**Patellofemoral bone marrow lesions: natural history and associations with pain and structure**

Zhaohua Zhu1,3, Changhai Ding1,2, 3, Xingzhong Jin1, Benny Antony1, Weiyu Han1, Laura L Laslett1, Flavia Cicuttini 2, Graeme Jones1

**Author Affiliations**

1 Menzies Research Institute Tasmania, University of Tasmania, Hobart, Tasmania, Australia

2 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

3 Arthritis Research Institute, 1st Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China

**Correspondence to**

Graeme Jones, Menzies Research Institute Tasmania, University of Tasmania, Private Bag 23, Hobart, Tasmania 7000, Australia; G.jones@utas.edu.au

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**Competing interests**

The authors declare that they have no competing interests.

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**ABSTRACT**

**Objective:** To describe the natural history of patellofemoral joint (PFJ) bone marrow lesions (BMLs) over 2.6 years and associations between change in PFJ BMLs, knee pain and knee cartilage morphology in older adults over 5 years.

**Methods:** Prospective population-based cohort study of men and women aged 50-80 years (mean age 63 years, n=406) was performed. PFJ BMLs, knee cartilage volume and cartilage defect scores (0-4) were measured using Whole-Organ Magnetic Resonance Imaging Score (WORMS) system at baseline and 2.6 years. Knee pain was assessed by Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scores at baseline and 5 years.

**Results:** At baseline, 27% (n=109) had PFJ BMLs, 24% of these increased (change in score of ≥ 1) at follow-up, 44% persisted, 32% decreased and 21% resolved completely. Of those without PFJ BMLs at baseline, 20% of participants developed PFJ BMLs over 2.6 years. In multivariable analyses, change in PFJ BMLs was deleteriously associated with change in total knee pain (β: 0.67, 95% CI: 0.03-1.31) and knee pain when going up/down stairs (β: 0.24, 95% CI: 0.04-0.44) over 5 years. Baseline PFJ and tibiofemroal joint (TFJ) cartilage volume were protective for PFJ BMLs (RR: 0.69, 95% CI: 0.52-0.90 for PFJ) while baseline PFJ cartilage defects were associated with an increase in PFJ BMLs (RR: 1.73, 95% CI: 1.38-2.17) over 2.6 years. TFJ cartilage defects were not associated with increases in PFJ BMLs.

**Conclusions:** PFJ BMLs are not static and change is clinically relevant. PFJ cartilage morphology predicts increases in PFJ BMLs.

**Keywords:** osteoarthritis; bone marrow lesions; patellofemoral joints; pain; cartilage morphology

**Significance and Innovations**

* This is the first population-based longitudinal study that describes the natural history of patellofemoral joint (PFJ) BMLs. PFJ BMLs were not static, with over one third participants showing change over 2.6 years of follow-up.
* Changes in PFJ BMLs over 2.6 years were associated with change in knee pain when going up or down stairs over 5 years, suggesting that changes in PFJ BMLs are clinically relevant.
* Baseline PFJ cartilage volume was associated with a decrease in PFJ BMLs and baseline PFJ cartilage defects were associated with an increase in PFJ BMLs, indicating a site-specific effect of cartilage morphology on PFJ BMLs.

**Introduction**

Structural abnormalities in the subchondral bone are key players in the pathogenesis of osteoarthritis (OA) ([1](#_ENREF_1)). Bone marrow lesions (BMLs) are ill-defined hyperintense features seen on magnetic resonance (MR) images. In the whole knee, they precede cartilage pathology, including cartilage defects and cartilage volume loss ([2](#_ENREF_2), [3](#_ENREF_3)). BMLs are associated with knee pain ([4](#_ENREF_4)) and predict disease progression ([5](#_ENREF_5), [6](#_ENREF_6)). Incident BMLs and increases in BML sizes are linked to the development of knee pain in pain-free subjects ([7](#_ENREF_7)); and increases in BML size are associated with increasing knee pain over time ([8](#_ENREF_8)). Kothari et al.([9](#_ENREF_9)) and Aitken et al. ([10](#_ENREF_10)) reported that baseline BMLs were associated with cartilage loss in the same subregion. Raynauld et al. ([11](#_ENREF_11)) found that an increase in BML size was associated with cartilage volume loss in the medial but not in lateral compartment.

The natural history of BMLs has been reported in some longitudinal studies. The MOST (Multi-center Osteoarthritis) study ([12](#_ENREF_12)) showed that one-third of knees without baseline BMLs developed new lesions at follow-up, 50% of the prevalent BMLs either regressed or resolved. Previous analyses from our cohort ([13](#_ENREF_13)) assessed knee joint BMLs at four sites (medial tibial, medial femoral, lateral tibial, and lateral femoral sites). This showed that 43% of participants had BMLs, of these 25% decreased in size and 24% increased in 2.7 years follow up. In a younger cohort, Foong. et al followed 198 patients over eight years and found that knee BML size remained stable in over half of the participants ([14](#_ENREF_14)). However, both of these studies reported BMLs in the tibiofemoral compartment or total knee BMLs, and did not report patellar BMLs. The patellofemoral joint (PFJ) is a common site of pain ([15](#_ENREF_15)) and contributes to functional limitation among OA patients ([16](#_ENREF_16)); thus, it is important to assess patellar sources of knee pain. Despite the high prevalence of PFJ OA, there are very few clinical or epidemiological studies that investigate PFJ OA particularly and the natural history of PFJ BMLs had not yet been described.

The aim of this study was, therefore, to describe the natural history of MRI-detected PFJ BMLs over 2.6 years and evaluate the association between increases in PFJ BMLs, knee pain and knee cartilage morphology in older adults.

**MATERIALS & METHODS**

**Subjects**

This study was performed as part of the Tasmanian Older Adult Cohort (TASOAC) study, a population-based study that was designed to identify the genetic, environmental, and biochemical factors associated with the development and progression of OA at multiple sites. Subjects between 50 and 80 years old were randomly selected from the electoral roll in Southern Tasmania (population 229,000), with an equal number of males and females. Baseline examinations were first taken in 2002 and follow-up measures were taken at approximately 2.6 years later. This study was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee. Written informed consent was obtained from all subjects.

**Anthropometrics**

Weight was measured with shoes, socks and bulky clothing removed using electronic scales (nearest 0.1kg). Height was measured with shoes, socks and headgear removed using a stadiometer (nearest 0.1cm). Body mass index (BMI) was calculated using height and weight (kg/m2).

**Magnetic Resonance Imaging**

MRI scans of the right knees were performed on two occasions and imaged in the sagittal plane on a 1.5-T whole body magnetic resonance unit (Picker, Cleveland, OH) using a commercial transmit-receive extremity coil. The image sequences used are listed as follows: (1) a T1-weighted fat saturation 3D gradient recall acquisition in the steady state; flip angle 30°; repetition time 31 ms; echo time 6.71 ms; field of view 16 cm; 60 partitions; 512×512 matrix; acquisition time 11 min 56 s; one acquisition. Sagittal images were obtained at a partition thickness of 1.5 mm and an in-plane resolution of 0.31×0.31 (512×512 pixels). (2) a T2-weighted fat saturation 3-D fast spin echo, flip angle 90, repetition time 3067 ms, echo time 112 ms, field of view 16 cm, 15 partitions, 228x256-pixel matrix; sagittal images were obtained at a partition thickness of 4 mm with a between-slices gap of 0.5 to 1.0 mm. The image database was transferred to an independent computer workstation using the software program Osirix (University of Geneva, Geneva, Switzerland) as previously described ([17](#_ENREF_17), [18](#_ENREF_18)).

**Subchondral BML evaluation**

Subchondral BMLs were measured by one observer (ZZ) trained by readers with long experience in scoring knee MRIs (CD) on T2-weighted MR images and were defined as increased signal areas adjoining to the subchondral bone at the patellar and trochlear sites of knees. The MRI slice with the greatest BML size were selected and scored using Whole-Organ Magnetic Resonance Imaging Score (WORMS) method ([19](#_ENREF_19)). Baseline and follow-up MRIs were scored in pairs in chronological order to minimise measurement error ([13](#_ENREF_13)) (Figure 1). PFJ compartment BMLs were obtained by summing the BML scores of patella and trochlea. Each BML was scored according to the maximal percentage of bone area that the lesion occupied on the slice. We scored grade 0 if no bone marrow lesions were present; grade 1 if lesion size ≤25% of the region on the same slice; grade 2, 25% to 50% of the region on the same slice; grade 3, >50% of the region on the same slice ([19](#_ENREF_19)). The inter-rater reliability of this BML scoring system is excellent, as reported previously ([11](#_ENREF_11)). The intraclass correlation coefficient (ICC) was 0.94 for intra-observer repeatability. An increase of 1 or more grade on the 0 to 3 point scale from baseline to follow-up in BMLs was defined as an increase in BML. Those whose scores remained the same or decreased by 1 or more grade were regarded as stable or having regressed.

**Cartilage defects assessment**

Cartilage defects were assessed by a trained observer (CD) on T1-weighted MR image according to previously described criteria ([2](#_ENREF_2), [20](#_ENREF_20)): grade 0 = normal cartilage; grade 1 = focal blistering and intracartilaginous low-signal intensity area with an intact surface and bottom; grade 2 = irregularities on the surface or bottom and loss of thickness less than 50%; grade 3 = deep ulceration with loss of thickness more than 50%; grade 4 = full-thickness chondral wear with exposure of subchondral bone. The highest grade was used if more than one defects existed at one site. Medial tibial, lateral tibial, medial femoral, lateral femoral, trochlear and patellar compartments were measured. Scores for patellofemoral and tibiofemoral compartment were obtained by summing the individual defect scores in relevant regions. Intraclass correlation coefficients (ICCs) ranged from 0.80 to 0.95 for intraobserver reliability ([21](#_ENREF_21)).

**Cartilage volume measurement**

Knee tibial and patellar cartilage volumes were measured on T1-weighted MR images by a single trained observer at baseline as previously described ([2](#_ENREF_2)). The volumes of individual cartilage plates (medial tibial, lateral tibial, medial femoral, lateral femoral, patellar and trochlear) were isolated from the total volume by manually drawing disarticulation contours around the cartilage boundaries on a section by section basis. These data were then resampled by means of bilinear and cubic interpolation (area of 312×312 um and 1.5 mm thickness, continuous sections) for the final 3-dimensional rendering. The volume of patellofemoral and tibiofemoral compartments were obtained by summing the pertinent cartilage plates within compartments. The coefficient of variation (CV) for cartilage volume measures was 2.1% for medial tibial, and 2.2% for lateral tibial, 2.7% for medial femoral, 2.8% for lateral femoral, 2.6% for trochlea and 2.6% for patella ([22](#_ENREF_22)).

**Meniscal damage**

Meniscal damage was assessed by a trained observer on T1-weighted MR images as previously described ([23](#_ENREF_23)). The proportion of the menisci affected by a tear, partical or full extrusion was scored separately (yes/no) at the anterior, middle and posterior horns (medially/laterally). Anterior, middle and posterior scores were summed to get medial and lateral meniscal tear/extursion scores. The intra-and inter-observer correlation coefficient ranged from 0.86 to 0.96 for meniscal tear and 0.85 to 0.92 for meniscal extrusion ([24](#_ENREF_24)).

**WOMAC knee pain assessment**

Knee pain was assessed using the Western Ontario McMaster Osteoarthritis Index (WOMAC) ([25](#_ENREF_25)) at baseline, 2.6 and 5 years later using a 10-point scale from 0 (no pain) to 9 (most severe pain). The 5 subscales (walking on flat surface, going up/down stairs, at night, sitting/lying and standing upright) were assessed separately and summed to create a total pain score (0 to 45).

**Radiographic osteoarthritis**

A standing anteroposterior semiflexed view of the right and left knee with 15°of fixed knee flexion was performed in all subjects at baseline and scored individually for osteophytes and joint space narrowing (JSN) on a scale of 0-3 (0=normal and 3=severe) according to the Altman atlas as previously described ([26](#_ENREF_26)). Medial tibiofemoral or lateral tibiofemoral JSN was scored separately, while osteophytes were scored at each site of medial tibia, medial femur, lateral tibia and lateral femur. The prevalence of medial or lateral tibiofemoral JSN or osteophytes was defined as the presence of radiographic osteoarthritis (ROA) ([27](#_ENREF_27)).

**Smoking**

Smoking status (never, or ever) was determined by questionnaire from the following questions: “Have you ever smoked cigarettes on a regular basis?”

**Knee** **bone size measurement**

Knee tibial plateau bone areas were measured using the software program Osiris as previously described ([18](#_ENREF_18)). Medial and lateral tibial plateau bone areas were uniform in nature and can be measured directly from the reformatted axial images. The CVs for these measures are 2.2-2.6% ([26](#_ENREF_26)).

**Data analysis**

Student’s t-tests and χ2 tests were used to compare differences between subjects with and without an increase in PFJ BMLs. Crude and adjusted linear regression was used to assess whether PFJ BML changes over 2.6 years were associated with changes in knee pain in the different sub-scales over 5 years, before and after adjustment for potential confounders ( age, sex, BMI, baseline patellar BML, ROA, smoking status). Crude and adjusted log binomial regression was used to examine the associations between increases in PFJ BMLs as an outcome, and baseline cartilage volumes as well as baseline cartilage defect scores as predictors, both before and after adjustment for potential confounders. A *p*-value less than 0.05 (2-tailed) was considered statistically significant. All statistical analyses were performed on Stata version 12.0 for Windows (StataCorp, College Station, TX, USA).

**RESULTS**

**Characteristics of the study population**

1100 participants aged between 51 and 81 (mean 63 years) were recruited to the TASOAC study. 406 subjects completed MRI measures at baseline and follow-up. MRI scans were discontinued after this sample due to decommissioning of the MRI scanner. WOMAC knee pain data were available on these subjects at 5 years’ follow-up. As previously reported ([28](#_ENREF_28)), study participants who did not complete MRI measures were similar to the remainder of the cohort in terms of demographics, smoking status, cartilage defects, BMLs, cartilage volume and ROA at baseline.

The characteristics of the study sample grouped by increase or no increase in PFJ BMLs at 2.6 years follow-up are presented in Table 1. Subjects who had an increase in PFJ BMLs had a higher patellar cartilage defect score and lower patellar cartilage volume at baseline and were less likely to have smoked but were similar in terms of BMI. There were no significant differences in age, sex, BMI, knee pain and ROA (%) between people with increased PFJ BMLs and those without (Table 1).

**Natural history of PFJ BMLs**

109 of 406 participants (27%) who completed follow-up had PFJ BMLs at baseline. Of these participants, 49 (45%) persisted, 26 (24%) increased in grade, and 34 (31%) improved including 23 (21%) which completely resolved. PFJ BMLs were absent in a total of 297 subjects at baseline, of which 59 devloped new BMLs (19.7% of knees) over 2.6 years (Figure 2).

Grade 1 BMLs (≤25% of the region on the same slice) changed most often, accounting for the majority of newly induced lesions (76.3%), and lesions that resolved over 2.6 years (87%).

**WOMAC pain and PFJ BMLs**

Table 2 describes the association between changes in PFJ BMLs over 2.6 years and changes in WOMAC knee pain over 5 years. A change in PFJ BML score over 2.6 years was associated with a change in total WOMAC pain and knee pain when going up and down stairs over 5 years, after adjustment for age, sex, BMI, ROA, smoking status, , baseline PFJ BMLs and baseline cartilage defects. No statistically significant associations between PFJ BMLs changes and changes in other WOMAC knee pain subscales were observed.

**Cartilage volume/defects and PFJ BMLs**

Table 3 describes the relationship between baseline cartilage volume, baseline cartilage defects, and increases in PFJ BMLs over 2.6 years. Higher PFJ and TFJ cartilage volume at baseline was associated with reduced risks of having an increase in PFJ BMLs. This result remained significant after adjustment for age, sex, BMI, smoking status, ROA, baseline patellar BMLs, and baseline total cartilage defects, total cartilage volume, meniscal tears and meniscal extrusion. Baseline PFJ cartilage defects were associated with increased odds of having an increase in PFJ BMLs; this association also remained significant after adjustment for age, sex, BMI, ROA, smoking status and baseline patellar BMLs and further adjustment for baseline PFJ BMLs, baseline total tibiofemoral BMLs, total cartilage defects, total cartilage volume, meniscal tears and meniscal extrusion. There were no significant associations between cartilage defects at the tibiofemoral compartment and increases in PFJ BMLs.

Figure 3 shows the association between baseline PFJ cartilage defects and increase in PFJ BMLs. There was a higher rate of increased PFJ BMLs in those with higher baseline PFJ cartilage defects scores especially grade 3 and 4.

**Discussion**

This is the first population-based longitudinal study that describes the natural history of PFJ BMLs and the associations with WOMAC knee pain as well as knee structures. PFJ BMLs were not static, with over one third participants showing change (both increasing and decreasing) over 2.6 years of follow-up. Changes in PFJ BMLs over 2.6 years were associated with change in knee pain when going up or down stairs over 5 years, suggesting that changes in PFJ BMLs are clinically relevant. Furthermore, baseline PFJ cartilage volume was associated with a decrease in PFJ BMLs and baseline PFJ cartilage defects were associated with an increase in PFJ BMLs, indicating a site-specific effect of cartilage morphology on PFJ BMLs.

We found that approximately half of the pre-existing PFJ BMLs showed a change in size over 2.6 years, with one third of pre-existing PFJ BMLs decreasing in score over 2.6 years. The regression rate was higher than some previous studies which assessed BMLs in whole knee ([3](#_ENREF_3), [29](#_ENREF_29)), but lower than that in a study which described knee joints BMLs in a cohort with symptomatic knee OA over 30 months ([30](#_ENREF_30)). The majority of the subjects whose BMLs resolved (87%) and those with new BMLs (76%) had grade 1 PFJ BMLs, suggesting that milder PFJ BMLs when BMLs have a greater potential to reverse.

Many studies have linked TF BMLs and knee pain ([4](#_ENREF_4), [31-33](#_ENREF_31)). Our team previously reported that tibiofemoral BMLs were associated with knee pain ([13](#_ENREF_13)) and patellar BMLs were deleteriously associated with increased knee pain especially going up/down stairs ([34](#_ENREF_34)). However, associations between knee pain and PFJ BMLs has been less frequently reported ([35-37](#_ENREF_35)). The current study found that the change in PFJ BMLs over 2.6 years was associated with changes in total WOMAC pain score and knee pain when going up and down stairs over 5 years. This model was not same time frame but does allow assessment of whether changes in PFJ BMLs over 2.6 years predict changes in WOMAC knee pain over 5 years. The results were expected given that PFJ structural changes are commonly thought to be the causes of anterior knee pain during activities in which the knee is flexed, such as squatting and going up and down stairs ([38](#_ENREF_38)).

Previous studies assessing the whole knee suggest that subchondral bone might play a role in cartilage degradation and in the early development of knee clinical symptoms ([39](#_ENREF_39)), with subchondral BMLs predicting increased progression of cartilage defects and loss of cartilage volume ([3](#_ENREF_3), [40](#_ENREF_40)). However, change in BMLs may be secondary to the cartilage damage. This finding was in line with our previous finding that baseline cartilage defects predicted BML progression in the tibiofemoral compartment ([10](#_ENREF_10)). In order to confirm this hypothesis in the PFJ, we examined whether baseline cartilage morphology could predict increases in PFJ BMLs. Baseline PFJ cartilage volume was associated with a decrease in PFJ BMLs and baseline PFJ cartilage defects were associated with an increase in PFJ BMLs over 2.6 years. Meniscal pathology have been reported to have a substantially increased risk of both incident and enlarging BML over 30 months ([41](#_ENREF_41)), however, in our current study, significant associations between cartilage morphology and increases in PFJ BMLs remained unchanged after further adjustment for meniscal tears and meniscal extrusion, indicating independent associations between PFJ cartilage morphology and PFJ BMLs. The current study also found that tibiofemoral cartilagedefects were not associated with changes in PFJ BMLs, suggesting compartment specific associations. This is consistent with the tibiofemoral compartment ([9](#_ENREF_9), [10](#_ENREF_10)). Somking has been found to be related to knee BMLs ([42](#_ENREF_42)) as well as knee pain and cartilage defects ([43](#_ENREF_43), [44](#_ENREF_44)). So it was considered as a potential confounder. However, no significant differences were made after smoking status was adjusted in multivariable analyses.

There are several potential limitations in this study. First, follow-up MRI scans were only available for the current study in 406 out of 1100 participants. However, between the current study sample and the rest of cohort were similar in terms of demographics, ROA, baseline cartilage volume, defects and BMLs (data not shown). Secondly, BML scores were measured by grading the slice with the greatest BML size using a semi-quantitative scale (0 to 3) rather than a quantitative measure of area or volume, which is likely to be more sensitive. Considering the slice thickness (4 mm) and interslice gap (0.5 to 1.0mm) of our imaging protocol, some lesions (especially small ones) may be underestimated if most of them lies within the interslice gap. Thirdly, we were not able to measure knee alignment, which has been linked to BMLs ([45](#_ENREF_45), [46](#_ENREF_46)). However, it remains uncertain whether this is a cause effect association. Fourth, patella axial and lateral firm were not included in the radiographic examination, which may impair the veracity of ROA assessment.

**Conclusions**

PFJ BMLs are not static and change is clinically relevant. PFJ cartilage morphology predicts increases in PFJ BMLs

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**Authors’ contributions**

ZZ was responsible for data collection, data management and patellafemoral BMLs measurement, analysis and interpretation of data, preparation of the manuscript. XJ and LL participated in analysis and interpretation of the data and critically revised the manuscript. BA participated in the statistical analysis and manuscript preparation. WH participated in the acquisition, analysis and interpretation of data. FC designed and carried out the study planning, participanted in analysis and interpretation of data. CD and GJ had full access to all of the data in this study and take responsibility for the integrity of the data and the accuracy of the data analysis. CD and GJ designed and carried out the study planning, participated in the acquisition, analysis and interpretation of data, and manuscript preparation. All authors have read and approved the final manuscript.

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**Table 1.** Characteristics of the participants.

|  |
| --- |
|  Patellofemoral joint BMLs |
|  | No Increase(n=321) | Increase(n=85) | *p* value |
| Age | 62.9±7.1 | 61.8±7.6 | 0.25 |
| Females (%) | 50 | 50 | 0.86 |
| BMI (kg/m2 ) | 27.5±4.3 | 28.0±4.9 | 0.38 |
| ROA present (%) | 70 | 61 | 0.75 |
| Knee pain (%) | 50 | 40 | 0.54 |
| Ever smoked (%) | 50 | 40 | **0.04** |
| Tibia Bone size (cm2) | 33.6±4.9 | 32.7±4.2 | 0.13 |
| PFJ BMLs at baseline (%) | 26 | 30 | 0.38 |
| TFJ BMLs at baseline (%) | 32 | 42 | 0.09 |
|  PFJ Cartilage defect score at baseline | 3.2±1.5 | 4.0±1.6 | **<0.01** |
| TFJ Cartilage defect score at baseline | 4.2±1.8 | 4.4±1.6 | 0.37 |
|  PFJ cartilage volume at baseline (ml) | 6.5±1.6 | 6.2±1.5 | 0.07 |
| TFJ cartilage volume at baseline (ml) | 10.4±2.6 | 10.1±2.1 | 0.29 |

Abbreviation: ROA, radiographic osteoarthritis; BMI, body mass index; PFJ, patellofemoral joint; TFJ, tibiofemoral joint; BMLs, bone marrow lesions. \*Data are given as mean ± SD unless otherwise indicated. Student’s t-test or chi-square test (where appropriate) were used to test for significant differences between two groups. An increase in patellofemoral joint (PFJ) BMLs is defined as a change in BMLs of ≥1 from baseline to follow-up (vs. no increase).

**Table 2.** Associations between change in PFJ BMLs over 2.6 years and changes in WOMAC pain over 5 years.

|  |  |  |  |
| --- | --- | --- | --- |
|   | Univariable | Multivariable \* | Multivariable\*\* |
|  | β (95% CI) | β (95% CI) | β (95% CI) |
|  Total WOMAC knee pain | **0.78 (0.15, 1.40)** | **0.81(0.17, 1.45)** | **0.67 (0.03, 1.31)** |
|  Pain walking on a flat surface | 0.03 (-0.12, 0.18) | 0.03 (-0.12, 0.19) | 0.02 (-0.14, 0.18) |
|  Pain going up and down stairs | **0.28 (0.07, 0.48)** | **0.27 (0.07, 0.47)** | **0.24 (0.04, 0.44)** |
|  Pain at night when in bed | **0.22 (0.03, 0.41)** | **0.22 (0.02, 0.42)** | 0.17 (-0.03, 0.37) |
|  Pain sitting or lying | 0.12 (-0.02, 0.27) | 0.13 (-0.02, 0.28) | 0.11 (-0.05, 0.26) |
|  Pain standing upright | 0.13 (-0.02, 0.29) | 0.15 (-0.01, 0.32) | 0.15 (-0.03, 0.29) |

\*Adjusted for age, sex, BMI, ROAand smoking status, \*\*further adjusted for baseline patellofemoral BML, baseline tibiofemoral BMLs, baseline patella cartilage defect, baseline tibiofemoral cartilage defect and baseline knee pain. Bold denotes statistical significance.

**Table 3.** Associations between baseline cartilage volume, baseline cartilage defects, and increases in PFJ BMLs over 2.6 years.

|  |  |  |  |
| --- | --- | --- | --- |
|   | Univariable | Multivariable \* | Multivariable \*\* |
|  | RR (95% CI) | RR (95% CI) | RR (95% CI) |
| Baseline PFJ cartilage volume (ml) | **0.88 (0.77, 0.99)** | **0.71 (0.57, 0.87)** | **0.69 (0.52, 0.90)** |
| Baseline TFJ cartilage volume (ml) | 0.96 (0.89, 1.03) | **0.85 (0.74, 0.97)** | **0.67 (0.49, 0.92)** |
| Baseline PFJ cartilage defects (per grade) | **1.48 (1.24, 1.76)** | **1.46 (1.22, 1.76)** | **1.73 (1.38, 2.17)** |
| Baseline TFJ cartilage defects (per grade) | 1.04 (0.96, 1.13) | 1.03 (0.93, 1.14) | 0.99 (0.89, 1.10) |

PFJ, patellofemoral joint; TFJ, tibiofemoral joint; \*Adjusted for age, sex, BMI, baseline patella BMLs, smoking status and ROA. \*\* further adjusted for baseline PFJ BMLs, baseline total tibiofemoral BMLs, total cartilage defects and total cartilage volume, meniscal extrusion and meniscal tears. Bold denotes statistical significance.



**Figure 1. Examples of change in BMLs over 2.6 years**

**Figure 2.** Natural history of patellofemoral bone marrow lesions over 2.6 years in older adults.

**Figure 3 .** Association between patellofemoral cartilage defect grades at baseline and increases in PFJ BMLs.