporated to the full model (data not shown). There were no statistically significant differences in muscle strength changes in the groups with inflammatory markers (CRP or ESR) elevated at only one point of assessment (baseline or follow up) compared with the reference group, before or after adjustment for relevant confounders.

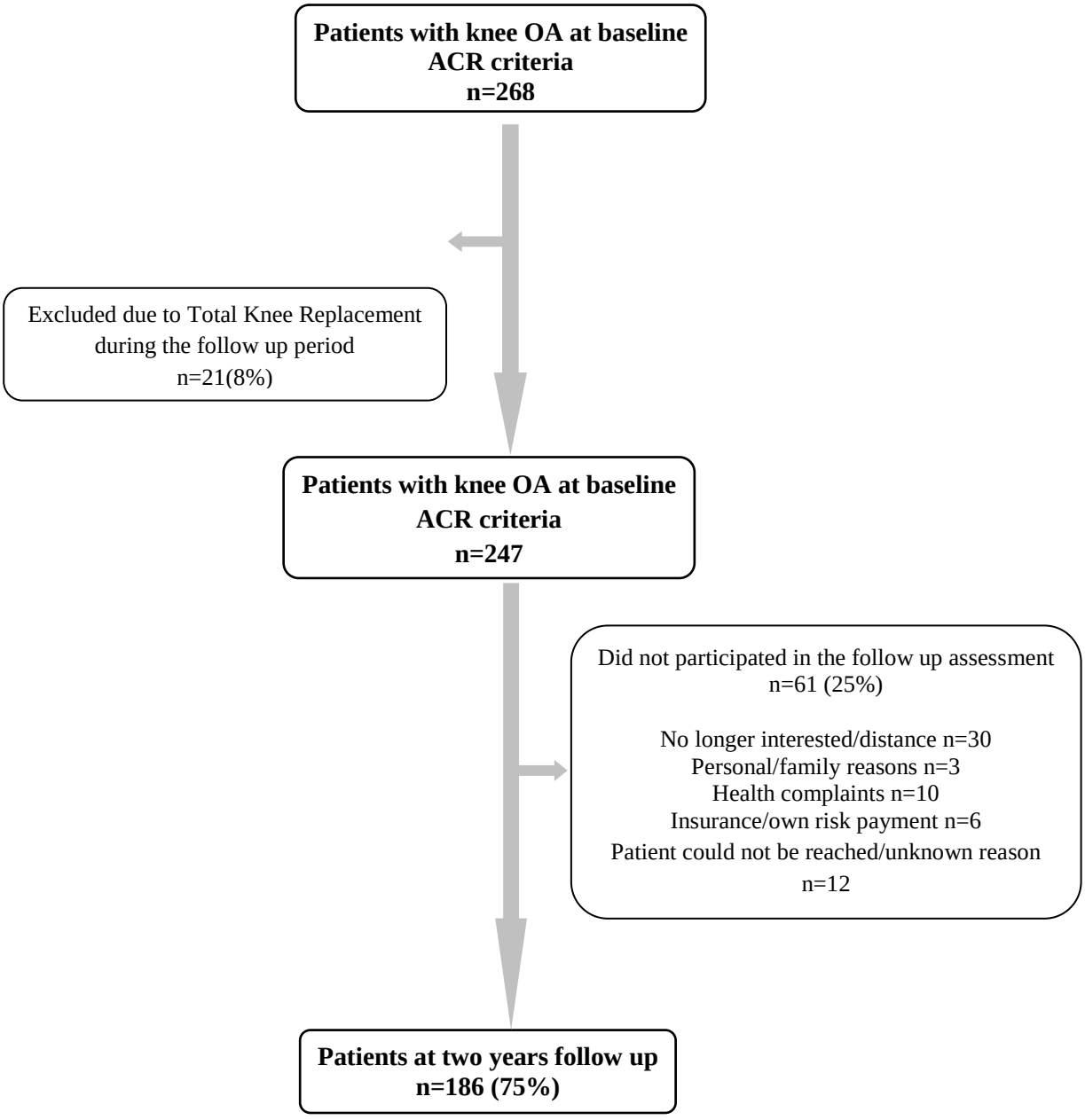

Figure 1. Patients course during the study

Table 1. Characteristics of the study population (n=186)

	Baseline		Two-years follow up	
	n		n	
Age, years	186	61(7.3)	-	-
Female, n(%)	186	127(68)	-	-
Radiographic OA- K/L score ≥2, n (%)	184	130(70)	186	123(66)
WOMAC pain score (0-20)	183	7.9(3.8)	185	7.0(4.3)*
WOMAC stiffness score (0-8)	179	3.7(1.7)	186	3.5(2.0)*
WOMAC physical function score (0-68)	183	28.6(13.4)	186	27.0(15.3)
Comorbidities count (CIRS ≥2)	184	0.8(1.0)	175	1.1(1.0)*
NSAIDs (yes), n (%)	185	30(16)	186	38(20)
BMI, kg/m²	185	29.3(5.5)	186	29.3(5.4)
Physical activity ≥30min (times per week)	-	No information	183	3.0(1.3)
PT treatment during the past 2 years (yes), n (%)	-	No information	186	149(80)
[a]Knee Muscle strength (Nm/kg)	177	0.88(0.4)	183	0.95(0.4)*
Inflammatory markers				
CRP, mg/l	183		184	
Median, IQR		2(1-4)		2(1-3)
Mean, sd		3.4(5.4)		2.9(3.1)
>3mg/l, n(%)		50(27)		45(24)
ESR, mm/h	183		186	
Median, IQR		9(5-15)		7(4-12)
Mean, sd		11.6(8.9)		9.5(8.4)*
≥20mm/h, n(%)		34(18)		25(13)

Mean ± standard deviation (sd), unless other stated. *significant difference between baseline and follow up assessment ($p<0.05$). OA= osteoarthritis; K/L= Kellgren/Lawrence, PT= physiotherapy, CRP=C-reactive protein, ESR=Erythrocyte sedimentation rate. [a]Mean quadriceps and hamstring muscles in OA knees.

Discussion

This study investigated the association of elevated serum inflammatory markers (i.e., CRP and ESR) and changes in knee muscle strength in a group of patients with established knee OA, over two years. We found that a persistently elevated level of serum CRP values was associated with lower gain in muscle strength compared with patients with not elevated levels at both times of assessment. Previous studies have documented the cross-sectional relationship between elevated inflammatory markers and lower muscle strength in patients with knee OA (6;7). However, to the best of our knowledge this is the first study on the longitudinal association between levels of serum inflammatory and knee muscle strength in patients with knee OA.

There was an overall increase in knee muscle strength after two years in the study population. The improvement of muscle strength could be explained by the fact that the patients of this study were initially referred to our outpatient rehabilitation centre to receive medical attention, and eighty percent of the study population reported to have received some type of physical therapy intervention during the follow up period. This may have resulted in increased muscle strength.

The relationship between elevated inflammatory markers and lower knee muscle strength is coherent with findings from previous cross-sectional studies carried out in patients with OA (6;7;33), in patients with rheumatoid arthritis (RA) (34) and in the general elderly population. Schaap et al. (35) described an association between baseline elevated serum inflammatory markers and a decline in knee and hand strength after 5 years, in a group of older adults (35;36).

In the present study, when change in BMI (29) over two years was incorporated in the fully adjusted model, elevated levels of serum CRP at both baseline and two-years follow up were still significantly associated with lower gain in muscle strength compared with patients with not elevated levels at both times of assessment. Nevertheless, in our previous cross-sectional study the association between inflammatory markers and muscle strength was not independent of BMI (6). A possible production and secretion of several pro-inflammatory cytokines by the adipose tissue, and/or a non-hepatic production of CRP through the stimulation of adiposities might

Table 2. Associations of CRP with muscle strength change in patients with knee OA

Independent Factors	Muscle Strength change (Nm/kg)	
	β	p-value
CRP (crude)		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.05	0.51
Not elevated at baseline and elevated at follow up	-0.09	0.22
Elevated at both times of assessment	-0.17	0.02
CRP [a, b]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.06	0.38
Not elevated at baseline and elevated at follow up	-0.06	0.38
Elevated at both times of assessment	-0.17	0.02
CRP [a, b, c]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.06	0.44
Not elevated at baseline and elevated at follow up	-0.06	0.42
Elevated at both times of assessment	-0.16	0.03
CRP [a, b, c, d]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.03	0.71
Not elevated at baseline and elevated at follow up	-0.07	0.38
Elevated at both times of assessment	-0.18	0.02
CRP [a, b, c, d, e]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.01	0.92
Not elevated at baseline and elevated at follow up	-0.09	0.25
Elevated at both times of assessment	-0.20	0.01
CRP [a, b, c, d, e, f]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.01	0.90
Not elevated at baseline and elevated at follow up	-0.09	0.26
Elevated at both times of assessment	-0.19	0.01
CRP [a, b, c, d, e, f, g]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.01	0.93
Not elevated at baseline and elevated at follow up	-0.09	0.25
Elevated at both times of assessment	-0.19	0.01
CRP [a, b, c, d, e, f, g, h]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	0.05	0.57
Not elevated at baseline and elevated at follow up	-0.09	0.25
Elevated at both times of assessment	-0.21	0.01

Linear regression analysis using muscle strength change as dependent factor. CRP= C-reactive protein. All the models were adjusted for baseline muscle strength. Additionally confounders adjusting the model included: a-age; b-gender; c-comorbidities change; d-NSAID change; e- BMI change; f-WOMAC pain change; g-Kellgren/Lawrence score change, h-Physical activity follow up. Reduced numbers of patients in the multivariate linear regression analyses due to random missing in the outcome measure or selected predictors.

Table 3. Associations of ESR with muscle strength change in patients with knee OA

Independent Factors	**Muscle Strength change (Nm/kg)**	
	β	**p-value**
ESR(crude)		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.07	0.34
Not elevated at baseline and elevated at follow up	-0.05	0.48
Elevated at both times of assessment	-0.11	0.16
ESR [a, b]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.06	0.39
Not elevated at baseline and elevated at follow up	-0.05	0.46
Elevated at both times of assessment	-0.09	0.19
ESR [a, b, c]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.06	0.41
Not elevated at baseline and elevated at follow up	-0.01	0.95
Elevated at both times of assessment	-0.08	0.26
ESR [a, b, c, d]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.08	0.28
Not elevated at baseline and elevated at follow up	0.01	0.99
Elevated at both times of assessment	-0.08	0.27
ESR [a, b, c, d, e]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.09	0.24
Not elevated at baseline and elevated at follow up	0.04	0.96
Elevated at both times of assessment	-0.08	0.31
ESR [a, b, c, d, e, f]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.10	0.20
Not elevated at baseline and elevated at follow up	-0.03	0.76
Elevated at both times of assessment	-0.07	0.35
ESR [a, b, c, d, e, f, g]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.10	0.19
Not elevated at baseline and elevated at follow up	-0.01	0.86
Elevated at both times of assessment	-0.07	0.34
ESR [a, b, c, d, e, f, g, h]		
Not elevated at baseline and at follow up	Ref.	
Elevated at baseline and not elevated at follow up	-0.10	0.17
Not elevated at baseline and elevated at follow up	-0.02	0.79
Elevated at both times of assessment	-0.07	0.38

Linear regression analysis using muscle strength change as dependent factor. ESR= Erythrocyte sedimentation rate. All the models were adjusted for baseline muscle strength. Additionally confounders adjusting the model included: a-age; b-gender; c-comorbidities change; d-NSAID change; e-BMI change; f-WOMAC pain change; g- Kellgren/Lawrence score change, h-Physical activity follow up. Reduced numbers of patients in the multivariate linear regression analyses due to random missing in the outcome measure or selected predictors.

help to explain the strong association between systemic inflammatory markers and BMI, previously reported (32;37;38). BMI is a relevant confounder in the association between inflammatory markers and muscle strength. However, small changes in BMI over time do not influence the association between elevated inflammatory markers and change in muscle strength.

In older adults, elevated levels of inflammatory markers have not only been associated with lower muscle strength, but also with loss of muscle mass and sarcopenia (29;35;39). These associations might be explained by the catabolic effect of inflammatory markers on muscle tissue (16;40). Higher levels of inflammatory factors might contribute to reducing the muscle's regenerative potential, probably through lowering protein synthesis rates in the skeletal muscle (17). Additionally, results from studies carried out in rats suggested that inflammatory factors might cause muscle breakdown (41;42). Bodell et al. (43) indicated that long exposure of skeletal muscle to interleukin-6 (IL-6) can retard muscle growth in rats, possibly due to the interaction with key growth factors. Although, these mechanisms have not been intensively studied in humans, the same mechanism as found in rat models might be involved in the development of muscle weakness in patients with knee OA.

The changes in muscle strength after two years were not associated with persistently elevated levels of serum ESR. A possible explanation might be that ESR can be affected by multiple factors such as gender, age, temperature, smoking, levels of plasma proteins and red blood cell factors (44). Additionally, ESR is less sensitive than CRP to changes in the onset of acute-inflammation, and has shown low/moderate reproducibility with wide range of normal results compared to the high reproducibility of CRP with narrow range of normal results. Looking at different inflammatory markers (i.e., IL-6, Tumor Necrosis Factor (TNF)) in future studies might provide further support for the long-term association between inflammation and muscle strength .

There were no statistically significant differences in muscle strength changes in the groups with elevated inflammatory markers at only one point of assessment (baseline or follow up) compared with the reference group (not elevated levels at both baseline and at follow up), before or after adjusting for relevant confounders. We suggest that longer exposure of skeletal-muscle tissue to elevated levels of inflammatory markers might be

required to induce changes in muscle strength, especially when using systemic inflammatory markers such as CRP which is highly sensitive to changes in the onset of acute-phase response. On the other hand, it is important to consider that the small number of subjects in the groups with elevated inflammatory markers at only one time of assessment might have affected these results.

Some limitations of this study have to be considered. First, 25% of patients dropped out the study at follow up. However, the relevant baseline characteristics were not statistically different between patients who completed and did not complete the follow up assessment, which makes us believe that this loss of patients at follow up did not impact the results of our study. Second, though this is a longitudinal study, we can only prove that associations exist but it is not possible to establish the causality underlying them. Therefore, further experimental studies should be undertaken to clarify the causality. Third, absence of standard conditions at the time of the blood collection (i.e., fasting conditions, preceding physical activity, time of sample collection, etc.) might have caused random variations in the levels of inflammatory markers. However, in the present study blood samples were collected as part of the medical care and additional parameters could not be controlled. Fourth, we gathered information on inflammatory markers and muscle strength at baseline and at two-years follow up, but we have no information about those variables in between these measurement points. Studies that include more than two time measurements might be necessary to further understand the longitudinal association between inflammation and muscle strength. Fifth, information about the percentage of body fat of the patients was not available. Therefore, we cannot conclude whether changes in fat mass during the follow-up period were or were not associated with changes in CRP and ESR levels. However, BMI, a proxy measure of body composition was used as potential confounder in the present study. Sixth, in the present study, only knee muscle strength was assessed. However other skeletal muscles might be also affected by persistently elevated levels of inflammatory markers. A key strength of our study is the large number of patients with knee OA (n=186) studied and a longitudinal design, compared with the smaller sample populations included in previous cross-sectional studies (7;45).

From a clinical perspective, the results of this study may contribute to more targeted treatment. Although further evidence is needed, targeting low-grade inflammation by

pharmacological, nutritional and/or lifestyle factors (46) might contribute to limiting sarcopenia and decreased muscle strength in patients with knee OA. On the other hand, it is also possible that an increase in muscle strength (through muscle training) might contribute to a decrease in circulating inflammatory markers in patients with OA. In this respect, previous literature has suggested that physical activity might contribute to mitigating inflammation (47). Furthermore, decreases in circulating levels of inflammatory markers (i.e., CRP and TNF) were associated with an increase in muscle strength in a group of post-menopausal women receiving resistance training (48), as well as in elderly individuals with knee OA receiving a whole-body vibration program (49). It is also feasible that both mechanisms are involved. Indeed, further longitudinal studies involving controlled and tailored interventions are needed to elucidate the clinical relevance of the association between inflammation and lower muscle strength in patients with knee OA.

Conclusions

Our results indicate that persistently elevated CRP levels are independently related to a lower gain in muscle strength over time in patients with established knee OA. Although the mechanism to explain this relationship is not fully elucidated, these results suggest inflammation as a relevant factor influencing muscle strength in this group of patients.

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