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Osteoarthritis and Cartilage

T_2 mapping of the articular cartilage as a biomarker for knee osteoarthritis: An analysis of the population-based Rotterdam Study

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ABSTRACT

Objective: Only few studies have investigated quantitative magnetic resonance imaging (MRI) T_2 mapping of knee cartilage in population-based cohorts. Our objective was to evaluate the association between T_2 relaxation times of different cartilage segments and the presence of knee MRI-based osteoarthritis (OA) and patient characteristics in a large population-based cohort.
Design: In this cross-sectional study, we included 673 females (mean age: 59.8 years; standard deviation: 3.7) scanned with 1.5T-MRI from a sub-cohort of the Rotterdam Study. T_2 relaxation times were calculated in six femoral and tibial cartilage regions of interest. Associations between T_2 relaxation times, MRI Osteoarthritis Knee Score (MOAKS)-based tibiofemoral OA, and Knee injury and Osteoarthritis Outcome Score (KOOS)-based symptom status were evaluated using multivariate fixed effects regression analyses.
Results: A total of 1332 knees were included, of which 237 (17.7%) had MRI-based OA. Patients with OA had higher T_2 relaxation times across all cartilage segments, and T_2 values positively correlated with BMI (r = 0.17–0.46), the strongest correlations being in the lateral compartment. Weak associations were found between T_2 relaxation times and age. After adjustments, T_2 values in the lateral weight-bearing femur (OR: 0.67; 95%CI: 0.56–0.79), lateral tibia (OR: 1.11; 95%CI: 1.00–1.24), lateral posterior femur (OR: 1.48; 95%CI: 1.28–1.72), and medial posterior femur (OR: 1.14; 95%CI: 1.01–1.30), were associated with the presence of OA. T_2 relaxation times were not associated with the KOOS-based symptom status.
Conclusion: In this population-based cohort, T_2 values were associated with BMI. Additionally, T_2 values in the lateral cartilage subregions were associated with MRI-based OA.

Introduction

The global burden of osteoarthritis (OA) poses a major public health challenge with substantial morbidity, and it is projected to increase further in the coming decades with rising life expectancy and aging populations [1]. OA is characterized by degradation and loss of cartilage, subchondral bone sclerosis, inflammation of the synovium, and osteophyte formation [2].

Because of the involvement of multiple different tissues in OA, magnetic resonance imaging (MRI) is considered the imaging modality of choice for evaluating the whole knee joint in OA. A widely applied and well-validated method for evaluating knee OA is the semi-quantitative MRI Osteoarthritis Knee Score (MOAKS) [3], which has previously been reported in large-scale observational studies into OA, including in the Osteoarthritis Initiative (OAI) [3,4]. MOAKS provides a robust evaluation of the entire knee joint, including articular cartilage integrity, meniscus and ligaments, osteophytes, synovitis and effusion, bone marrow abnormalities, cystic lesions, and loose bodies [3]. However, conventional MRI has limitations as it aims at identifying morphological changes in damaged knee cartilage, which are mostly observed in relatively advanced stages of degeneration [5].

T_2 mapping is a noninvasive MRI method which can quantitatively assess biochemical changes in cartilage, including the integrity

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of collagen network, and collagen and water content, thus this technique is able to provide more information on zonal variation and regional cartilage degeneration in the early stages of OA [6,7]. In advanced stages of OA, T_2 mapping has limitations due to the loss of cartilage tissue and the reduced dynamic range of T_2 values [8].

While there is ample evidence that T_2 mapping is an imaging biomarker for OA progression [6,9,10], few studies have been published specifically investigating T_2 mapping in large population-based cohorts, other than the Osteoarthritis Initiative (OAI) [11]. Such cohorts reduce the risk of selection bias and may provide insights into early cartilage degeneration. Therefore, the aim of our study was to investigate the association between T_2 relaxation times of different cartilage segments and the presence of MRI-based knee OA and patient characteristics in a large population-based cohort.

Methods

Patient population

Our study sample was derived from a sub-study (RS-III-1) of the Rotterdam Study, a population-based prospective cohort study in the Netherlands established to investigate the prevalence and determinants of chronic diseases in middle-aged and older populations. The design of the Rotterdam Study has been published in detail previously [12]. In 2006, the first 1116 females between the ages of 45–60 were invited to enroll in a sub-study (RS-III-1) investigating early signs of knee OA [13,14]. The Rotterdam Study was approved by the medical ethics committee of the Erasmus MC University Medical Center Rotterdam, and written informed consent was obtained from all included patients. Participants were invited to visit the research center for questionnaires, physical examinations, and MRI at baseline and after five years of follow-up. The Knee injury and Osteoarthritis Outcome Score (KOOS) subscales were assessed for the subsets of pain, symptoms, Activities of Daily Living (ADL), Function in Sport and Recreation, and knee-related Quality of Life (QoL) at the time of follow-up imaging.

MRI acquisition

All subjects were scanned on a 1.5 Tesla (T) MRI scanner (Signa Excite 2, General Electric Healthcare) with an eight-channel cardiac coil that allowed imaging of both knees in one session without repositioning. MRI was acquired at baseline and five-year follow-up time point. The scanning protocol consisted of sagittal fast spin echo (FSE) proton density–weighted, FSE T_2-weighted with fat suppression, spoiled gradient echo with fat suppression, and fast imaging employing steady-state acquisition (FIESTA) sequences at both time points and were used for semi-quantitative MRI scoring. The second time-point included an additional sagittal multi-echo spin echo sequence with fat suppression for the purpose of T_2 mapping (Supplementary Table 1).

Image analysis

Full-thickness masks of the tibiofemoral cartilage were segmented on six slices (three central slices of the medial compartment and three central slices of the lateral compartment). Segmentation masks were further divided into a femoral weight-bearing (WB), tibial WB, and femoral posterior region of interest (ROI) for both the medial and lateral knee compartment as in a previous study [9]. The outer perimeters of the menisci demarcated the WB ROIs of the femur and tibia. The posterior ROIs contained the femoral cartilage behind the posterior border of the menisci. Segmentation was performed using ITK-SNAP (www.itksnap.org) [15] by a researcher with five years of experience in musculoskeletal imaging and investigative radiology (N.I.H.) who was blinded to the clinical data (Supplementary Figure 1). For intra-observer repeatability, the same reader re-segmented a random subset of 30 knees. For inter-observer repeatability, a researcher with 15 years of experience in musculoskeletal image analysis (J.H.) independently segmented the same subset. Post-processing of the T_2 mapping knee MRI images was performed using an in-house developed MATLAB software tool previously described by Bron et al. [16]. T_2 relaxation times were weighted by the reciprocal of the uncertainty of the estimated T_2 relaxation time in each voxel to reduce effects of possible outliers within ROIs. This uncertainty was measured with the square root of the Cramer-Rao lower bound, which defines a lower bound for the standard deviation (SD) of the estimated T_2 relaxation time [16].

MRI-based OA assessment

MRIs were scored by two experienced readers using the MOAKS [3]. All readers were extensively trained by a musculoskeletal radiologist (E.O.) with more than 15 years of experience with clinical and research musculoskeletal MRI [17]. A previously proposed definition for the identification of tibiofemoral OA on MRI was used [13,14,18,19]. Tibiofemoral OA was defined as the presence of a definite osteophyte and full-thickness cartilage loss, or one of these features and two of the following features: (1) subchondral bone marrow lesion or cyst not associated with meniscal or ligamentous attachments, (2) meniscal maceration or degeneration (including a horizontal tear), or (3) partial thickness cartilage loss. Grade 1 and 2 cartilage lesions were classified as partial thickness lesions and grade 3 lesions as full-thickness lesions. Grade 2 and 3 osteophytes were classified as definite osteophytes. Bone marrow lesions and cysts were present when scored as grade 1 or higher. Meniscus abnormalities were defined as the presence of intrasubstance degeneration, tears, or maceration. Meniscal subluxation or bone attrition was not assessed.

Statistical analysis

Differences between groups were calculated using Student's t-tests for continuous data. BMI was subdivided into three different strata (strata 1: "normal range" = 18–24.9 kg/m^2; strata 2: "overweight range" = 25–29.9 kg/m^2; strata 3: "obese range" 30–45 kg/m^2) to assess the effects of obesity on T_2 values for the different cartilage segments with one-way analysis of variance (ANOVA). Intra- and inter-observer repeatability of the T_2 measurements was assessed by calculating the root-mean-square coefficient of variation (CV_{RMS}) for each cartilage region [20]. Correlations between T_2 values and age and BMI were estimated using Pearson's correlation coefficient.

Analyses were performed using linear and logistic mixed effects regression models to account for correlations between knees within participants. All models included both knees of each participant and all six cartilage subregions, thus mutually adjusting for each other. A random intercept for each participant accounted for within subject correlation. No interaction terms were included in any model. Associations between T_2 relaxation times and patient characteristics were assessed using linear mixed effects regression models with a single cartilage subregion as the outcome variable (continuous). Fixed effects included BMI (continuous), age (continuous), and the remaining five cartilage subregions (continuous). This analysis was performed separately for each of the six cartilage subregions. Logistic mixed effects regression was performed with OA status at baseline and at follow-up as outcome variable (yes/no). Fixed effects included BMI (continuous), age (continuous), all six separate cartilage subregions (continuous), family OA history (yes/no), as independent variables. The model was optimized using Bound Optimization BY Quadratic Approximation (BOBYQA). This analysis

was repeated after stratifying by cartilage loss status (no loss vs. partial/full-thickness loss). KOOS subscales were transformed to a previously proposed definition of a symptomatic knee [21]. This was chosen due to the skewed distribution of each KOOS subscale as our cohort comprised a largely asymptomatic population. Furthermore, it helped to mitigate convergence issues in mixed effects models, which have also been reported in previous studies [22]. For the logistic mixed effects regression analysis of a symptomatic knee (outcome: yes/no), fixed effects included BMI (continuous), age (continuous), and all six separate cartilage subregions (continuous). BOBYQA optimizer was used. Statistical analyses were performed using R, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). The lme4 package was used for mixed effects analyses. A p-value < 0.05 was considered statistically significant.

Results

Patient characteristics

Of the 1116 females invited to participate, a total of 891 agreed to enroll, of whom 673 had sufficient MR image quality at both time points and T_2 mapping data available at the follow-up time point. A total of 1332 knees were included, comprising 671 left (50.4%) and 661 right (49.6%) knees. At the time of the follow-up MRI scan, the mean age of our population was 59.8 years (SD: 3.7) and mean BMI was 26.9 kg/m^2 (SD: 4.7) One hundred thirty-six knees were classified as having OA at baseline, and 237 knees having OA at the second time point (when T_2 mapping was performed). The mean time between scans was 5.1 years (SD: 0.4). At the time of the follow-up MRI scan, participants with OA were older (61.3 *vs* 59.4 years) and had a higher BMI (28.4 *vs.* 26.5 kg/m^2) compared to subjects without OA. Subjects with OA had, on average, higher T_2 values for each subregion, and lower KOOS subscale scores (Table 1).

The intra-observer CV_{RMS} ranged from 0.93% to 2.03%, while the inter-observer CV_{RMS} values were slightly higher, ranging from 1.23% to 2.94% (Supplementary Table 2).

T_2 relaxation times in relation to BMI and age

Subjects with BMI in the obese range had higher ($p < 0.001$) mean T_2 values than subjects with BMI in the normal range and subjects with BMI in the overweight range for all cartilage segments, in both the medial and lateral compartment. Moreover, subject with BMI in the overweight range had higher ($p < 0.001$) T_2 values compared to subjects with BMI in the normal range.

Scatter plots of BMI and age with T_2 relaxation times of the cartilage subregions with corresponding trend lines based on the (univariate) Pearson correlation coefficients are displayed in Figs. 1 and 2, respectively. The correlation between T_2 relaxation times and BMI was stronger in the lateral compartment (r = 0.42 – 0.46) than in the medial compartment (r = 0.18 – 0.40). For age, the correlations were weaker (r = −0.09 – 0.06).

Mixed effects linear regression analysis between T_2 values and patient characteristics is shown in Table 2. BMI was positively associated with T_2 relaxation times in the lateral femur weight-bearing (ß 0.06; 95% CI: 0.04, 0.08), lateral tibia weight-bearing (ß 0.07; 95% CI: 0.04, 0.10), lateral femur posterior (ß 0.06; 95% CI: 0.03, 0.09), medial tibia weight-bearing (ß 0.03; 95% CI: 0.004, 0.05), and medial femur posterior cartilage (ß 0.11; 95% CI: 0.08, 0.15) compartments. T_2 relaxation times of the medial femur weight-bearing cartilage was negatively associated with BMI (ß −0.07; 95% CI: −0.10, −0.05). T_2 relaxation times of the lateral femur posterior cartilage were positively associated with age (ß 0.05; 95% CI: 0.02, 0.08), whereas T_2 relaxation times of the medial femur weight-bearing cartilage were negatively associated with age (ß −0.03; 95% CI: −0.06, −0.001).

MRI-based OA status and T_2 relaxation times

Univariate T_2 relaxation times for each region by MRI-based OA status are shown in Fig. 3. Mixed effects logistic regression analyses between T_2 relaxation times and MRI-based OA status at different time-points with adjustments for each subregion, age, BMI, and family history of OA are shown in Table 3. Analyses stratified by

Variable	Total population	No MRI-based OA	MRI-based OA
	N = 1332	N = 1065	N = 237
Knee side (Left/Right)	671/661	520/545	135/102
Age in years	59.7 (4.7)	59.4 (3.7)	61.3 (3.3)
BMI in kg/m^2	26.9 (4.7)	26.5 (4.4)	28.4 (5.5)
Cartilage loss (none/partial/full thickness/NA)	940/229/134/29	888/161/16/0	52/67/118/0
Family history of OA	560 (42%)	446 (42%)	99 (42%)
KOOS-defined symptomatic knee	419 (31.5%)	282 (26.5%)	129 (54.4%)
KOOS ADL	98.5 (88.2, 100.0)	98.5 (89.7, 100.0)	92.7 (77.9, 100.0)
KOOS Symptoms	92.9 (78.6, 100.0)	92.9 (82.1, 100.0)	79.2 (64.3, 92.9)
KOOS QoL	87.5 (68.8, 100.0)	93.8 (75, 100.0)	75.0 (50.0, 93.8)
KOOS Pain	97.2 (83.3, 100.0)	97.2 (88.9, 100.0)	86.1 (69.4, 100.0)
KOOS Sport	90.0 (60.0, 100.0)	95.0 (68.8, 100.0)	67.5 (35.0, 100.0)
T2 times in ms			
Lateral			
Femur WB	35.4 (2.3)	35.3 (2.3)	35.7 (2.4)
Tibia WB	35.0 (3.0)	34.8 (2.9)	35.8 (3.6)
Femur posterior	35.9 (2.5)	35.6 (2.4)	37.0 (2.5)
Medial			
Femur WB	36.7 (2.1)	36.6 (2.0)	36.9 (2.3)
Tibia WB	34.8 (2.0	34.7 (1.8)	35.1 (2.5)
Femur posterior	37.1 (3.1)	36.9 (2.4)	38.1 (5.1)

Data provided as mean (standard deviation) for normally distributed numerical data, and median (interquartile range) for skewed data. ADL: Activities of Daily Living; FU: follow-up; OA: osteoarthritis; QoL: quality of life WB: weight-bearing.

Table 1

Osteoarthritis and Cartilage

Population characteristics at the follow-up (time point of T2 mapping).

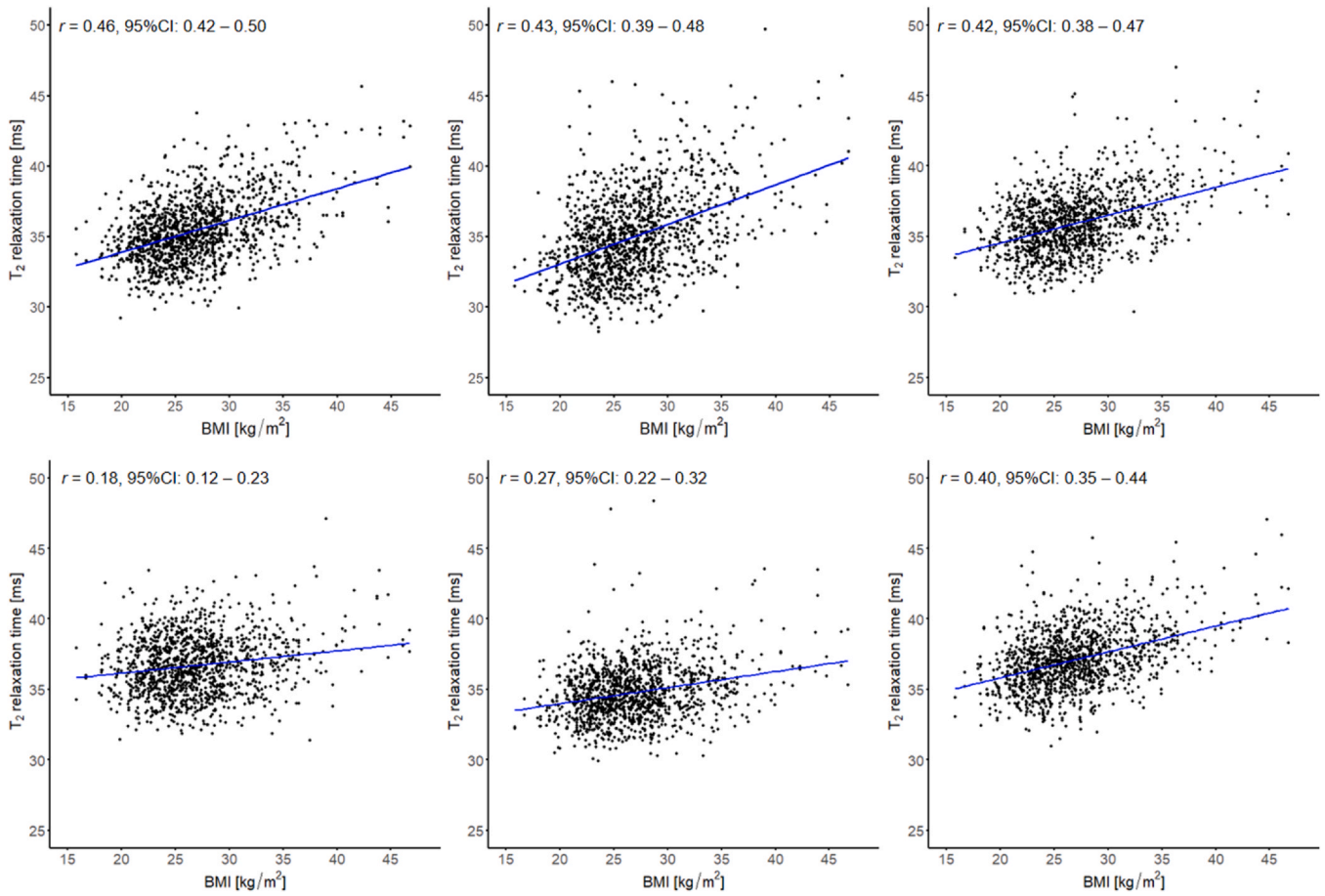

Fig. 1

Osteoarthritis and Cartilage

Scatter plots of BMI and mean T_2 with trend lines. Each circle represents the cartilage T_2 value of one patient. A. lateral femur weight-bearing B. lateral tibia weight-bearing C. lateral femur posterior D. medial femur weight-bearing E. medial tibia weight-bearing F. medial femur posterior.

cartilage loss are shown in Supplementary Tables 3 and 4. Increases of 1 ms in T_2 relaxation times of the lateral femur weight-bearing cartilage (OR: 0.67; 95%CI: 0.56–0.79), lateral tibia weight-bearing cartilage (OR: 1.11; 95%CI: 1.00–1.24), and lateral posterior femur cartilage (OR: 1.48; 95%CI: 1.28–1.72) were associated with OA at both time points in multivariate analyses. In contrast, only the T2 relaxation times of the posterior femur cartilage subregion in the medial compartment at follow-up (OR: 1.14; 95%CI: 1.01–1.30) were associated with OA status. The presence of OA was also associated with increasing age (+1 year, OR: 1.17; 95%CI: 1.09–1.26), increasing BMI (+1 kg/m^2, OR: 1.10; 95%CI: 1.03–1.17).

KOOS-defined symptoms and T_2 relaxation times

Table 4 displays the associations between T_2 relaxation times and the KOOS-based definition of a symptomatic knee, adjusted for age and BMI. In the mixed effects logistic regression model, none of the cartilage segments were associated with the KOOS-based definition of a symptomatic knee.

Discussion

In this population-based cohort study of females, we studied the relationship between T_2 relaxation times of tibiofemoral knee cartilage with patient characteristics, MRI-based OA status at various points in time, and KOOS-based outcome. We observed positive correlations between T_2 relaxation times and BMI. The absolute mean cartilage T_2 values were higher in all cartilage subregions for participants with OA. After adjustments, T_2 relaxation times in the lateral compartment were associated with the presence of OA.

In the BMI analyses, the increase in T_2 relaxation time per unit BMI was comparable to or lower than previously reported [9]. We found correlations between T_2 values and BMI in both compartments, which was more profound in the lateral compartment. However, the associations weakened after adjusting for other cartilage subregions and

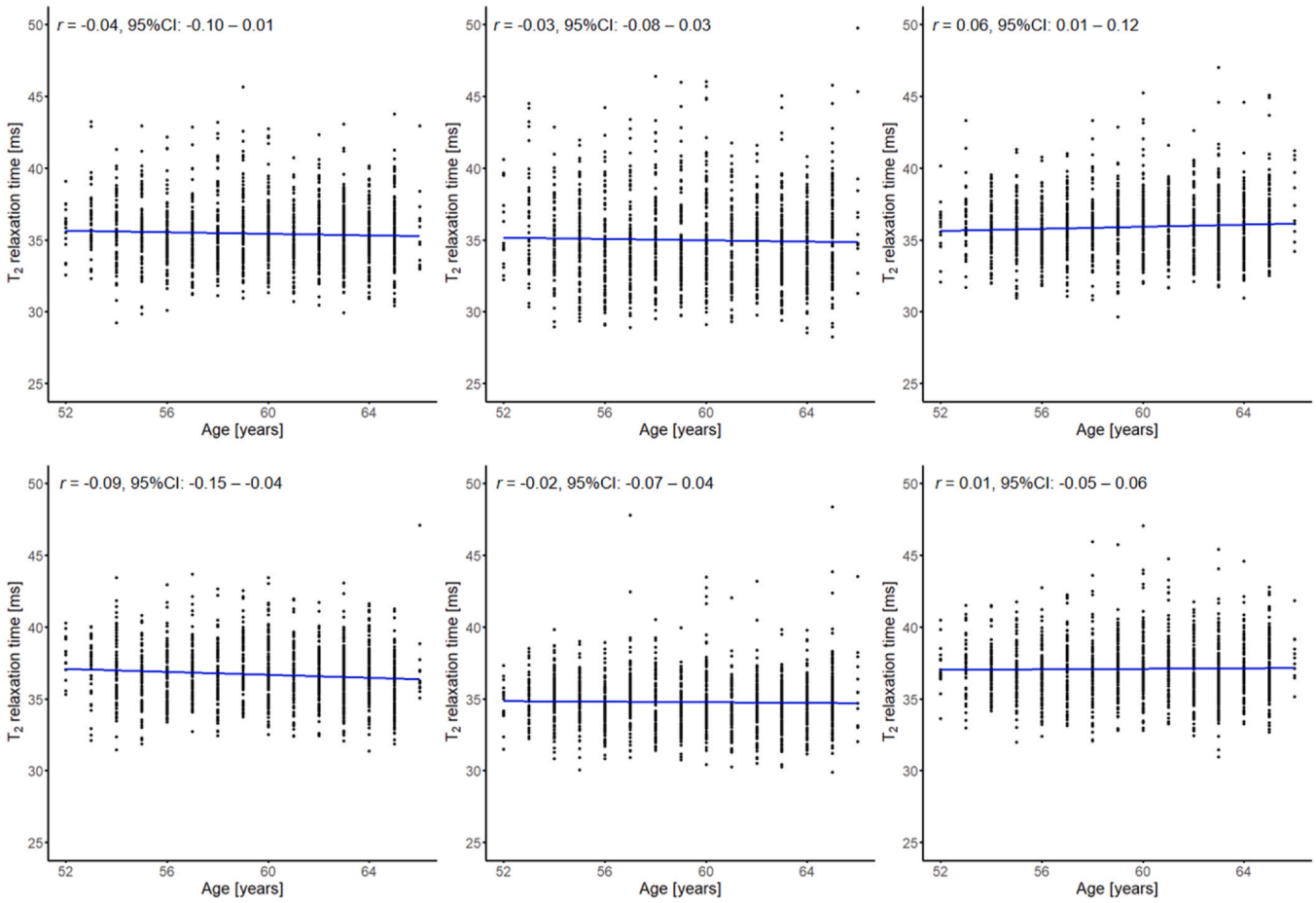

Fig. 2 Osteoarthritis and Cartilage

Scatter plots of age and mean T_2 with trend lines. Each circle represents cartilage T_2 value of one patient. A. lateral femur weight-bearing B. lateral tibia weight-bearing C. lateral femur posterior D. medial femur weight-bearing E. medial tibia weight-bearing F. medial femur posterior.

	Unit	BMI (kg/m^2)	Age (years)
		ß (95% CI)	ß (95% CI)
Lateral			
Femur WB	+1ms	**0.06 (0.04, 0.08)**	−0.02 (−0.04, 0.004)
Tibia WB	+1ms	**0.07 (0.04, 0.10)**	−0.01 (−0.05, 0.02)
Femur posterior	+1ms	**0.06 (0.03, 0.09)**	**0.05 (0.02, 0.08)**
Medial			
Femur WB	+1ms	**−0.07 (−0.10, −0.05)**	**-0.03 (−0.06, −0.001)**
Tibia WB	+1ms	**0.03 (0.004, 0.05)**	0.01 (−0.01, 0.04)
Femur posterior	+1ms	**0.11 (0.08, 0.15)**	0.01 (−0.03, 0.05)

WB: weight-bearing. Significant associations shown in bold. All cartilage subregions were included in a single model. Analysis performed with N_{knees} = 1332 and $N_{subjects}$ = 673.

Table 2 Osteoarthritis and Cartilage

Mixed effects linear regression analyses between age and BMI and cartilage T_2 values.

age. Our findings for the relations between T_2 values and BMI are in line with the results of a study using an unselected clinical population of 109 patients [9]. One previous study reported an association between BMI and T_2 values in the lateral tibia [11]. In contrast, no positive relation was observed between T_2 relaxation times and age. Our observed relations with age are in line with Joseph et al. who found weak associations between T_2 values and increasing age in 481 subjects of the OAI [11]. It should be noted that there are important differences between the Rotterdam Study and the study populations of the aforementioned studies. The Rotterdam Study is a population-based cohort, whereas the OAI and MOST studies consist of patients with established OA or at risk for OA.

In participants with MRI-based OA, T_2 relaxation times were consistently higher compared to subjects without OA in our cohort, although these mean differences were not as large as described in previous studies [24]. Most of the studies reporting T_2 mapping in OA included selected patients with advanced OA with healthy controls as a reference group, or large cohorts with symptomatic patients. The small differences we observed may be attributed to the population-based design of our study and may have limited clinical significance at the individual level. However, even small differences in T_2 values could be relevant at the population level as they potentially indicate early cartilage changes in relation to potential risk factors for OA. Further longitudinal studies are needed to determine whether these small differences predict OA incidence or progression.

In the mixed effects logistic regression analyses adjusted for each subregion, age, BMI, and family history of OA, the lateral cartilage

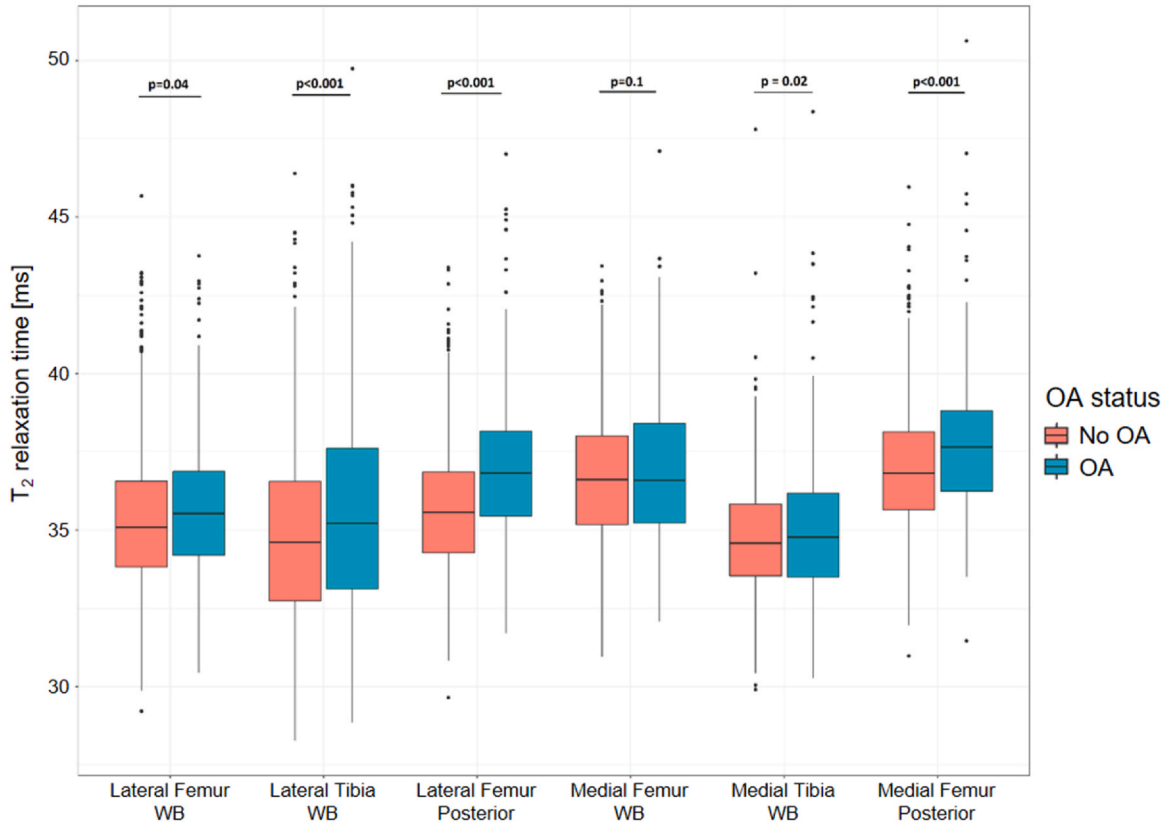

Fig. 3 Osteoarthritis and Cartilage

Differences in mean T_2 by cartilage segment between subjects with MRI-based OA and without MRI-based OA. WB = weight-bearing.

	Unit	OA baseline (n=136)	OA follow-up (n=237)
		Odds ratio (95%CI)	**Odds ratio (95%CI)**
Age	+1 year	**1.21 (1.10 – 1.32)**	**1.17 (1.09 – 1.26)**
BMI	+1 kg/m^2	**1.11 (1.03 – 1.20)**	**1.10 (1.03 – 1.17)**
Family history OA	yes	0.78 (0.42 – 1.45)	0.95 (0.56 – 1.60)
Lateral			
Femur WB	+1 ms	**0.72 (0.60 – 0.87)**	**0.67 (0.56 – 0.79)**
Tibia WB	+1 ms	**1.13 (1.00 – 1.28)**	**1.11 (1.00 – 1.24)**
Femur posterior	+1 ms	**1.49 (1.25 – 1.77)**	**1.48 (1.28 – 1.72)**
Medial			
Femur WB	+1 ms	0.96 (0.81 – 1.13)	0.92 (0.80 – 1.06)
Tibia WB	+1 ms	0.99 (0.84 – 1.17)	1.02 (0.89 – 1.18)
Femur posterior	+1 ms	1.09 (0.93 – 1.26)	**1.14 (1.01 – 1.30)**

All subregions fitted in the same mixed effects regression model with adjustments for age, BMI, and OA family history. WB: weight bearing. Significant relations shown in bold. Analysis performed with N_{knees} = 1332 and $N_{subjects}$ = 673.

Table 3 Osteoarthritis and Cartilage

Mixed effects logistic regression analyses between MRI-based OA status and T_2 relaxation times.

	Unit	KOOS-defined symptomatic knee
		Odds ratio (95%CI)
Lateral		
Femur WB	+1 ms	0.89 (0.63, 1.24)
Tibia WB	+1 ms	1.02 (0.81, 1.28)
Femur posterior	+1 ms	1.10 (0.81, 1.28)
Medial		
Femur WB	+1 ms	0.92 (0.68, 1.23)
Tibia WB	+1 ms	1.08 (0.80, 1.48)
Femur posterior	+1 ms	1.11 (0.84, 1.47)

All subregions fit in the same model. Adjustments made for age and BMI. WB: weight-bearing. Analysis performed with N_{knees} = 1332 and $N_{subjects}$ = 673.

Table 4 Osteoarthritis and Cartilage

Mixed effects logistic regression analysis of T_2 relaxation times and KOOS-defined symptomatic knee.

regions were associated with the presence of MRI-based OA at baseline (i.e. five years prior to T_2 mapping). At follow-up (i.e., at the time of T_2 mapping), the same cartilage regions remained associated with MRI-based OA with similar strength, despite substantially higher number of patients with OA compared to baseline. After stratifying by cartilage loss, T_2 values of the lateral posterior femur cartilage remained associated with MRI-based OA at both baseline and follow-up. We found that associations between T_2 values and both BMI and MRI-based OA were more pronounced in the lateral compartment. One possible explanation is that our study included a large sample of low-risk female participants, and among them, early cartilage changes may occur in the lateral compartment.

We did not observe associations between T_2 values and KOOS-based definition of a symptomatic knee. One previous study reported elevated T_2 values in individuals with knee pain, defined as a Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index pain score ≥5, using a subset of 126 participants from the OAI [23]. Another study found weak to moderate correlations between T_2 values and WOMAC pain and function scores, but not with stiffness scores [24]. In contrast, a more recent study reported no associations between T_2 values and KOOS subscales in a clinical population [9]. Variations in study populations and differences in statistical models used may explain some of the inconsistent findings.

Major strengths of the current study include the large cohort derived from a sample which can be generalizable to an asymptomatic unselected female population. Furthermore, the relation between T_2 relaxation times in different subregions and patient-specific characteristics such as age and BMI, OA status, and KOOS-defined symptoms, was extensively assessed.

However, the limitations of our study should also be mentioned. First, T_2 mapping was not performed at the baseline time point of the cohort and therefore, we could not use T_2 values to predict OA incidence or progression. Second, because of the limited spatial resolution, we were not able to further divide the cartilage in different layers (e.g. deep and superficial). Third, the patellar and trochlear cartilage were not included in the analysis. Fourth, the lack of a longitudinal T_2 data limits the interpretation regarding the exact T_2 differences over time. Future studies investigating longitudinal changes in T_2 in knee OA are warranted.

Conclusion

In this open population-based cohort study of females, T_2 relaxation times were positively correlated with BMI, the strongest correlations being in the lateral knee compartment. Weak correlations were observed between age and T_2 relaxation times. Furthermore, T_2 values in the lateral cartilage subregions were associated with the MRI-based OA status. These findings suggest that early cartilage changes may be more pronounced in the lateral compartment, particularly in low-risk populations.

Author contributions

Conception and design of the study, or acquisition of data, or analysis and interpretation of data: all authors; drafting the article or revising it critically for important intellectual content: all authors; final approval of the version to be submitted: all authors. JH (j.hirvasniemi@erasmusmc.nl) and EO (e.oei@erasmusmc.nl) take responsibility for the integrity of the work as a whole, from inception to finished article.

Conflict of Interest

The authors report no conflicts of interests.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.joca.2025.09.009.

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