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Associations between serum IL-8 and knee symptoms, joint structures, and cartilage or bone biomarkers in patients with knee osteoarthritis

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Abstract

Objective The aim of this study was to investigate cross-sectional associations between serum levels of IL-8 and the above outcomes in patients with knee osteoarthritis (OA).

Methods A total of 160 subjects with clinical knee OA were included. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and Lequesne index were used to assess the joint symptom. Magnetic resonance imaging was used to measure knee structural abnormalities including infrapatellar fat pad (IPFP) signal intensity alternation. Knee radiographic OA was assessed by radiography using the Kellgren-Lawrence (K-L) grading system. Enzyme-linked immunosorbent assay was used to measure the serum levels of IL-8 and cartilage or bone biomarkers.

Results In multivariable analyses, serum IL-8 was positively associated with WOMAC weight-bearing pain (β 2.85, $P = 0.028$), WOMAC physical dysfunction (β 12.71, $P = 0.048$), and Lequesne index (β 1.65, $P = 0.015$), and had positive associations with IPFP signal intensity alteration (OR 3.18, $P = 0.011$) and serum levels of N-telopeptide of type I collagen (NTXI), N-terminal procollagen III propeptide (PIIINP), matrix metalloproteinase (MMP)3, and MMP13 (β 0.24–1.44, all $P < 0.05$) in patients with clinical knee OA. Furthermore, there were positive associations between IL-8 and WOMAC score (β 22.49, $P = 0.037$), K-L grades (OR 3.88, $P = 0.013$), and IPFP signal intensity alteration (OR 3.20, $P = 0.033$) in patients with radiographic OA.

Conclusions Serum levels of IL-8 were positively associated with increased knee symptoms, IPFP signal intensity alteration, and serum levels of bone and/or cartilage biomarkers, suggesting that IL-8 may have a role to play in knee OA.

Key Point

- *This study systemically investigates the associations between serum IL 8 and knee symptoms, joint structures, and cartilage or bone biomarkers in patients with knee osteoarthritis, and some significant associations have been found, suggesting that IL 8 may have a role to play in knee OA.*

Keywords IL-8 · Magnetic resonance imaging · Osteoarthritis

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Background

Osteoarthritis (OA) is the most common form of joint disease characterized by joint structural changes, and is most common in the knees [1, 2]. It is the leading cause of joint pain and physical disability, which causes a large socioeconomic healthcare burden [1]. OA is viewed as a whole-organ disease of the joint including breakdown of cartilage, remodelling of the underlying bone, formation of ectopic bone, hypertrophy of the joint capsule, and inflammation of the synovial lining [3]. Although the pathogenesis of OA is unclear, low-grade chronic inflammation is thought to play a central role in OA [1, 3]. Age, sex, and body mass index (BMI) are well-known risk factors for OA [4].

Interleukin-8 (IL-8) is a member of the CXC chemokine family [5]. It is a major mediator of inflammation, acting as a chemoattractant for neutrophils, basophils, and T cells, and is a potent angiogenic factor [5]. High levels of IL-8 have been found in the serum, synovial fluid, synovium, and subchondral bone of patients with OA [6–8], and the levels of IL-8 in synovial fluid were associated with radiographic scores and pain on movement in OA patients [7, 9]. There were reports that the IL-8 gene polymorphisms were associated with the prevalence of OA [5], and hypomethylation of *IL-8* in chondrocytes and synovial membrane could have positive effects on OA progression [10, 11]. Therefore, IL-8 may be involved in the pathogenesis of OA; however, there are no observational studies exploring the associations between serum IL-8 and knee symptoms, joint structural changes, and cartilage or bone biomarkers in knee OA patients so far. The aim of this study, therefore, was to investigate the cross-sectional associations of serum levels of IL-8 with knee symptoms, joint structural changes including joint radiographic OA, cartilage defects, bone marrow lesions (BMLs), effusion-synovitis, and signal intensity alternation of infrapatellar fat pad (IPFP) measured using magnetic resonance imaging (MRI), and serum cartilage or bone biomarkers including cartilage oligomeric matrix protein (COMP), cross-linked C-telopeptide of type I collagen (CTXI), cross-linked N-telopeptide of type I collagen (NTXI), N-terminal procollagen III propeptide (PIIINP), and matrix metalloproteinase (MMP)3, 10, and 13 in patients with knee OA.

Methods

Subjects

This study was part of the Anhui Osteoarthritis (AHOA) Study, a clinical study of 205 patients aimed to identify the environmental and biochemical factors associated with the progression of knee OA. Patients with clinical knee OA, diagnosed using American College of Rheumatology criteria [12], were consecutively recruited from the Department of Rheumatology and Immunology in the First Affiliated Hospital of Anhui Medical University, from January 2012 to November 2013. We excluded institutionalized patients, patients with rheumatoid arthritis or other inflammatory diseases, patients with severe knee OA who were planning to have knee arthroplasty in 2 years (this study was ongoing with 2 years of follow-up), and patients with contraindications to MRI. Forty-five patients were excluded from the study because of incomplete data, leaving 160 patients.

Anthropometrics

Weight was measured to the nearest 0.1 kg (with shoes, socks, and bulky clothing removed) by weighing scales. Height was measured to the nearest 0.1 cm (with shoes, socks, and headgear removed) by a height meter. BMI was calculated as [weight (kg)/height $(m)^2$].

Joint symptom assessments

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Lequesne index were acquired by questionnaires and were used to assess the joint symptom of knee OA patients. The WOMAC pain was divided into weight-bearing pain (walking on flat surface, going up/down stairs, and when standing upright) and non-weight-bearing pain (at night while in bed and when sitting/lying).

Serum IL-8 and cartilage or bone biomarkers measurements

Fasting blood samples were collected from patients in the morning. Serum was separated, aliquoted into 1.5-ml eppendorf tubes, and stored at − 80 °C until analysis. Serum levels of IL-8, COMP, CTXI, NTXI, PIIINP, MMP3, MMP10, and MMP13 were measured by using enzyme-linked immunosorbent assay (ELISA) (eBioscience, USA, for IL-8, and Elabscience, China, for others) kits according to the manufacturer's instructions.

Knee radiographic assessments

A standing anteroposterior semiflexed view of the symptomatic knee (the severer one if both knees were affected; the right one if both knees were equally painful) with 15-degree flexion was performed in all participants. Kellgren-Lawrence (K-L) grading system was used to assess the radiographic severity of OA. The K-L grading system (grades 0–4) was graded as previously reported [13]. Radiographic OA (ROA) was defined as K-L grade ≥ 2.

MRI assessment

MRI of the selected knee was performed with a 3.0-T whole-body magnetic resonance imaging unit (Signa HDxT 3.0 T; GE Healthcare, Little Chalfont, UK), using a commercial transmit/receive extremity coil. The sequence and parameters were reported previously [1]. Images were checked for image noise and structural abnormalities interfering with segmentation. All images were grouped together and read in randomized order, with the reader blinded to subject information and status.

Regional subdivision of the articular surfaces was based on Whole-Organ Magnetic Resonance Imaging Score (WORMS) of knee OA: femur and tibia are divided into medial and lateral sites, with the trochlear groove of the femur considered as a part of the medial site. The femoral and tibial surfaces are further subdivided into anterior (A), central (C), and posterior (P) subregions [14].

Cartilage defects (0 to 4 scale) were assessed at the medial femoral, lateral femoral, medial tibial, lateral tibial, and patellar sites using T2-weighted images as previously reported [15]. A cartilage defect had to be present in at least two consecutive slices. The highest score at a subregion of each region was used to represent the score of this region. Total cartilage defect scores were obtained by summing the scores of medial and lateral tibial, medial and lateral femoral, and patellar sites.

BMLs were defined as discrete area of increased signal adjacent to subcortical bone at the tibia and femur on T2-weight MRI using a semiquantitative (0–3) scoring system based on the WORMS of knee OA: grade 0, none; grade 1, no more than 25% of the region; grade 2, 25% to 50% of the region; grade 3, more than 50% of the region. The highest score at a subregion of each region was used to represent the score of this region. Total BML scores were obtained by summing the scores of medial and lateral tibial, medial and lateral femoral, and patellar sites [14].

IPFP signal intensity alteration on T2-weighted MRI was recorded if hyperintense signal alterations were observed within the IPFP. Signal intensity alteration, defined as discrete areas of increased signal within the IPFP, was graded as follows: grade 0, none; grade 1, less than 10% of the region; grade 2, 10 to 20% of the region; and grade 3, more than 20% of the region [16] (Fig. 1).

Effusion-synovitis was assessed as the presence of intra-articular fluid-equivalent signal on sagittal T2-weighted MRI. Effusion-synovitis was investigated in the four regions (suprapatellar pouch, central portion, posterior femoral recess, subpopliteal recess) according to the anatomy of the knee joint synovial cavity [17]. They were the following: (1) suprapatellar pouch, extends superiorly from the upper surface of the patellar, between the posterior suprapatellar fat pad (quadriceps femoris tendon) and the anterior surface of the femur; (2) central portion, lies between the central femoral and tibial condyles, around the ligaments and menisci; (3) posterior femoral recess, lies behind the posterior portion of each femoral condyle and the deep surface of the lateral and medial heads of the gastrocnemius; (4) subpopliteal recess, lies posteriorly between the lateral meniscus and the popliteal tendon. The size of effusion-synovitis in each of the regions was directly generated in the entire series of images using OsiriX software. A total area of all the regions in the same slice was summed as effusion-synovitis area of this slice. A maximal area in one slice was selected to represent effusion-synovitis area of the knee.

Statistical analysis

Student's t tests, chi-squared tests, and Mann-Whitney U tests were used to compare means, proportions, and medians, respectively. Cartilage or bone biomarkers were not normally distributed, so the Box-Cox transformations for cartilage or bone biomarkers were performed. The calculated λ values were 0, 0.34, 0, 0, 0, 0.41, and 1.5 for COMP, CTXI, NTXI, PIIINP, MMP3, MMP10, and MMP13, respectively; therefore, natural log transformations were performed for COMP, NTXI, PIIINP, and MMP3, and other transformations were calculated using the λ values. Linear regression analyses were used to examine the associations between IL-8 (the independent variable) and knee symptoms scores, effusion-synovitis area, and transformed bone/cartilage biomarkers before and after adjustment for age, sex, and BMI. Ordinal logistic regression analyses were used to examine the associations between IL-8 (the independent variable) and K-L grades, cartilage defects, BMLs, and IPFP signal intensity alternation before and after adjustment for age, sex, and BMI. Standard diagnostic checks of model fit and residuals were routinely done, and data points with large residuals and/or high influence were investigated for data errors. A p value < 0.05 (two-tailed) or 95% confidence interval (CI) not including the null point (for linear regression) or 1 (for ordinal regression) was considered statistically significant. All statistical analyses were performed using SPSS 13.0 for Windows (SPSS, Chicago, IL, USA).

Results

A total of 160 subjects (88.1% females) aged between 34 and 74 years (mean 55.4 years) were included in the analyses. There were no significant differences in demographic factors (age, sex, and BMI) between these participants and those excluded ($n = 45$; data not shown). The median IL-8 level was 0.20831 ng/ml. Characteristics of the participants are presented in Table 1. Patients with higher and lower levels of IL-8 (split at the median level) were similar in age, gender, height, weight, BMI, WOMAC score, Lequesne index, prevalence of

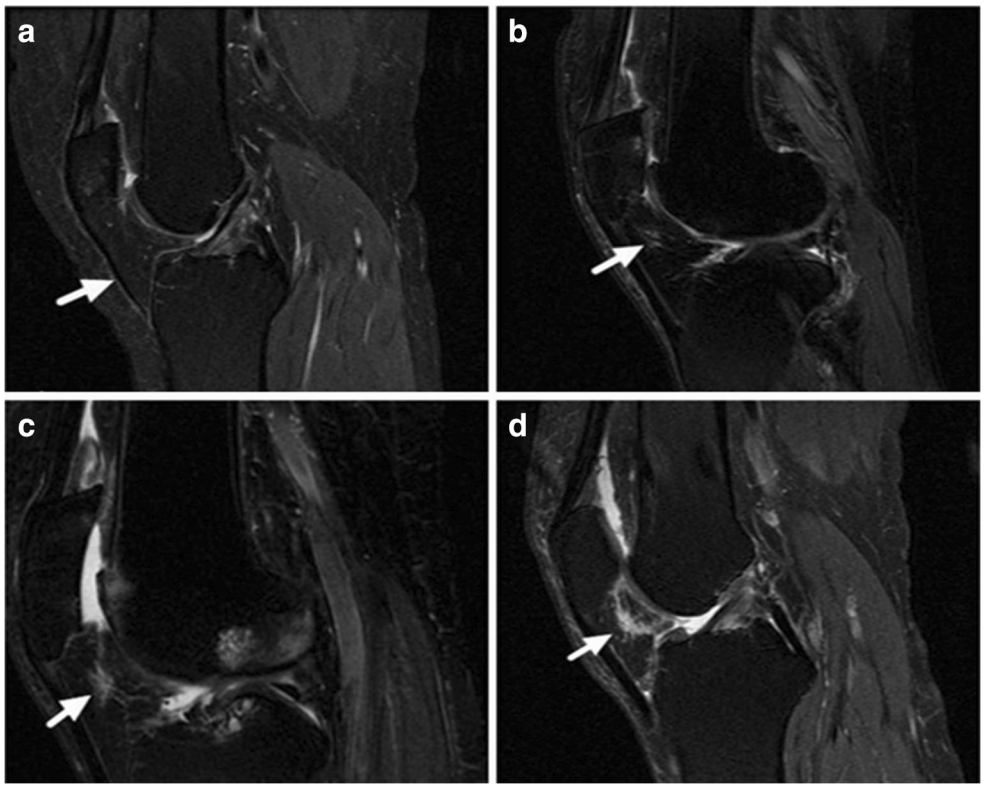

Fig. 1 Grading of IPFP signal intensity alteration on T2-weighted MRI. **a** Grade 0 of IPFP signal intensity alteration. **b** Grade 1 of IPFP signal intensity alteration. **c** Grade 2 of IPFP signal intensity alteration. **d** Grade 3 of IPFP signal intensity alteration

knee ROA, cartilage defects score, BML score, effusion-synovitis area, proportions of IPFP signal intensity alteration of ≥2, and levels of COMP, NTXI, MMP3, MMP10, and MMP13. However, patients with higher level of IL-8 had higher level of PIIINP and lower level of CTXI.

There was no significant association between serum levels of IL-8 and total WOMAC score in univariable analysis, but after adjustment for age, sex, and BMI, the association has a trend of significance (Table 2). The associations between serum levels of IL-8 and WOMAC pain did not reach statistical significance before and after adjustment for age, sex, and BMI, but serum IL-8 had a positively significant association with weight-bearing pain in univariable and multivariable analyses (Table 2). Serum IL-8 was not significantly associated with WOMAC physical dysfunction in univariable analysis, but this association became significant after adjustment for age, sex and BMI (Table 2). Serum IL-8 was not associated with WOMAC stiffness in both univariable and multivariable analyses (Table 2). Moreover, serum IL-8 had a positively significant association with Lequesne index before and after adjustment for age, sex, and BMI (Table 2, Fig. 2).

Serum IL-8 was significantly and positively associated with IPFP signal intensity alteration before and after adjustment for age, sex, and BMI (Table 3). Associations between serum IL-8 and K-L grades, cartilage defects, BMLs, and effusion-synovitis area did not reach statistical significance (data not shown).

Associations between serum IL-8 and serum biomarkers are shown in Table 3. Serum IL-8 was significantly and positively associated with NTXI, PIIINP, MMP3, and MMP13 before and after adjustment for age, sex, and BMI (Table 3). We did not find significant associations between serum IL-8 and COMP, CTXI, and MMP10 (data not shown).

In these clinical knee OA patients, 142 out of 160 had ROA. We further analyzed the associations between serum IL-8 and knee symptoms and structural changes in these ROA patients. Serum IL-8 was significantly and positively associated with WOMAC score, K-L grades, and IPFP signal intensity alteration in multivariable analyses after adjustment for age, sex, and BMI (Table 4). We did not find significant associations between serum IL-8 and Lequesne index, cartilage defects, BMLs, and effusion-synovitis in ROA patients.

Discussion

To the best of our knowledge, this is the first epidemiological study to investigate the associations between serum levels of IL-8 and knee symptoms, joint structural changes, and cartilage or bone biomarkers in patients with knee OA. We found that after adjustment for age, sex, and BMI, serum levels of IL-8 were positively associated with weight-bearing pain and physical dysfunction assessed by WOMAC and knee symptoms assessed by Lequesne index. IL-8 was also significantly associated with increased IPFP signal intensity alteration as

Table 1 Characteristics of participants (split by median level of IL-8)

	IL-8 ≤ median ($n = 81$)	IL-8 > median ($n = 79$)	P values
Age, years[a]	56.46 (9.03)	54.28 (8.04)	0.111
Female sex, %[b]	85.2	91.1	0.192
Height, cm[a]	159.18 (6.80)	158.69 (6.74)	0.653
Weight, kg[a]	65.04 (10.74)	64.29 (9.21)	0.640
BMI, kg/m^{2}[a]	25.64 (3.78)	25.54 (3.34)	0.861
WOMAC score			
Pain[a]	22.05 (9.79)	21.79 (9.00)	0.960
Stiffness[a]	6.93 (4.47)	7.39 (4.02)	0.492
Physical dysfunction[a]	71.94 (32.48)	73.78 (30.98)	0.718
Total[a]	99.67 (45.19)	100.50 (44.65)	0.907
Lequesne index[a]	14.14 (3.26)	14.76 (3.35)	0.239
Knee ROA, %[b]	75.4	68.5	0.293
Total cartilage defect score[a]	11.62 (2.91)	11.73 (3.22)	0.831
Total BMLs score[a]	3.56 (2.73)	2.98 (2.70)	0.343
Effusion-synovitis area, cm^{2}[a]	1.70 (1.26)	1.57 (1.84)	0.602
IPFP signal intensity alteration ≥ 2, %[b]	34.8	41.2	0.382
COMP, ng/ml[c]	115.50 (80.75, 176.25)	110.00 (74.5, 153.5)	0.327
CTXI, ng/ml[c]	0.48 (0.36, 0.72)	0.40 (0.28, 0.56)	*0.031*
NTXI, ng/ml[c]	614.69 (538.87, 787.64)	626.15 (564.69, 729.23)	0.785
PIIINP, pg/ml[c]	70.64 (21.48, 123.3)	135.96 (57.28, 213.02)	*< 0.001*
MMP3, ng/ml[c]	0.54 (0.32, 0.68)	0.52 (0.30, 0.76)	0.789
MMP10, ng/ml[c]	15.86 (7.14, 29.71)	13.10 (6.89, 31.75)	0.791
MMP13, ng/ml[c]	74.54 (63.06, 123.87)	122.24 (64.98, 124.95)	0.053

n, number of patients; *BMI*, body mass index; *WOMAC*, Western Ontario and McMaster Universities Arthritis Index; *ROA*, radiographic osteoarthritis; *BMLs*, bone marrow lesions; *IPFP*, infrapatellar fat pad; *COMP*, cartilage oligomeric matrix protein; *CTXI*, cross-linked C-telopeptide of type I collagen; *NTXI*, cross-linked N-telopeptide of type I collagen; *PIIINP*, N-terminal procollagen III propeptide; *MMP*, matrix metalloproteinase

IL-8 median level: 0.20831 ng/ml. Data in italics denote statistically significant results

[a] *t* tests were used for mean (standard deviation)

[b] χ^2 tests were used for proportions

[c] Mann-Whitney *U* tests were used for median (interquartile range)

well as serum levels of NTXI, PIIINP, MMP3, and MMP13, but was not associated with other joint structures and cartilage/bone biomarkers. Besides, in patients with knee ROA, IL-8 was positively associated with total WOMAC score, K-L grades, and IPFP signal intensity alteration after adjustment for age, sex, and BMI.

IL-8 is primarily produced by adipocytes and macrophages [18], and can also be expressed by OA chondrocytes,

Table 2 Associations between IL-8 and knee symptoms

	Univariable β (95% CI)	P value	Multivariable* β (95% CI)	P value
Total WOMAC	14.47 (− 3.78, 32.91)	0.119	16.84 (− 0.46, 34.15)	0.056
Pain	2.76 (− 1.11, 6.62)	0.161	3.39 (− 0.40, 7.18)	0.079
Weight-bearing pain	*2.80 (0.19, 5.41)*	*0.036*	*2.85 (0.31, 5.39)*	*0.028*
Non-weight-bearing pain	0.10 (− 1.75, 1.94)	0.919	0.19 (− 1.65, 2.03)	0.841
Stiffness	1.21 (− 0.54, 2.97)	0.173	1.45 (− 0.29, 3.19)	0.101
Physical dysfunction	10.62 (− 2.41, 23.64)	0.109	*12.71 (0.10, 25.33)*	*0.048*
Lequesne index	*1.56 (0.21, 2.91)*	*0.023*	*1.65 (0.32, 2.98)*	*0.015*

Dependent variables: WOMAC score/Lequesne index. Independent variable: IL-8

*Adjusted for age, sex, and BMI. Data in italics denote statistically significant results

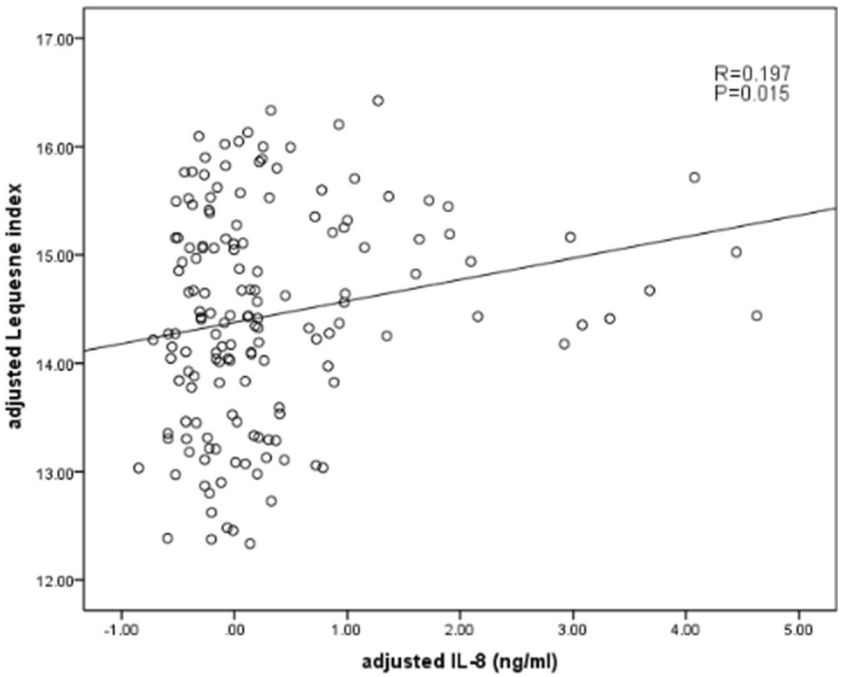

Fig. 2 Association between serum IL-8 and Lequesne index in patients with clinical knee osteoarthritis. Scatter plot showing association between serum IL-8 and Lequesne index in multivariable analysis. Greater IL-8 level was associated with higher Lequesne index in patients with clinical knee osteoarthritis.

fibroblast-like synoviocytes, and IPFP [10, 19, 20]. IL-8 may play roles in the pathophysiology of OA by inducing a number of pathogenic processes such as (1) releasing matrix-degrading metalloproteinases; (2) neutrophil accumulation; (3) leukocyte activation and homing to the synovium; and (4) inducing chondrocyte hypertrophy and differentiation [10, 18]. Furthermore, IL-8 could also play roles in maintenance and perpetuation of chronic synovial inflammation as it has angiogenic function [21].

The most common symptoms of knee OA are pain, stiffness, and physical dysfunction, which affect the quality of life in OA patients [22]. The presence of frequent knee pain and more severe knee symptoms is associated with faster cartilage loss and radiographic progression in knee OA [23]. Symptom severity was positively correlated with synovial fluid IL-8 in patients with knee OA [24]. In our study, IL-8 was positively associated with WOMAC weight-bearing pain and dysfunction and Lequesne index in patients with clinical knee OA, and had a positive association with total WOMAC score in knee ROA patients. These suggest that systemic IL-8 may have a detrimental effect on knee OA symptoms, but the causal relationship and the underlying mechanisms need to be examined by future longitudinal studies and experimental researches.

IPFP is an intracapsular extra-synovial structure in the anterior knee joint [25]. It is composed of adipose tissue structurally similar to subcutaneous fat [25]. IPFP was reported to have biphasic effects in knee OA: it may play a protective role physiologically through improving the distribution of the lubricant effect of intra-articular joint fluid by increasing the synovial surface, and reducing the impact of loading by absorbing forces generated in the knee joint, and can also play a

Table 3 Associations between IL-8 and IPFP signal intensity alteration and cartilage/bone biomarkers in knee OA

	Unadjusted OR/β (95% CI)	*P* value	Multivariable* OR/β (95% CI)	*P* value
IPFP signal intensity alteration (OR)	*2.42 (1.03, 5.69)*	*0.044*	*3.18 (1.30, 7.76)*	*0.011*
NTXI (β)	*0.21 (0.06, 0.36)*	*0.007*	*0.24 (0.08, 0.39)*	*0.003*
PIIINP (β)	*1.41 (0.93, 1.90)*	*< 0.001*	*1.44 (0.93, 1.94)*	*< 0.001*
MMP3 (β)	*0.30 (0.02, 0.59)*	*0.038*	*0.31 (0.02, 0.60)*	*0.039*
MMP13 (β)	*0.28 (0.05, 0.50)*	*0.016*	*0.30 (0.06, 0.53)*	*0.013*

Dependent variables: IPFP signal intensity alteration/cartilage or bone biomarkers (after Box-Cox transformation). Independent variable: IL-8

*Adjusted for age, sex, and BMI. Data in italics denote statistically significant results

Table 4 Associations between IL-8 and knee symptom and structural changes in patients with knee ROA

	Unadjusted OR/β (95% CI)	*P* value	Multivariable* OR/β (95% CI)	*P* value
WOMAC score (β)	18.63 (− 3.15, 40.41)	0.093	*22.49 (1.35, 43.62)*	*0.037*
K-L grades (OR)	*2.71 (1.01, 7.23)*	*0.047*	*3.88 (1.33, 11.32)*	*0.013*
IPFP signal intensity alteration (OR)	2.62 (0.93, 7.38)	0.069	*3.20 (1.10, 9.33)*	*0.033*

Dependent variables: WOMAC score/K-L grades/IPFP signal intensity alteration. Independent variable: IL-8

*Adjusted for age, sex, and BMI. Data in italics denote statistically significant results

detrimental role pathologically due to its metabolic and pro-inflammatory effects [1, 25]. MRI-detected IPFP signal intensity alteration has been used as a surrogate for whole knee joint synovitis [25]. Previous studies showed that IPFP signal intensity alteration was detrimentally associated with knee OA. A nested case-control study demonstrated that IPFP signal intensity change was associated with the development of radiographic knee OA [26]. A study with both cross-sectional and longitudinal analyses reported that the signal intensity changes in IPFP were positively associated with the prevalence and/or incidence of knee pain, cartilage defects, BMLs, and ROA in older adults [27]. There has been no study evaluating the relationship between serum IL-8 and IPFP signal intensity alteration in knee OA so far. Our study showed positive associations between IL-8 and IPFP signal intensity alteration in both clinical knee OA and ROA patients. These suggest that IL-8 could induce IPFP signal intensity alteration, or in an opposite way, abnormal IPFP could produce increased IL-8 into blood, in patients with knee OA. The cause-effect relationship needs to be further investigated.

NTXI, a bone resorption marker, is inversely associated with bone mineral density and directly associated with osteoporosis and fracture risk [1]. PIIINP is a biomarker of type III collagen propetide turnover and is over-expressed in the serum and synovial fluid of OA patients [28]. MMPs were proved to induce cartilage degradation and promote the development of OA [1]. Among these MMPs, MMP3 is responsible for disrupting the collagen cross-link of telopeptide of type II and type IX collagens resulting in disruption of fiber structure and function [29]; MMP13 is an enzyme which plays an important role in type II collagen degradation in articular cartilage [30]. We found that IL-8 was positively associated with serum levels of NTXI, PIIINP, MMP3, and MMP13, suggesting that IL-8 may be associated with increased cartilage breakdown and bone resorption in patients with knee OA. In contrast, we did not find significant association between IL-8 and other cartilage/bone biomarkers including COMP, CTXI, and MMP10. Serum IL-8 was not significantly associated with MRI measures such as cartilage defects, BMLs, and effusion-synovitis. The underlying reasons for these inconsistent results are unclear, and further cohort studies are required to confirm these findings.

There are several limitations in this study. First, it was a cross-sectional study so causalities were unknown. These need to be verified by further cohort studies. Second, the subjects were recruited from the clinics consecutively rather than from the community randomly, so the results may not be generalizable to patients with general knee OA. Third, the sample size was modest, and it is possible that with a larger sample more significant associations can be detected. Fourth, the signal intensity alteration of IPFP was assessed by unenhanced MRI, which was nonspecific, and its pathology was largely unclear [31]. Last, wide 95% CIs of some statistically significant results may be caused by high variation of the coefficients, which should be interpreted with caution.

Conclusions

Serum levels of IL-8 were positively associated with increased knee symptoms, IPFP signal intensity alteration and serum levels of bone/cartilage biomarkers in patients with clinical knee OA, suggesting that IL-8 may have a role to play in knee OA. Further longitudinal studies with larger sample sizes are required to confirm these findings.

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Compliance with ethical standards

Disclosures None.

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