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Association of Blood Pressure with Knee Cartilage Composition and Structural Knee Abnormalities: Data from the Osteoarthritis Initiative

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Abstract

Objective.—To investigate the associations of systolic blood pressure (SBP) and diastolic blood pressure (DBP) with changes in knee cartilage composition and joint structure over 48-months, using magnetic resonance imaging (MRI) data from the Osteoarthritis Initiative (OAI).

Materials and methods.—1126 participants with right knee Kellgren-Lawrence (KL) score 0–2 at baseline, no history of rheumatoid arthritis, blood pressure measurements at baseline and cartilage T2 measurements at baseline and 48-months were selected from the OAI. Cartilage composition was assessed using MRI T2 measurements, including laminar and grey-level co-occurrence matrix texture analyses. Structural knee abnormalities were graded using the Whole-Organ Magnetic Resonance Imaging Score (WORMS). We performed linear regression, adjusting for age, sex, body mass index, physical activity, smoking status, alcohol use, KL score, number of anti-hypertensive medications and number of nonsteroidal anti-inflammatory drugs.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

Informed consent was obtained from all individual participants included in the study. The OAI study was compliant with the Health Insurance Portability and Accountability Act and was approved by the local institutional review board of each OAI participating center. All procedures performed in this study were in accordance with the ethical standards of the local institutional review board and with the 1964 Helsinki declaration and its later amendments.

Results.—Higher baseline DBP was associated with greater increases in global T2 (coefficient: 0.22 (95% CI: 0.09, 0.34), $P = 0.004$), global superficial layer T2 (coefficient: 0.39 (95% CI: 0.20, 0.58), $P = 0.001$), global contrast (coefficient: 15.67 (95% CI: 8.81, 22.53), $P < 0.001$), global entropy (coefficient: 0.02 (95% CI: 0.01, 0.03) $P = 0.011$) and global variance (coefficient: 9.14 (95% CI: 5.18, 13.09), $P < 0.001$). Compared to DBP, the associations of SBP with change in cartilage T2 parameters and WORMS subscores showed estimates of smaller magnitude.

Conclusion.—Higher baseline DBP was associated with higher and more heterogenous cartilage T2 values over 48-months, indicating increased cartilage matrix degenerative changes.

Keywords

Knee osteoarthritis; blood pressure; magnetic resonance imaging; cartilage

Introduction

Osteoarthritis (OA) is a highly prevalent, disabling musculoskeletal disorder [1]. Current treatment options for OA are limited and primarily target the symptoms and disability caused by OA [1, 2]. Due to the chronic nature of OA and lack of longitudinal studies investigating OA biomarkers, our understanding of risk factors for the early development of OA is limited.

Given its potential significance in improving OA preventative strategies, there has been growing interest in studying the association of OA with metabolic syndrome (MS). Several studies have shown associations between OA and MS components, including systolic blood pressure (SBP) and diastolic blood pressure (DBP) [3–8]. Lo et al. showed that high SBP was associated with increased incidence of radiographic knee OA [5]. Another study investigating the relationship of MS components with radiographic knee OA in the Framingham Offspring cohort reported an association between high DBP and incident radiographic OA [6]. Many of the previous studies classified subjects based on radiographic measures, which are generally insensitive for early and mild OA. Furthermore, we have not found any studies that evaluated the association of blood pressure with knee cartilage composition and morphological changes as assessed with magnetic resonance imaging (MRI).

MRI-based T2 relaxation time measurement is a quantitative imaging technique that characterizes the biochemical properties of cartilage composition and measures early degenerative changes in the cartilage extracellular matrix [9]. Several studies have demonstrated that, in addition to mean T2, the laminar organization and spatial distribution of T2 values may be important when investigating early OA pathogenesis [10–13]. Laminar analysis, which partitions knee cartilage into a deep bone layer and superficial articular layer, measures early laminar disruption within cartilage that may occur prior to changes in full-thickness cartilage mean T2 values [12]. Grey-level co-occurrence matrix (GLCM) texture analysis evaluates the spatial distribution of T2 values. GLCM texture parameters (contrast, entropy, variance) supplement standard T2 measurements by providing information at a pixel level and measuring cartilage heterogeneity. Higher contrast, entropy and variance are associated with a more inhomogeneous cartilage texture and are features of

early degenerative changes when there is more fluid in the cartilage and a more heterogeneous collagen architecture.

The goals of our study were therefore to investigate whether SBP and DBP are associated with changes in knee cartilage composition and structural knee abnormalities over 48-months, assessed using MRI-based T2 relaxation time measurements and modified whole-organ magnetic resonance imaging scores (WORMS), respectively.

Materials and methods

Study participants and selection

The Osteoarthritis Initiative (OAI) is a multicenter, longitudinal observational study of the evolution of OA. The OAI enrolled 4796 study participants ages 45–79 years with either risk factors for the development of knee OA, established symptomatic knee OA or no OA risk factors. The aim of the OAI is to establish a public domain research resource for investigating and validating biomarkers of knee OA onset and progression, including those derived from MRI (https://data-archive.nimh.nih.gov/oai). Informed consent was reviewed and approved for each participant by the local institutional review board of the OAI participating center.

In this study, we selected OAI participants who had no or mild radiographic tibiofemoral OA (Kellgren-Lawrence (KL) score 0–2) in the right knee at baseline, blood pressure measurements at baseline and cartilage T2 measurements in the right knee at baseline and 48-months (Fig. 1). Participants with a history of rheumatoid arthritis or another inflammatory arthropathy were excluded. Participants with radiographic KL score ≥ 3 in the right knee were excluded given that previous studies have shown T2 measurements may be limited for the evaluation of cartilage degeneration once advanced cartilage loss occurs [14]. T2 measurements and WORMS were analyzed in prior studies with different aims from the current study [14–22]. Based on our inclusion and exclusion criteria, right knees from 1126 participants were selected and analyzed.

Blood pressure measurements

Blood pressure measurements in the OAI study protocol closely followed the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) [23] and were assessed by trained OAI staff using the auscultatory method. Participants were asked to avoid drinking caffeine, exercising or smoking for at least 30 minutes prior to blood pressure assessment. Furthermore, participants were asked to sit in a chair with feet on the floor and arm supported at heart level for at least 5 minutes prior to measurement. An estimated SBP was first measured using the palpated radial obliteration pressure and subsequently an appropriately sized cuff was inflated 20–30 mmHg above this level for auscultatory determination. SBP and DBP were measured using a conventional mercury sphygomomanometer and stethoscope. Blood pressure measurements from the OAI baseline, 12-, 24-, 36- and 48-month visits were used in this study. These data are publicly available (AllClinical_SAS, versions 0.2.2, 1.2.1, 3.2.1, 5.2.1).

Participant characteristics

For all participants that fulfilled the selection criteria, age, gender, body mass index (BMI), Physical Activity Scale for the Elderly (PASE), smoking status and alcohol use at baseline were collected. These data are publicly available (AllClinical_SAS, version 0.2.2; Enrollees_SAS, version 22).

Medications

Information about prescription medication use was obtained using a standardized medication inventory form for the OAI. Participants brought in all medications that they took during the 30 days preceding the OAI baseline visit. Medications were classified and coded using the Iowa Drug Information System ingredient database. Medication inventory data were reviewed to identify anti-hypertensive medications (AHM) whose primary indication was the treatment of hypertension including beta blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, thiazides, chlorthalidone, dihydropyridine calcium channel blockers and aliskiren. Nonsteroidal anti-inflammatory drugs (NSAID), which are known to increase blood pressure [24], were also identified including ibuprofen, flurbiprofen, naproxen, oxaprozin, celecoxib, rofecoxib, valdecoxib, diclofenac, sulindac, etodolac, ketorolac, nabumetone, indomethacin, tolmetin, piroxicam and meloxicam. These data are publicly available (MIF00_SAS, version 0.2.2).

MRI protocol

MR images were acquired using four 3.0T scanners (Siemens Magnetom Trio; Siemens Healthcare, Erlangen, Germany) with quadrature transmit-receive coils (USA Instruments, Aurora, OH, USA) at the OAI clinical sites. For cartilage T2 measurements, a sagittal 2D multislice multiecho (MSME) sequence (echo times [TE] = 10–70 ms; repetition time [TR] = 2700 ms) was used. The following sequences were used for analysis of structural knee abnormalities: a sagittal 2D intermediate-weighted (IW) fat-suppressed turbo spin-echo (TSE) sequence (TR = 3200 ms; TE = 30 ms), a coronal 2D IW non-fat suppressed TSE sequence (TR = 3700 ms; TE = 29 ms) and a 3D dual echo steady-state gradient-echo with selective water excitation sequence (TR = 16.3 ms; TE = 4.7 ms). Details regarding the MR acquisition protocols have been described previously [25].

Image Analysis

Radiographic KL score—Fixed flexion knee radiographs were obtained at the OAI baseline visit and central readers assessed radiographic severity in the tibiofemoral compartment using the Kellgren-Lawrence (KL) score [26]. Participants with KL scores 0 (no radiographic features of OA), KL score 1 (doubtful joint space narrowing with possible osteophytes) and KL score 2 (possible joint space narrow with definite osteophytes) in the right knee at baseline were selected. Baseline radiographic KL scores are publicly available (kXR_SQ_BU00_SAS, version 0.8).

T2 measurements—For T2 analysis, semiautomatic cartilage segmentation of five knee regions (patella, lateral/medial femur, and lateral/medial tibia) was performed using an in-house, spline-based algorithm written in MatLab (MathWorks, Natick, MA) as described

previously [19]. The trochlear region was excluded from the analysis due to interfering flow artifacts from the popliteal artery. Furthermore, cartilage sections with compromised image quality or artifacts limiting segmentation were excluded from the analysis. T2 maps were computed from the MSME images on a pixel-by pixel basis using six echoes (TE = 20–70 ms) after excluding the first echo in order to optimize the signal-to-noise ratio [27–30]. Mean T2 values were computed for each cartilage region, and the global T2 values were computed as the mean of all knee regions.

Laminar and GLCM texture analyses—Laminar analysis divided the cartilage of each segmented region into two layers of equal thickness: a superficial articular layer and a deep bone layer adjacent to the cartilage-bone interface [12]. In addition, texture analysis was performed to assess the grey level distributions of pixels based on the GLCM as described by Haralick et al [31]. Based on our previous work, three GLCM texture parameters were included in the analysis: contrast, entropy and variance [32]. Contrast is a measure of the differences in neighboring pixel values with higher contrast indicating a greater probability of neighboring pixels with large differences in T2 values. Entropy represents the probability of finding another pixel pair with the same value in the entire image. A higher entropy suggests a more random distribution of T2 values. Variance is a measure of the distribution of pixel values about the region mean. Therefore, a higher variance reflects a high number of pixels with T2 values dispersed from the mean T2.

WORMS scoring—MR images of the right knee at baseline and 48-months were previously graded using the modified semi-quantitative Whole-Organ Magnetic Resonance Imaging Score (WORMS) [33]. The modified WORMS has been described in detail in earlier studies [15–17, 20] and assesses structural abnormalities of the knee joint on a numeric grading system, with higher scores indicating increased severity of morphological findings. Structural abnormalities included cartilage lesions, bone marrow edema pattern (BMEP) and effusion. Cartilage lesions (graded 0–6) and BMEP (graded 0–4) were assessed in the same six regions (patella, lateral/medial femur, lateral/medial tibia, trochlea). Effusion was scored according to WORMS as previously described [33]. For cartilage lesions and BMEP, the WORMS max score was defined as the maximum lesion score in any knee region.

Reproducibility—Cartilage T2 and WORMS reproducibility results have been described previously [19, 21, 22]. To assess inter- and intrareader reproducibilities for cartilage T2 measurements, coefficients of variation (CV) were calculated on a percentage basis as the root mean square average. The interreader reproducibility error for mean T2 across ranged from 1.2% in the patella to 1.9% in the lateral tibia [19]. The intrareader reproducibility for mean T2 ranged from 0.8% in the medial femur to 3.2% in the patella [21].

Three radiologists with 8-, 6-, and 6-years of experience performed WORMS readings; each study was read by two radiologists independently and both were blinded to clinical data. In equivocal cases, a consensus reading was performed with a musculoskeletal radiologist with 25-years of experience. For interreader reproducibility of WORMS readings, the intraclass correlation coefficients (ICC) ranged from 0.97 (95% CI: 0.95–0.98) for WORMS cartilage to 0.75 (95% CI: 0.52–0.86) for WORMS effusion [22]. The ICCs for intrareader

reproducibility ranged from 0.99 (95% CI: 0.98–0.99) and 0.99 (95% CI: 0.99–0.99) for WORMS cartilage to 0.90 (95% CI: 0.81–0.94) and 0.74 (95% CI: 0.52–0.86) for WORMS effusion [22]. Similar inter- and intrareader reproducibilities have been published previously [15, 20].

Statistical Analysis

Statistical analysis was performed using Stata software (Version 15, College Station, TX, USA: StataCorp LP). Linear regression models were performed using standardized values for baseline SBP and DBP as primary predictors and change in cartilage T2 and WORMS subscores over 48-months as primary outcomes. To make interpretation easier, we report standardized coefficients – the change in outcome per standard deviation change in the predictors. Standardized values for predictors were calculated by subtracting the mean value across all participants from the value for each participant and dividing by the standard deviation. Based on prior analyses [8, 17, 18, 32], the change in laminar parameters (superficial layer T2, deep layer T2) and GLCM texture parameters (contrast, entropy, variance) over 48-months were considered as secondary outcomes. Models were adjusted for baseline age, sex, BMI, PASE, smoking status, alcohol use, KL score, number of anti-hypertensive medications (AHMs) and number of nonsteroidal anti-inflammatory drugs (NSAIDs) reported at baseline. All predictors, outcomes and covariates (except sex, smoking status, alcohol use) were analyzed as continuous variables. Furthermore, we performed a sensitivity analysis to assess whether the results differed when the blood pressure for each participant was averaged across five visits. Average SBP and DBP were calculated as the mean of baseline, 12-, 24-, 36- and 48-month SBP and DBP measurements for each participant, respectively. Standardized values for average SBP and DBP were subsequently calculated as previously described. We conducted an additional sensitivity analysis to test the robustness of our results, excluding participants with mild radiographic tibiofemoral OA in either knee (KL $\geq$ 2). To evaluate whether the associations of SBP and DBP with change in cartilage T2, laminar parameters, GLCM texture parameters and WORMS subscores were modified by number of AHMs, we included interaction terms between number of AHMs and SBP and DBP. Models with and without these interaction terms were compared using the likelihood ratio test. In addition, linear regression models were assessed for departures from linearity using component-plus-residual plots. P-values were adjusted for multiple comparisons across all models using the Benjamini-Hochberg procedure. Two-way false discovery rate (FDR) adjusted P-values < 0.05 were considered statistically significant.

Results

Participant characteristics

Participant characteristics are summarized in Table 1. The average age of all study participants was 58.8 (8.7) years with a higher proportion of females (59.1%). The average BMI was 28.3 (4.4) kg/m^2, the average SBP was 122.4 (15.4) mmHg, and the average DBP was 75.4 (9.7) mmHg. 408 (36.2%) participants reported taking at least one AHM and 170 (15.1%) participants reported taking at least one NSAID at baseline.

Change in cartilage T2 and laminar parameters over 48-months

A one standard deviation increase in baseline DBP (9.66 mmHg) was associated with greater increases in global T2 (coefficient: 0.22 (95% CI: 0.09, 0.34), *FDR-adjusted P* = 0.004; Fig. 2) and global superficial layer T2 (coefficient: 0.39 (95% CI: 0.20, 0.58), *FDR-adjusted P* = 0.001) over 48-months as shown in Table 2. This suggests that an increase in baseline DBP was associated with worsening of T2 values and increase degeneration in the global and superficial layers of knee cartilage. Compared to baseline DBP, a weaker effect was observed for the associations of baseline SBP with changes in global T2, global deep layer T2 and global superficial layer T2. Similar results were observed when using average SBP and DBP as predictors (Online Resource 1).

Change in GLCM texture parameters over 48-months

As shown in Table 2, higher baseline DBP was associated with increases in GLCM global contrast (coefficient: 15.67 (95% CI: 8.81, 22.53), *FDR-adjusted P* < 0.001), GLCM global entropy (coefficient: 0.02 (95% CI: 0.01, 0.03), *FDR-adjusted P* = 0.01), and GLCM global variance (coefficient: 9.14 (95% CI: 5.18, 13.09), *FDR-adjusted P* < 0.001) over 48-months. This indicates that an increase in baseline DBP was associated with more heterogenous cartilage T2 values, suggesting a more disordered cartilage composition. Similar results were observed when using average SBP and DBP over the five visits as predictors except for the association of average DBP with change in GLCM global entropy which was no longer significant after adjustment for multiple comparisons (Online Resource 1). Compared to baseline DBP, the associations of baseline SBP with changes in global contrast, global entropy and global variance over 48-months demonstrated estimates of smaller magnitude. Furthermore, there was no evidence of departures from linearity in the associations of baseline DBP and SBP with change in cartilage T2, laminar parameters and GLCM texture parameters.

Change in WORMS subscores over 48-months

There were no strong associations of baseline SBP or baseline DBP with changes in WORMS subscores (Table 3). Similar results were observed in the models using average SBP and DBP as predictors (Online Resource 2).

In a sensitivity analysis excluding participants with KL ≥ 2 in either knee, the estimates of the associations of baseline DBP with change in cartilage T2 and WORMS subscores were consistent in direction though they were smaller in magnitude. There was no consistent evidence for interactions between number of AHMs and either SBP or DBP for change in cartilage T2, laminar parameters, GLCM texture parameters and WORMS subscores (all *FDR-adjusted P* values for likelihood ratio test > 0.05).

Discussion

This study investigated the associations of SBP and DBP with changes in knee articular cartilage composition using MRI T2 relaxation time measures and structural knee abnormalities over 48-months as endpoints. Higher DBP was associated with a greater

increase in cartilage T2 parameters, suggesting accelerated deterioration of the cartilage matrix and a more heterogenous cartilage composition.

Previous studies have reported associations of hypertension with incident knee OA after adjustment for BMI [3–6]. The Research on Osteoarthritis and Osteoporosis Disability study reported that hypertension was associated with radiographic knee OA occurrence and progression [3]. Moreover, higher SBP but not DBP was associated with knee OA occurrence and progression; however, this association did not persist after adjustment for other MS components. Hussain et al. found that hypertension was associated with increased incidence of severe knee OA requiring total knee replacement [4]. In a meta-analysis of eight studies, Zhang et al. reported that there was a significant relationship between hypertension and radiographic and symptomatic knee OA [7]. A previous study from our group investigating the association of metabolic risk factors with cartilage degeneration assessed by T2 relaxation time demonstrated that hypertension was individually associated with baseline T2 [8]. Nonetheless, this association did not persist after adjustment for BMI. In the OAI cohort, Lo et al. demonstrated that high SBP, but not DBP, was associated with incident radiographic OA [5]. Furthermore, participants taking three or more antihypertensive medications had decreased odds of developing incident OA compared to those not taking any antihypertensive medications [5]. The Framingham OA study reported an association of high DBP with incident radiographic OA and the relationship between high SBP and incident radiographic OA was nearly significant as well [6]. Our results did not show a strong association of SBP with change in knee cartilage composition and structural abnormalities. In addition, there was no consistent evidence for interactions between number of AHMs and SBP and DBP for our outcomes. In contrast to previous studies which used either arthroplasty or radiographs as outcome measures for incident knee OA, our study utilized MRI-based parameters to assess longitudinal changes in cartilage composition and structural abnormalities. Nonetheless, there may still be potential associations of SBP with change in knee cartilage composition and structural abnormalities that we were not able detect in this study due to insufficient statistical power. Compared to the estimates of the associations of DBP with change in cartilage T2 parameters, the estimates for SBP were generally smaller in magnitude though in the same direction with overlapping confidence intervals.

The mechanism of the relationship between blood pressure and OA is unclear. Hypertension is more prevalent among individuals with OA and the two diseases share multiple risk factors, including age, obesity and other cardiovascular risk factors [34]. There is growing evidence supporting the role of vascular pathology in OA development and progression [35, 36]. Hypertension promotes microvasculature remodeling which may lead to reduced blood flow to subchondral bone and compromised nutrient and oxygen exchange into articular cartilage [35–37]. Given that hypertension confers a prothrombotic state [38], thrombotic blockage of microvasculature would further potentiate the deleterious effects of impaired subchondral perfusion. In animal models, spontaneously hypertensive rats had altered subchondral bone structure, thinner hyaline cartilage, superficial disruption to the articular surfaces and other OA-like lesions compared to control rats [39]. It is intriguing that the associations of DBP with change in cartilage composition were stronger than those of SBP with change in cartilage composition. DBP, a reflection of peripheral vascular resistance,

may be a more important determinant of small artery structure and media-to-lumen ratio than SBP [40].

Cartilage T2 parameters quantify the early biochemical stages of cartilage degeneration and have both clinical and prognostic significance. Elevated cartilage T2 values are associated with increased cartilage degeneration [41] and knee pain [20] and can predict morphological degeneration [21] and radiographic OA [10]. Carballido-Gamio et al. reported that GLCM entropy of cartilage T2 was higher in participants with mild knee OA as compared with controls [42]. In addition, participants with risk factors for knee OA but without symptomatic or radiographic OA were found to have higher and more heterogenous cartilage T2 values compared to healthy controls [17]. Thus, cartilage T2 parameters may serve as useful biomarkers for OA and identification of OA-related risk factors. The clinical significance of our results (e.g. a 0.22 increase in change in global T2 per 9.66 mmHg increase in baseline DBP) are best understood in the context of other longitudinal studies which reported increases of 0.04, 0.10 and 0.02 in change in global T2 per one point increase in WOMAC stiffness, disability and pain over 48-months, respectively [43]. Past studies have shown that targeting OA-related risk factors, such as obesity, can prevent incidence and progression of OA, relieve symptoms and improve quality of life [44]. Consequently, a greater understanding of how other risk factors, such as hypertension, contribute to the degenerative process of OA would aid in developing effective treatment and preventative strategies for knee OA.

We acknowledge that this study has a few limitations. First, there are multiple factors that influence blood pressure and many of these were not available to be assessed in the OAI including family history of hypertension, sodium intake and medication dosage. The observed associations do not establish causality and further studies, including mendelian randomization studies, are necessary to assess causal relationships between blood pressure and knee osteoarthritis. Furthermore, we could not assess the reliability of blood pressure measurements used in our study. It is well established that blood pressure values oscillate over the short-term [45] as well as long-term periods [46]. Therefore, we aimed to reduce the influence of blood pressure variability on our results in a sensitivity analysis using the average SBP and DBP measurements for each participant across the baseline, 12-, 24-, 36- and 48-month visits. Moreover, issues related to variability in medication frequency and duration of use as well as confounding by indication may account for why there was no strong evidence for interactions between number of AHMs and SBP and DBP observed in our study. Finally, data on smoking behavior and alcohol intake in the OAI was self-reported and may have been subject to recall bias and purposeful underreporting due to social desirability biases.

In conclusion, this study showed that higher DBP was associated with greater increases in cartilage T2 parameters over 48-months, signifying accelerated cartilage degeneration. While further mechanistic studies are needed to elucidate the pathophysiology behind this relationship, these results are significant given the lack of research on the association of blood pressure with cartilage composition and joint structures as well as clinical approaches for OA management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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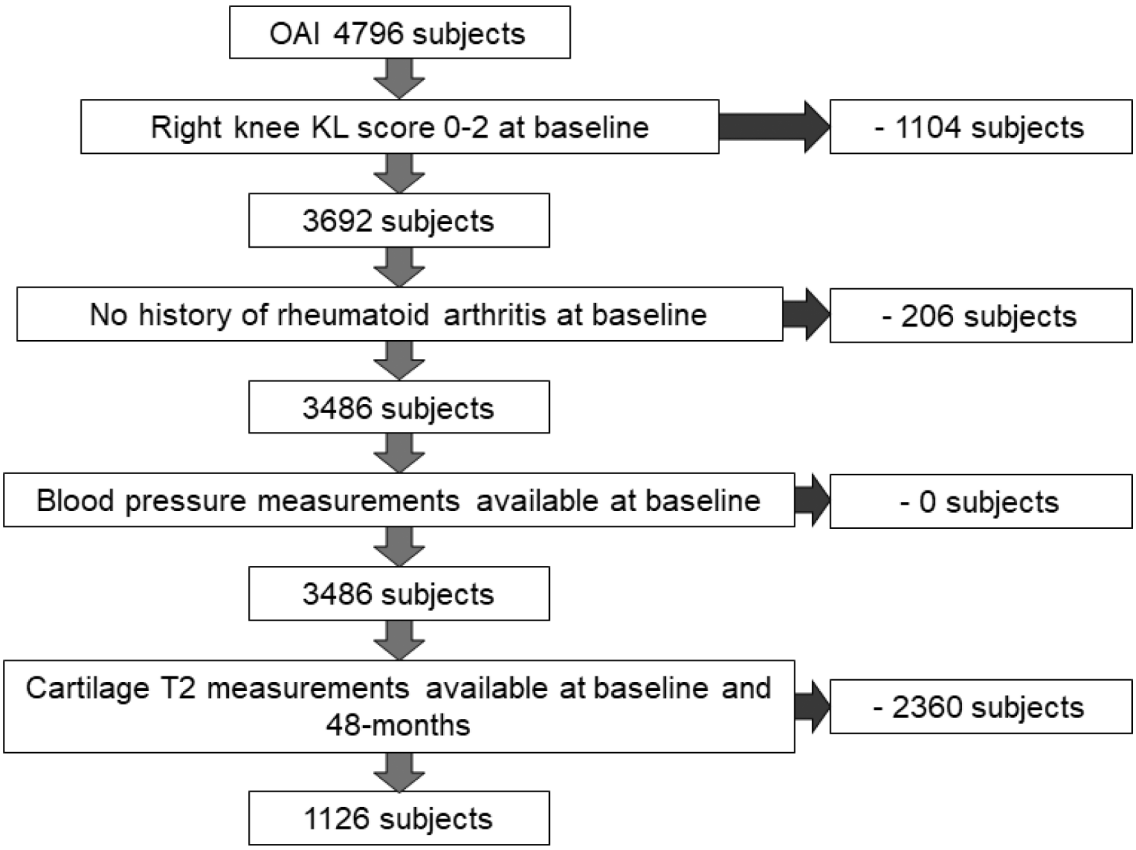

Fig. 1.
Flowchart demonstrating participant selection from the Osteoarthritis Initiative (OAI). KL = Kellgren-Lawrence

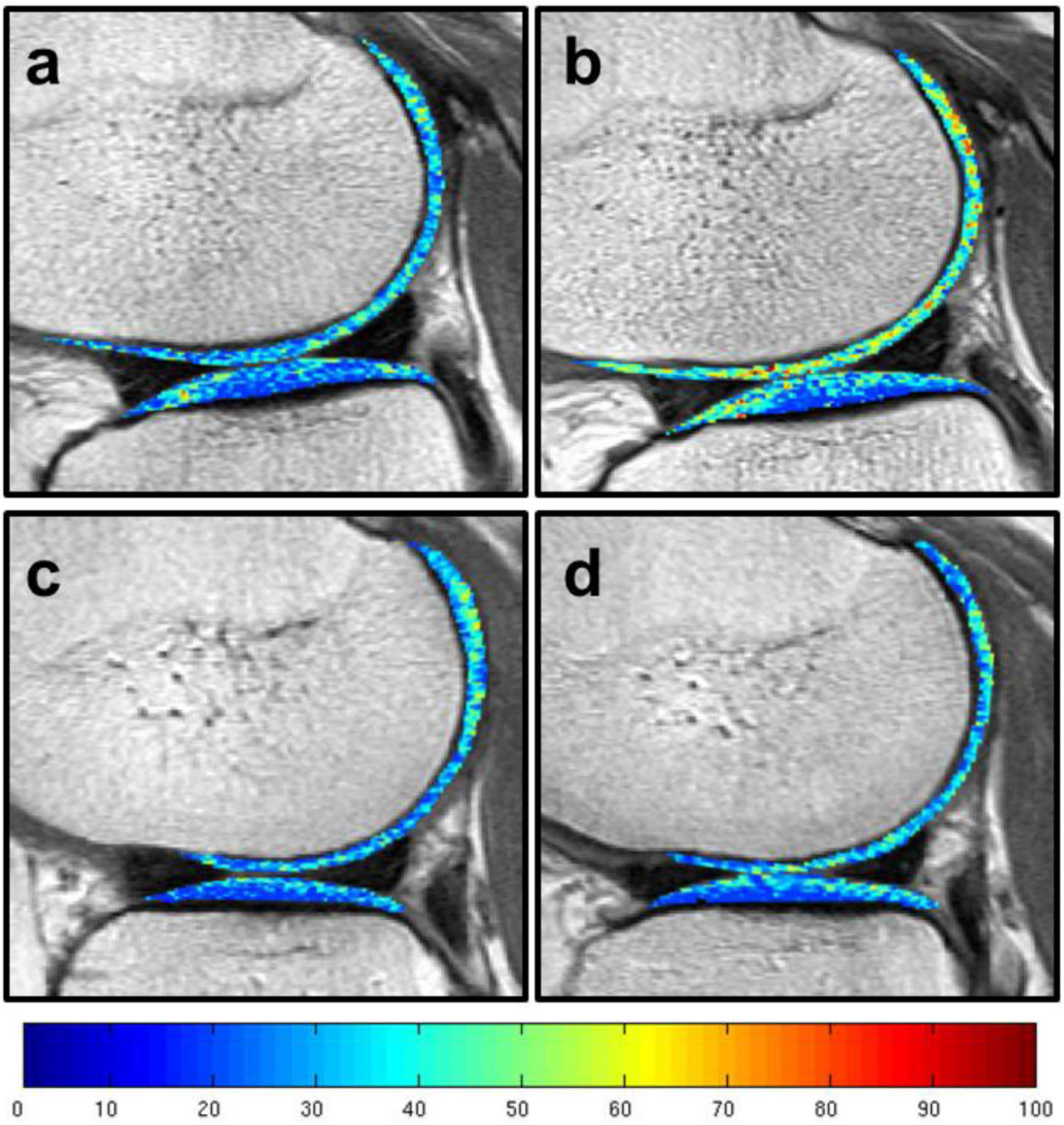

Fig. 2.

Representative T2 color maps (values are in milliseconds) overlaid on sagittal 2D multislice multiecho (MSME) sequences showing the lateral knee compartment in a study participant with a diastolic blood pressure (DBP) of 94 mmHg (A, B) and a participant with a DBP of 58 mmHg (C, D) over 48-months. Blue color represents lower T2 values while red represents higher T2 values. In comparison to the T2 color map at baseline showing predominantly lower T2 values (A), the T2 color map of the participant with the DBP of 94 mmHg shows overall elevated T2 values in the cartilage of the lateral femoral condyle and lateral tibia after 48-months (B) indicating progressive cartilage matrix degeneration. The T2 color maps of the participant with the DBP of 58 mmHg show predominately lower T2 values at both time points (C, D)

Table 1.

Baseline descriptive characteristics of participants

	All participants (n = 1126)
Age, mean (SD) years	58.8 (8.7)
Body mass index, mean (SD) kg/m^2	28.3 (4.4)
Female, n (%)	666 (59.1)
Physical Activity Scale for the Elderly, mean (SD)	167.0 (83.1)
Smoking status, n (%)	
Never	647 (57.7)
Former	50 (4.5)
Current	423 (37.7)
Current, but never regular	2 (0.2)
Alcohol use, n (%)	911 (81.1)
Right knee Kellgren-Lawrence, n (%)	
Grade 0	538 (47.8)
Grade 1	268 (23.8)
Grade 2	320 (28.4)
WOMAC Pain Score (range, 0–20), mean (SD)	1.7 (2.7)
Systolic blood pressure, mean (SD) mmHg	122.4 (15.4)
Systolic blood pressure, min - max mmHg	82 – 180
Diastolic blood pressure, mean (SD) mmHg	75.4 (9.7)
Diastolic blood pressure, min - max mmHg	50 – 110
Number of AHMs, n (%)	
0	718 (63.8)
1	223 (19.8)
2	134 (11.9)
3	43 (3.8)
4	6 (0.5)
5	2 (0.2)
Number of NSAIDs, n (%)	
0	956 (84.9)
1	160 (14.2)
2	10 (0.9)

Data are given as means (standard deviation), n (% of total) or range (minimum to maximum). WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; AHM = anti-hypertensive medication; NSAID = nonsteroidal anti-inflammatory drug.

Table 2.

Association of baseline systolic blood pressure (SBP) and baseline diastolic blood pressure (DBP) with longitudinal change in cartilage T2, laminar parameters and GLCM texture parameters over 48-months.

Change in cartilage T2 parameters over 48-months	Adjusted for baseline age, sex, BMI, PASE, smoking status, alcohol use, KL score, number of AHMs and number of NSAIDs					
	SBP			DBP		
	Coeff.	[95% CI]	*P**	Coeff.	[95% CI]	*P**
Global knee T2	0.08	[−0.05, 0.21]	0.48	0.22	[0.09, 0.34]	**0.004**
Global deep layer T2	0.08	[−0.09, 0.25]	0.59	0.18	[0.02, 0.35]	0.12
Global superficial layer T2	0.18	[−0.02, 0.37]	0.23	0.39	[0.20, 0.58]	**0.001**
Global contrast	4.78	[−2.22, 11.78]	0.43	15.67	[8.81, 22.53]	**<0.001**
Global entropy	0.00	[−0.01, 0.01]	0.96	0.02	[0.01, 0.03]	**0.01**
Global variance	1.76	[−2.28, 5.80]	0.62	9.14	[5.18, 13.09]	**<0.001**

Data are given as coefficients (Coeff.) associated with a one standard deviation increase in baseline SBP (15.41 mmHg) or baseline DBP (9.66 mmHg) with [95% confidence intervals] and computed as the absolute change between baseline and 48-months. False discovery rate (FDR) was controlled using the Benjamini-Hochberg procedure.

* FDR-adjusted *P*-values < 0.05 are in bold.

GLCM = grey-level co-occurrence matrix; BMI = body mass index; PASE = Physical Activity Scale for the Elderly; KL = Kellgren-Lawrence; AHM = anti-hypertensive medication; NSAID = nonsteroidal anti-inflammatory drug.

Table 3.

Association of baseline systolic blood pressure (SBP) and baseline diastolic blood pressure (DBP) with longitudinal change in WORMS subscores over 48-months.

Change in WORMS subscores over 48-months	Adjusted for baseline age, sex, BMI, PASE, smoking status, alcohol use, KL score, number of AHMs and number of NSAIDs					
	SBP			DBP		
	Coeff.	[95% CI]	*P**	Coeff.	[95% CI]	*P**
WORMS cartilage max	0.07	[−0.03, 0.17]	0.37	0.06	[−0.03, 0.15]	0.47
WORMS BMEP max	0.03	[−0.03, 0.10]	0.56	0.02	[−0.04, 0.08]	0.71
WORMS effusion	0.04	[0.00, 0.07]	0.23	0.04	[0.01, 0.08]	0.09

Data are given as coefficients (Coeff.) associated with a one standard deviation increase in baseline SBP (15.41 mmHg) or baseline DBP (9.66 mmHg) with [95% confidence intervals] and computed as the absolute change between baseline and 48-months. WORMS max scores were defined as the maximum lesion score in any knee region. False discovery rate (FDR) was controlled using the Benjamini-Hochberg procedure.

*FDR-adjusted *P*-values < 0.05 are in bold.

BMI = body mass index; PASE = Physical Activity Scale for the Elderly; KL = Kellgren-Lawrence; AHM = anti-hypertensive medication; NSAID = nonsteroidal anti-inflammatory drug; BMEP = bone marrow edema pattern.