PATELLAR TENDON ENTHESIS ABNORMALITIES AND THEIR ASSOCIATION WITH KNEE PAIN AND STRUCTURAL ABNORMALITIES IN OLDER ADULTS.

Authors

Siti Maisarah Mattap[1], Dawn Aitken[1], Karen Wills[1], Andrew Halliday[2], Changhai Ding[1,3], Weiyu Han[1, 3], Ishanka Munugoda[1], Stephen E Graves[4], Michelle Lorimer[5], Flavia Cicuttini[6], Graeme Jones[1], Laura L Laslett[1]

[1]Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia;

[2]Department of Medical Imaging, Royal Hobart Hospital, Hobart, Tasmania, Australia;

[3]Clinical Research Centre, Zhujiang Hospital, Southern Medical University, Guangzhou, China;

[4]Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), Adelaide, South Australia, Australia;

[5]South Australian Health and Medical Research Institute (SAHMRI), Adelaide, South Australia, Australia;

[6]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia.

Corresponding author and person to whom reprint requests should be addressed:

Siti Maisarah Mattap

Menzies Institute for Medical Research,

University of Tasmania,

https://doi.org/10.1016/j.joca.2018.11.009

Private Bag 23

Hobart TAS 7001

Australia;

siti.mattap@utas.edu.au

Co-authors emails

dawn.aitken@utas.edu.au

karen.wills@utas.edu.au

andrew.halliday@ths.tas.gov.au

changhai.ding@utas.edu.au

weiyu.han@utas.edu.au

ishanka.munugoda@utas.edu.au

segraves@aoanjrr.org.au

michelle.lorimer@sahmri.com

flavia.cicuttini@monash.edu

graeme.jones@utas.edu.au

laura.laslett@utas.edu.au

Abstract

Objective: To describe associations between presence of patellar tendon enthesis (PTE) abnormalities and symptoms, structural abnormalities, and total knee replacement (TKR) in older adult cohort.

Methods: PTE abnormalities (presence of abnormal bone signal and/or bone erosion), were measured on T2-weighted magnetic resonance images at baseline in 961 community-dwelling older adults. Knee pain and function limitation were assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Bone marrow lesions (BMLs),

https://doi.org/10.1016/j.joca.2018.11.009

cartilage volume and defects score, and infrapatellar fat pad (IPFP) area were measured using validated methods. Incidence of TKR was determined by data linkage.

Results: Participants with abnormal PTE bone signal and/or erosion was 20%**.** Cross-sectionally, presence of PTE abnormalities was associated with greater pain intensity while going up and down stairs (β=0.22 (95% CI; 0.03, 0.41)), greater risk of femoral BMLs (RR=1.46 (1.12, 1.90)) and worse tibial cartilage defects score (RR=1.70 (1.16, 2.47), and smaller IPFP area (β=-0.27 (-0.47, -0.06) cm^2), after adjustment of confounders. Longitudinally, presence of baseline PTE abnormalities was associated with a deleterious increase in tibial BML size (RR=1.52 (1.12, 2.05)) over 10.7 years but not symptoms, other structural changes, or TKR.

Conclusion: Patellar tendon enthesis abnormalities are common in older adults. Presence of cross-sectional but not longitudinal associations suggests they are commonly co-exist with other knee structural abnormalities but may not play a major role in symptom development or structural change, excepting tibial BMLs.

Keywords: patellar tendon enthesis, enthesis abnormalities, enthesopathy, osteoarthritis, MRI, knee

Introduction

The signature feature of knee osteoarthritis (OA) is cartilage volume loss; however, OA is a disease of the whole joint [1, 2]. In theory, it can begin in any joint structure, including the attachment site (enthesis) of a ligament and ligaments themselves [3-5].

Entheses have high tensile strength, enabling them to dissipate mechanical stress during joint movement at the bony interface [6]. The patellar tendon enthesis (PTE) is the attachment site

of the ligament, connecting the patella to the tibia. This provides a firm anchor point to keep the patella in position and allow smooth knee bending and straightening [7, 8]. Therefore, abnormalities at the PTE may result in abnormal function and pain, particularly with activities that involve stress on the patellofemoral joint e.g. knee bending, walking up and down stairs. Evidence from histopathological studies of cruciate ligaments in cadavers [9] and magnetic resonance (MR) images of collateral ligament insertions in interphalangeal joints in hand OA [10, 11] demonstrate that abnormal enthesis changes are present in early OA, strengthening the hypothesis that entheses may play a role in OA development.

While there is evidence for the importance of entheses from histopathology in knees, and MR images in hands, there is no data on associations between knee enthesis abnormalities and pain, physical function, and OA structural abnormalities in vivo, using non-invasive methods. Therefore, we aimed to describe associations between presence of PTE abnormalities visible on MR images and knee pain, physical function limitations, and OA structural abnormalities both cross-sectionally and longitudinally over 2.7 and 10.7 years and incidence of total knee replacement (TKR) over 13.3 years in a cohort of community-dwelling older adults. We hypothesised that presence of PTE abnormalities is associated with knee OA symptoms and structural abnormalities especially knee abnormalities at the patellofemoral compartment.

Method

Participants

This study uses data from the Tasmanian Older Adult Cohort (TASOAC) Study. TASOAC is a prospective population-based study. Participants aged between 50 and 80 years were randomly selected from the roll of electors in southern Tasmania (population 229 000), a comprehensive population listing, using sex-stratified simple random sampling without replacement (response rate 57%). Participants attended baseline clinic between March 2002 and September 2004 and follow-up clinics at (Phase 2) 2.7 and (Phase 4) 10.7 years later, on average. Additional information was available at 13.3 years through data linkage to the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Figure 2 outlines the study timeline. Persons were excluded if they were institutionalised or had contraindications to magnetic resonance imaging (MRI), including metal sutures, presence of shrapnel, iron filings in the eye and claustrophobia.

All participants gave written informed consent for the TASOAC study, and the research conducted was in compliance with the Declaration of Helsinki and was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee.

These analyses include 961 participants with baseline MRI (Figure 3), excluding 21 patients whose MR images had artefacts at the PTE sites. Participants with and without baseline MR images had similar demographic profiles (supplementary Table 1), excepting small differences in baseline BMI (mean±SD BMI 27.7 ±4.68 vs 28.9 ±5.13 kg/m^2), which were unlikely to be clinically important.

MRI

MRI scans of the right knee were performed at baseline, 2.7 and 10.7 years. Knees were imaged in the sagittal plane on a 1.5-T Picker unit (Cleveland, Ohio, USA; baseline and 2.7 years) and a Siemens unit (Espree, Pennsylvania, USA; 10.7 year). Image sequences included: (1) a T1-weighted fat saturation three-dimensional gradient recall acquisition in the

steady state, flip angle 30°, repetition time 31ms, echo time 6.71ms, field of view 16cm, 60 partitions, 512 × 512-pixel matrix, slice thickness of 1.5mm without an inter-slice gap; (2) a T2-weighted fat saturation two-dimensional fast spin echo, flip angle 90°, repetition time 3,067ms, echo time 112ms, field of view 16cm, 15 partitions, 228 × 256-pixel matrix, slice thickness of 4mm with a between-slice gap of 0.5 to 1.0mm.

PTE abnormalities

PTE abnormalities were assessed at baseline on T2-weighted MR images of the right knee, both proximally and distally by one trained observer (SMM), who was trained by a radiologist (AH). Participants with MR imaging artefacts which prevented clear views of PTE sites e.g. alternating bright and dark bands were excluded in the evaluation. As there was no standardised scoring system for PTE abnormalities and adjacent structural abnormalities, we developed a novel scoring system based on a previous study [9]. This system was quick to use, and implementation was straightforward, enabling reproducible scoring for a large number of participants. Features were classified as abnormal signals if the abnormalities were present on more than one consecutive slice. Presence of any abnormality was scored as 1, absence of any abnormality was scored as 0. Quantification abnormality size was not feasible due to image quality. We defined bone signal as an increase in signal intensity (bright abnormal signal) or any abnormal marks at the bone area adjacent to the enthesis site, such as black or white bands and irregular marking next to the cortical bone (Figure 1a and 1b). We defined bone erosion as a sharply bordered dark bone lesion which is visible in two planes with a cortical break seen in at least one plane [12] (Figure 1c and 1d); and tendon signal as an increase in signal intensity of the tendon adjacent to the enthesis (Figure 1e). Deep infrapatellar bursae are fluid-filled sacs at the distal end of the patellar tendon, between the patellar tendon and the tibia; they appear as a hyperintensities on MRI [13] (Figure 1f). Intra-observer reliability was assessed in 20 randomly selected participants after a 2-week interval between the readings using kappa-statistic.

The intra-rater agreement was excellent [14] for proximal tendon signal 0.88(95% CI; 0.64 to 1.00) distal tendon signal 0.99 (0.97 to 1.00); proximal bone signal 0.72 (0.37 to 1.00) distal

bone signal 0.82 (0.80 to 0.99); proximal, distal bone erosion, and deep infrapatellar bursa have small variability to calculate kappa.

Pain, physical function limitation, and total WOMAC score

Knee pain, physical function limitation, and total WOMAC score were assessed using the self-administered Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [15] scale, which was scored using a 10-point numeric rating scale from 0 (no pain, no functional deficit) to 9 (most severe pain, most functional deficit). The WOMAC is a valid knee OA patient reported measures of pain, function limitation, and stiffness [15-17]. This study includes 5 components of knee pain and 17 components of function limitation. Participants were asked to rate how much pain, stiffness, and functional deficits they experienced on the day of their questionnaire for their right knee. Knee pain was rated while walking on a flat surface, going up and down stairs, at night while in bed, sitting or lying and standing upright. Each of the pain subscales and physical function subscales are summed to form a score for knee pain (range 0-45), function limitation (range 0-153) and total WOMAC score (pain, physical function, and stiffness) (range 0- 216).

Evaluation of cartilage morphology

Cartilage defects were assessed by a trained observer at baseline and 2.7 years on T1-weighted MR images (score range, 0 – 4 where 0= normal and 4 indicating full-thickness chondral wear with exposure of subchondral bone), as previously described [18]. Intra-observer repeatability calculated in prior study was excellent (intraclass correlation coefficient (ICC) of 0.80 – 0.94) [18]. Change in cartilage defect score from baseline to follow-up was dichotomised to 0 and 1: 0 representing no change or a decrease in cartilage defects and 1 representing an increase of 1 or more on scale 0 – 4.

Knee tibial and patellar cartilage volume was measured by a trained observer on T1-weighted MR images at baseline and 10.7 years follow-up by means of image processing on an

independent workstation using Osiris software as previously described [18]. The coefficient of variation (CV) was 2.1% for the medial tibia, 2.2% for the lateral tibia, and 2.6% for patella as previously reported [18, 19].

Bone marrow lesions

Subchondral BMLs were assessed on T2-weighted fat saturation MRI by using OsiriX software at the medial and lateral sites of tibia and femur, and patella. BMLs were defined as areas of increased signal intensity on T2-weighted, located immediately under the articular cartilage. One trained observer scored the BMLs by measuring the maximum area of the lesion at each site in mm^2 using software cursors at baseline and over 10.7 years follow-up. Baseline and 10.7-year images were read paired with the chronological order known to the reader. Intra-observer reliability using two way mixed-effects model [20] was excellent (0.98 (0.96, 0.99)), at baseline and 10.7 years follow-up. A deleterious increase in BML size was defined as any change larger than the least significant criterion ($52mm^2$) [21, 22]; this takes into account measurement error and correlations between BML measurements at baseline and 10.7 years of follow-up.

Infrapatellar fat pad (IPFP) area

Baseline IPFP was measured by manually drawing disarticulation contours around the IPFP boundaries on a section-by-section basis on T2-weighted MR images, using Osiris software (University of Geneva). The maximum area was selected to represent the IPFP size. One observer graded IPFP area on all MRI scans; both intra- and inter-observer reliability calculated in previous study were excellent (ICC = 0.96 for intra-observer reliability, ICC = 0.92 for inter-observer reliability) [23].

TKR surgery

The incidence of primary TKR between 1 March 2002 and 21 September 2016 were determined by data linkage to the AOANJRR. The AOANJRR started data collection in Tasmania in September 2000 and collects data from both public and private hospitals. Data validation against State and Territory Health Department data is done using a sequential multi-level matching proces [24]. Matched data were then obtained which included the date, side of joint replacement, primary or revision joint replacement and the reason for the procedure (e.g., OA, osteonecrosis). In this study, we only considered TKRs that were due to OA.

Additional available baseline data

Weight was measured to the nearest 0.1 kg (with shoes, socks, and bulky clothing removed) by using a single pair of electronic scales (Seca Delta Model 707). Height was measured to the nearest 0.1 cm (with shoes and socks removed) by using a stadiometer. Body mass index (BMI) was calculated as kilograms per square meter. A standing anteroposterior semi-flexed view of right knee with 15° of fixed knee flexion was performed and scored individually for osteophytes and joint space narrowing (JSN) on a scale of 0 – 3 [25]. Presence of radiographic osteoarthritis was defined as any score ≥1 for JSN or osteophytes.

Knee extension strength of the dominant leg measured to the nearest kg using a seated isometric contraction of the knee extensors [26]. Meniscal damage was assessed by a trained observer on T1-weighted MR images as previously described [27], and defined as presence of tear or extrusion on the meniscus dichotomised as 0=absent and ≤1=present. Presence of intra-articular fluid-equivalent signal on T2-weighted MRI at the suprapatellar pouch (suprapatellar effusion) was determined as previously described [28].

Statistical analysis

The primary exposure for all analyses was presence of PTE abnormalities at baseline, defined as presence of abnormal bone signal and/or erosion at PTE.

As TASOAC is a community-based cohort, there is a mix of people with and without pain. The pain data is non-normally distributed with a large number of zeros, so exponential hurdle models were the most appropriate model to estimate associations between baseline PTE abnormalities and pain outcomes. The hurdle model has two parts: one model for the presence/absence of pain and a second, separate model for pain severity for those who reported pain. We report estimates from these models separately for each outcome as the relative risk of reporting pain and the coefficient for intensity of pain. The interaction between baseline PTE abnormalities and time was used to calculate estimated change in outcomes over 10.7 years associated with PTE abnormalities. Multivariable models were adjusted for age, sex, BMI, knee extension strength, and additionally adjusted for presence of medial tibiofemoral BMLs, cartilage defects, and suprapatellar effusions.

Log binomial regression was used to assess associations between presence of PTE abnormalities at baseline and prevalence of BMLs at baseline, deleterious increases in BML size over 10.7 years and risk of TKR incidence over 13.3 years, as well as associations with baseline cartilage defects, and risk of worsening of cartilage defects over 2.7 years. All models were adjusted for age, sex, BMI, and baseline cartilage defects.

Linear regression was used to estimate associations between PTE abnormalities and infrapatellar fat pad at baseline. The models were adjusted for age, sex, BMI, interaction between age and sex, cartilage defects, and BMLs.

Multilevel mixed effects regression models were used to estimate associations between PTE abnormalities and cartilage volume loss over 10.7 years. Each model included fixed effect terms for PTE abnormalities at baseline, time (years since baseline), and an interaction term for PTE abnormalities with time. The interaction term estimates the additional change in the outcome per year associated with the presence of PTE abnormalities at baseline. A random intercept was specified for each participant to account for individual differences in baseline cartilage volume, and the correlation between the repeated measurements over time was modelled using an exponential residual variance-covariance structure. Point estimates of

change in the cartilage volume loss over 10.7 years were reported for those with PTE abnormalities at baseline compared to those without PTE abnormalities. All models were adjusted for age, sex, BMI, and additionally adjusted for baseline BMLs and cartilage defects.

All statistical analyses were performed using Stata 15 (Stata-Corp, College Station, Texas, USA). The significant p-value was set at the value of less than 0.05 (two-tailed).

Results

Of the 7 abnormalities measured, presence of tendon signal and deep infrapatellar bursa was almost ubiquitous in this group (tendon signal (proximal 97%, distal 84%); deep infrapatellar bursa 93%). Bone signal was infrequent, and bone erosion was rare (bone signal (proximal 10%, distal 10%); erosion (proximal 2%, distal 2%)). Prevalence of tendon signal, bone signal, and bone erosion were similar between distal and proximal sites. Therefore, PTE abnormalities were defined as presence of bone signal and/or erosion. At baseline, 20% of participants (n=192/961) had bone signal and/or erosion at the PTE. Of these, 84% had bone signal or erosion at 1 site only, 15% at 2 sites, and <1% at ≥3 sites.

Participants with and without baseline PTE abnormalities had similar demographic and structural profiles (Table 1); however, participants with PTE abnormalities were older, less female, had greater pain, and poorer physical function. They had more OA structural abnormalities (greater proportion of medial and lateral tibiofemoral BMLs, any BMLs, tibial and femoral cartilage defects), compared to participants without PTE abnormalities (Table 1).

Associations between PTE abnormalities and knee pain, physical function limitation, and total WOMAC score.

Presence of PTE abnormalities at baseline was associated with higher risk of presence (vs absence) of pain whilst walking on flat surfaces, going up and down stairs, pain score, function limitations score, and total WOMAC score, in the unadjusted model (Table 2). However, associations remained significant only for presence of pain whilst going up and down stairs and pain score after adjustment for demographic factors but not structural abnormalities.

PTE abnormalities were associated with greater intensity of function limitation and total WOMAC score in the unadjusted model. This association persisted for physical function limitation after adjustment for demographic factors. Only the association between PTE abnormalities and pain intensity going up and down stairs remained statistically significant after further adjustment for structural abnormalities.

Longitudinally, presence of baseline PTE abnormalities were not associated with change in risk of presence (vs absence) or intensity of knee pain subscales, pain, physical function limitation, and total WOMAC score over 10.7 years in unadjusted data. Presence of PTE abnormalities at baseline conferred a 3% increase in risk of presence of physical function limitation over 10.7 years, after adjustment of demographic factors and knee extension strength (Table 2) but not after further adjustment for structural abnormalities.

Bone marrow lesions

Baseline PTE abnormalities were associated with higher risk of presence of tibial and femoral BMLs at baseline after adjustment for demographic confounders (Table 3). The association remained significant for presence of femoral BMLs but associations diminished for tibial BMLs after further adjustment for site-specific cartilage defects (RR=1.27 (95% CI; 0.99, 1.62)). PTE abnormalities were not associated with presence of patellar BMLs at baseline. Over 10.7 years, baseline PTE abnormalities conferred a doubling of risk (RR 1.94) of a deleterious tibial BML size increase (change >52mm^2), compared with a participant with no PTE abnormalities; associations persisted after adjustment for demographic and structural factors. PTE abnormalities were not associated with increases in femoral or patellar BML size.

Infrapatellar fat pad area

Cross-sectionally, PTE abnormalities at baseline were negatively associated with infrapatellar fat pad area, after adjustment for demographic factors (Table 3). This association strengthened after further adjustment for cartilage defects and BMLs.

Cartilage defects and volume

Participants with PTE abnormalities were more likely to have tibial and femoral cartilage defects at baseline (Table 4). Associations persisted after adjustment for demographic factors, but after adjustment for structural factors (site-specific BMLs), associations only persisted for tibial cartilage defects. PTE abnormalities were not associated with patellar cartilage defects at baseline. Longitudinally, presence of baseline PTE abnormalities were not associated with change of tibial, femoral, and patellar cartilage defect score over 2.7 years. PTE

abnormalities were associated with medial tibial cartilage volume loss over 10.7 years after adjustment for demographic factors but not after adjustment of structural factors (RR=1.14 (0.84, 1.55)) (Table 4). PTE abnormalities were not associated with cartilage volume loss in other compartments.

Total knee replacement

Baseline PTE abnormalities were not associated with the incidence of TKR surgery over 13.3 years (Table 4).

Discussion

This study demonstrates that presence of PTE abnormalities (bone signal and erosion) are associated with greater pain going up and down stairs, presence of femoral BMLs, worse tibial cartilage defect score and lower infrapatellar fat pad area cross-sectionally, independent of structural confounders. However, these associations did not persist longitudinally, excepting associations with increases in tibial BML size. PTE abnormalities were not associated with the change in cartilage defects over 2.7 years, cartilage volume loss over 10.7 years, or TKR over 13.3 years. This suggests that PTE abnormalities are not causally related to the knee OA process.

The prevalence of abnormal changes at the PTE site in our study was 20%, comprising bone signal or erosion at 1 enthesis site (17%), 2 sites (3%) or 3 sites (n=1 person only), assessed reproducibly and non-invasively using MR imaging. This is the first time that such abnormalities have been measured in a similar population; previous studies investigated knee cruciate ligaments, collateral ligaments and tendon of interphalangeal joints. The 2% prevalence of enthesis bone erosion in our sample is larger than 0% (0/18 participants) in MRI images of finger joints of 18 healthy participants (age 30-72) [10], however, this study had both a small sample size and a wide age range. Bone pathology was very common at the cruciate ligament enthesis (range 22% to 69%) assessed using MRI amongst osteoarthritic patients [9], which is consistent with prevalence estimates from our study, also in older adults (10% bone signal at one enthesis site).

PTE abnormalities were most strongly associated with knee pain going up and down stairs, as expected. This association was independent of demographic and structural covariates. This is the activity where patients first report knee pain [29], and is responsible for the largest stress on hips and knees during weight bearing [30, 31]. Pain while stair climbing can be explained through increase in patellofemoral pressure, lateral tilt, and force distribution on the patella [32]. Our results suggest that PTE abnormalities may be associated with knee pain intensity (possibly anterior knee pain); and that this stress may be associated with the abnormal changes that we see on the enthesis site cross-sectionally. However, the effect size was small and may not clinically important, as associations did not persist longitudinally. This is in contrast with other studies which showed that enthesis abnormalities were related to pain in inflammatory arthritis [33] and heel pain [34-36].

We are the first group to explore associations between enthesis abnormalities and joint function. We observed that PTE abnormalities were not associated with presence of functional limitation independent of demographic or structural factors cross-sectionally; however the effect sizes remained similar to pain score. PTE abnormalities were associated with severity of functional limitation after adjustment for demographic factors cross-sectionally, but were not independent of structural covariates. Longitudinally, presence of PTE abnormalities were associated with a small (3%) increase in risk of worsening functional limitation over 10.7 years after adjustment for demographic factors, but this was also not independent of structural factors.

While almost none of the associations between PTE abnormalities and pain or function were independent of structural factors, we did demonstrate that PTE abnormalities are associated with some structural factors: higher risk of the presence of femoral BMLs at baseline and deleterious increases in tibial BML size over 10.7 years. A weaker cross-sectional association was also seen for tibial BMLs (RR 1.27 (0.99, 1.62)) after full adjustment of covariates at baseline. Previous studies have shown that BMLs can originate from entheses [10, 11], and are commonly adjacent to ligament pathology [37]. Our study design collected data on which compartment the BMLs were in, but not specifically whether the BMLs were or were not adjacent to cruciate ligament enthesis and PTE sites. However, we hypothesise that the observed association is due to the impact of joint loading on the tibia [38, 39]. Ligament degeneration and instability changes the biomechanical joint environment and is one of the risk factors for knee osteoarthritis [40]. The patellar tendon provides joint stability [41], so this association may be due to reduced stability and strength of the patellar tendon attachments.

Presence of PTE abnormalities was associated with smaller infrapatellar fat pad area, and worse tibial cartilage defects cross-sectionally; but not change in these factors longitudinally. Larger infrapatellar IPFP at baseline is protective for knee pain and cartilage damage in this cohort [23, 42]. We have no longitudinal data on infrapatellar fat pad area.

The lack of consistency between cross-sectional and longitudinal associations with osteoarthritis outcomes raises questions regarding whether PTE abnormalities are related to osteoarthritis or whether it simply co-occurs with other osteoarthritic structural abnormalities. We also hypothesised that the abnormalities would be more strongly associated with patellar

abnormalities, but paradoxically our results showed no association with any patellar abnormalities. Associations between PTE abnormalities and knee pain were seen cross-sectionally but not longitudinally, supporting an absence of longitudinal associations with knee OA structural abnormalities. Tan et al. suggested that enthesopathy-related osteoarthritis could be a specific subcategory of osteoarthritis [43] based on images of interphalangeal joints; however our study suggests that it may not be a major player in development of knee osteoarthritis.

Strengths of our study include data from a randomly selected community-dwelling cohort, therefore the results can be generalized to community-dwelling older adults. Data collection continued for 10 years, enabling us to assess longitudinal associations. The scoring system used in this study to assess PTE abnormalities is a novel, non-invasive, simple to use, and reproducible system which used T2-weighted fat saturation MRI. Limitations of our study include a lack of standardised scoring system to assess PTE abnormalities, requiring us to develop one from the literature to suit our study. We were unable to measure the size or volume of deep infrapatellar bursae and presence of enthesophytes due to the available image quality. Better image quality would improve the sensitivity of the analysis; since we are unable to assess volume, this may underestimate the magnitude of any associations, as bursa size more than 2-3mm is considered abnormal [44].

Conclusions

Patellar tendon enthesis abnormalities are common in older adults. Presence of cross-sectional but not longitudinal associations suggests they commonly co-exist with other knee structural abnormalities, and they may be a marker of loading manifested through BMLs. However, they may not play a major role in symptom development or structural change with the exception of tibial BMLs.

DECLARATIONS

Ethics approval and consent to participate

All research conducted was in compliance with the Declaration of Helsinki and was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee. All TASOAC participants gave informed written consent at the start of the TASOAC study.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgements

We thank the participants who made this study possible, and Catrina Boon and Pip Boon for their role in collecting the data, and Jason Rogers for his expertise in entheseal pain.

Author's contributions

All authors were involved in drafting the article or revising it for important intellectual content. All authors have approved the final manuscript. Laura L Laslett (laura.laslett@utas.edu.au) takes responsibility for the integrity of the work as a whole, from inception to finished article.

Conception and design: Mattap, Aitken, Wills, Halliday, Cicuttini, Jones, Laslett

Analysis and interpretation of data: Mattap, Aitken, Wills, Jones, Laslett

Drafting of the article: Mattap

Critical revision of the article for important intellectual content: Mattap, Aitken, Wills, Halliday, Ding, Han, Munugoda, Graves, Lorimer, Cicuttini, Jones, Laslett

Final approval of the article: Mattap, Aitken, Wills, Halliday, Ding, Han, Munugoda, Graves, Lorimer, Cicuttini, Jones, Laslett

Statistical expertise: Wills

Obtaining of funding: Cicuttini, Jones

Collection and assembly of data: Mattap, Ding, Munugoda, Graves, Lorimer, Han

Role of funding source

This work was supported by the National Health and Medical Research Council of Australia; Tasmanian Community Fund; Masonic Centenary Medical Research Foundation; Royal Hobart Hospital Research Foundation; and Arthritis Foundation of Australia. The study

sponsor had no role in the design of the study; the collection, analysis, and interpretation of the data; or the writing of the article and the decision to submit it for publication.

SM Mattap is supported by the Farrell foundation elite postgraduate scholarship, G Jones and LL Laslett are supported by National Health and Medical Research Council. The researchers work independently of their funders.

Competing interest statement

The authors declare no competing interest.

Reference List

1. Lane NE, Brandt K, Hawker G, Peeva E, Schreyer E, Tsuji W, et al. OARSI-FDA initiative: defining the disease state of osteoarthritis. Osteoarthritis Cartilage 2011; 19: 478-482.
2. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis Rheum. 2012; 64: 1697-1707.
3. Quasnichka HL, Anderson-MacKenzie JM, Tarlton JF, Sims TJ, Billingham ME, Bailey AJ. Cruciate ligament laxity and femoral intercondylar notch narrowing in early-stage knee osteoarthritis. Arthritis Rheum. 2005; 52: 3100-3109.
4. Anderson-MacKenzie JM, Billingham ME, Bailey AJ. Collagen remodeling in the anterior cruciate ligament associated with developing spontaneous murine osteoarthritis. Biochem. Biophys. Res. Commun. 1999; 258: 763-767.
5. Setton LA, Elliott DM, Mow VC. Altered mechanics of cartilage with osteoarthritis: Human osteoarthritis and an experimental model of joint degeneration. Osteoarthritis Cartilage 1999; 7: 2-14.
6. Benjamin M, Ralphs JR. Fibrocartilage in tendons and ligaments — an adaptation to compressive load. J. Anat. 1998; 193: 481-494.
7. Lu HH, Thomopoulos S. Functional Attachment of Soft Tissues to Bone: Development, Healing, and Tissue Engineering. Annu Rev Biomed Eng 2013; 15: 201-226.
8. Basso O, Johnson D, Amis A. The anatomy of the patellar tendon. Knee Surg. Sports Traumatol. Arthrosc. 2001; 9: 2-5.
9. Binks DA, Bergin D, Freemont AJ, Hodgson RJ, Yonenaga T, McGonagle D, et al. Potential role of the posterior cruciate ligament synovio-entheseal complex in joint effusion in early osteoarthritis: a magnetic resonance imaging and histological evaluation of cadaveric tissue and data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2014; 22: 1310-1317.
10. Tan AL, Grainger AJ, Tanner SF, Shelley DM, Pease C, Emery P, et al. High-resolution magnetic resonance imaging for the assessment of hand osteoarthritis. Arthritis Rheum. 2005; 52: 2355-2365.
11. Tan AL, Toumi H, Benjamin M, Grainger AJ, Tanner SF, Emery P, et al. Combined high-resolution magnetic resonance imaging and histological examination to explore the role of ligaments and tendons in the phenotypic expression of early hand osteoarthritis. Ann. Rheum. Dis. 2006; 65: 1267-1272.
12. Østergaard M, Peterfy C, Conaghan P, McQueen F, Bird P, Ejbjerg B, et al. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. J. Rheumatol. 2003; 30: 1385-1386.
13. Chatra PS. Bursae around the knee joints. Indian J. Radiol. Imaging 2012; 22: 27-30.
14. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33: 159-174.
15. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J. Rheumatol. 1988; 15: 1833-1840.
16. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Care Res. (Hoboken) 2001; 45: 453-461.
17. White DK, Master H. Patient Reported Measures of Physical Function in Knee Osteoarthritis. Rheum. Dis. Clin. North Am. 2016; 42: 239-252.

18. Ding C, Garnero P, Cicuttini F, Scott F, Cooley H, Jones G. Knee cartilage defects: association with early radiographic osteoarthritis, decreased cartilage volume, increased joint surface area and type II collagen breakdown. Osteoarthritis Cartilage 2005; 13: 198-205.
19. Zhu Z, Ding C, Jin X, Antony B, Han W, Laslett LL, et al. Patellofemoral Bone Marrow Lesions: Natural History and Associations With Pain and Structure. Arthritis Care Res. (Hoboken) 2016; 68: 1647-1654.
20. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol. Bull. 1979; 86: 420-428.
21. Dore D, Quinn S, Ding C, Winzenberg T, Zhai G, Cicuttini F, et al. Natural history and clinical significance of MRI-detected bone marrow lesions at the knee: a prospective study in community dwelling older adults. Arthritis Res. Ther. 2010; 12: R223.
22. Nguyen TV, Eisman JA. Assessment of Significant Change in BMD: A New Approach. J. Bone Miner. Res. 2000; 15: 369-370.
23. Han W, Cai S, Liu Z, Jin X, Wang X, Antony B, et al. Infrapatellar fat pad in the knee: is local fat good or bad for knee osteoarthritis? Arthritis Res. Ther. 2014; 16: R145.
24. Australian Orthopaedic Association National Joint Replacement Registry. Annual Report - 2016. Adelaide2016.
25. Altman RD, Hochberg M, Murphy WA, Jr., Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. Osteoarthritis Cartilage 1995; 3 Suppl A: 3-70.
26. Scott D, Blizzard L, Fell J, Jones G. Prospective study of self-reported pain, radiographic osteoarthritis, sarcopenia progression, and falls risk in community-dwelling older adults. Arthritis Care Res. (Hoboken) 2012; 64: 30-37.
27. Berthiaume MJ, Raynauld JP, Martel-Pelletier J, Labonte F, Beaudoin G, Bloch DA, et al. Meniscal tear and extrusion are strongly associated with progression of symptomatic knee osteoarthritis as assessed by quantitative magnetic resonance imaging. Ann. Rheum. Dis. 2005; 64: 556-563.
28. Wang X, Jin X, Han W, Cao Y, Halliday A, Blizzard L, et al. Cross-sectional and Longitudinal Associations between Knee Joint Effusion Synovitis and Knee Pain in Older Adults. J. Rheumatol. 2016; 43: 121-130.
29. Hensor EM, Dube B, Kingsbury SR, Tennant A, Conaghan PG. Toward a clinical definition of early osteoarthritis: onset of patient-reported knee pain begins on stairs. Data from the osteoarthritis initiative. Arthritis Care Res. 2015; 67: 40-47.
30. Andriacchi TP, Andersson GB, Fermier RW, Stern D, Galante JO. A study of lower-limb mechanics during stair-climbing. JBJS 1980; 62: 749-757.
31. Costigan PA, Deluzio KJ, Wyss UP. Knee and hip kinetics during normal stair climbing. Gait Posture 2002; 16: 31-37.
32. Goudakos IG, König C, Schöttle PB, Taylor WR, Singh NB, Roberts I, et al. Stair climbing results in more challenging patellofemoral contact mechanics and kinematics than walking at early knee flexion under physiological-like quadriceps loading. J. Biomech. 2009; 42: 2590-2596.
33. Kiris A, Kaya A, Ozgocmen S, Kocakoc E. Assessment of enthesitis in ankylosing spondylitis by power Doppler ultrasonography. Skeletal Radiol. 2006; 35: 522-528.
34. Williams SK, Brage M. Heel pain—plantar fasciitis and Achilles enthesopathy. Clin. Sports Med. 2004; 23: 123-144.
35. Hyslop E, McInnes IB, Woodburn J, Turner DE. Foot problems in psoriatic arthritis: high burden and low care provision. Ann. Rheum. Dis. 2010; 69: 928.

36. Olivieri I, Barozzi L, Padula A, De Matteis M, Pierro A, Cantini F, et al. Retrocalcaneal bursitis in spondyloarthropathy: assessment by ultrasonography and magnetic resonance imaging. J. Rheumatol. 1998; 25: 1352-1357.
37. Hernandez-Molina G, Guermazi A, Niu J, Gale D, Goggins J, Amin S, et al. Central bone marrow lesions in symptomatic knee osteoarthritis and their relationship to anterior cruciate ligament tears and cartilage loss. Arthritis Rheum. 2008; 58: 130-136.
38. Beckwée D, Vaes P, Shahabpour M, Muyldermans R, Rommers N, Bautmans I. The Influence of Joint Loading on Bone Marrow Lesions in the Knee: A Systematic Review With Meta-analysis. Am. J. Sports Med. 2015; 43: 3093-3107.
39. Bennell KL, Creaby MW, Wrigley TV, Bowles K-A, Hinman RS, Cicuttini F, et al. Bone marrow lesions are related to dynamic knee loading in medial knee osteoarthritis. Ann. Rheum. Dis. 2010; 69: 1151-1154.
40. Øiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee Osteoarthritis after Anterior Cruciate Ligament Injury. Am. J. Sports Med. 2009; 37: 1434-1443.
41. Loudon JK. Biomechanics and Pathomechanics of the Patellofemoral Joint. Int. J. Sports Phys. Ther. 2016; 11: 820-830.
42. Pan F, Han W, Wang X, Liu Z, Jin X, Antony B, et al. A longitudinal study of the association between infrapatellar fat pad maximal area and changes in knee symptoms and structure in older adults. Ann. Rheum. Dis. 2015; 74: 1818-1824.
43. McGonagle D, Tan AL, Carey J, Benjamin M. The anatomical basis for a novel classification of osteoarthritis and allied disorders. J. Anat. 2010; 216: 279-291.
44. McCarthy CL, McNally EG. The MRI appearance of cystic lesions around the knee. Skeletal Radiol. 2004; 33: 187-209.

Tables

Table 1. Characteristics of participants divided by presence of PTE abnormalities at baseline (n=961).

	No PTE abnormalities n=769	PTE abnormalities n=192
Age	62.5 (7.1)	64.4 (8.2)
Female sex (%)	53	43
Body Mass Index (kg/m^2)	27.6 (4.6)	28.2 (4.8)
Knee Extension (kg)	30.2 (11.1)	30.2 (11.7)
Radiographic OA (%)	60	57
Any meniscal tears (%)	99.5	100
Any meniscal extrusion (%)	24	28
Suprapatellar effusion (%)	43	39
Any BMLs (%)	52	68
Tibial cartilage defects (%)	18	27
Femoral cartilage defects (%)	25	34
Any cartilage defects (%)	52	59
Infrapatellar fat pad area (cm^2)	7.6 (1.2)	7.6 (1.2)
Cartilage volume (cm^3)		
Medial tibial	22.8 (6.1)	23.5 (6.2)
Lateral tibial	27.3 (7)	28.3 (7.4)
Patellar	32.1 (9.6)	31.9 (9.1)
Medial femoral	40.5 (11.3)	40 (10.4)
Lateral femoral	44.7 (12.6)	45 (12.6)
WOMAC scales		
Pain (0-45)	3.3 (5.9)	4.4 (7.0)
Function limitation (0-153)	9.9 (19.6)	14.9 (25.1)
Total score (0-216)	14.7 (26.8)	21.5 (34.5)

Mean (SD) except for percentages.
Baseline any cartilage defects score was dichotomised to normal/focal blistering (0 and 1) and any loss of chondral thickness (2 or more).
Suprapatellar effusion was dichotomised to normal (0 and 1) and pathological effusion as any score of ≥2.
n, number; BMI, body mass index; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Associations of PTE abnormalities and pain, function limitation, and total WOMAC score at baseline and change over 10.7 years.

	Univariable		Multivariable 1		Multivariable 2	
	Present/absent RR (95% CI)	Intensity β (95% CI)	Present/absent RR (95% CI)	Intensity β (95% CI)	Present/absent RR (95% CI)	Intensity β (95% CI)
Baseline (n=961)						
Pain subscales						
Walking on flat surface	**1.24 (1.00, 1.52)**	0.10 (-0.06, 0.27)	1.18 (0.96, 1.46)	0.11 (-0.06, 0.28)	1.20 (0.90, 1.61)	0.15 (-0.08, 0.38)
Going up and down stairs	**1.26 (1.03, 1.54)**	0.14 (0.00, 0.29)	**1.25 (1.02, 1.54)**	0.12 (-0.03, 0.26)	1.20 (0.91, 1.58)	**0.22 (0.03, 0.41)**
At night while in bed	1.09 (0.89, 1.34)	-0.12 (-0.31, 0.07)	1.04 (0.84, 1.29)	-0.15 (-0.34, 0.04)	0.97 (0.72, 1.32)	-0.07 (-0.34, 0.20)
Sitting or lying	1.22 (0.99, 1.50)	0.02 (-0.16, 0.20)	1.17 (0.95, 1.46)	-0.01 (-0.19, 0.18)	1.05 (0.77, 1.42)	0.03 (-0.23, 0.28)
Standing upright	1.17 (0.95, 1.44)	0.10 (-0.08, 0.28)	1.11 (0.90, 1.38)	0.09 (-0.09, 0.27)	0.98 (0.73, 1.33)	0.18 (-0.07, 0.43)
Pain score	**1.26 (1.03, 1.54)**	0.11 (-0.10, 0.31)	**1.24 (1.01, 1.53)**	0.06 (-0.14, 0.26)	1.17 (0.88, 1.54)	0.14 (-0.13, 0.41)
Function limitation score	**1.25 (1.02, 1.53)**	**0.35 (0.08, 0.61)**	1.20 (0.97, 1.48)	**0.26 (0.01, 0.52)**	1.21 (0.91, 1.60)	0.27 (-0.08, 0.62)
Total WOMAC score	**1.23 (1.00, 1.51)**	**0.29 (0.04, 0.55)**	1.18 (0.95, 1.46)	0.22 (-0.02, 0.47)	1.12 (0.84, 1.49)	0.29 (-0.05, 0.63)
Change over 10.7 years						
Pain subscales						
Walking on flat surface	1.00 (0.97, 1.03)	0.00 (-0.03, 0.03)	1.00 (0.97, 1.03)	0.00 (-0.03, 0.03)	0.99 (0.96, 1.03)	0.01 (-0.03, 0.04)
Going up and down stairs	1.00 (0.97, 1.03)	-0.01 (-0.03, 0.02)	1.00 (0.97, 1.03)	-0.01 (-0.03, 0.02)	0.99 (0.95, 1.03)	-0.01 (-0.04, 0.02)
At night while in bed	1.02 (0.99, 1.05)	0.01 (-0.02, 0.05)	1.02 (0.99, 1.05)	0.01 (-0.02, 0.05)	1.03 (0.99, 1.06)	0.02 (-0.02, 0.05)
Sitting or lying	1.00 (0.97, 1.03)	0.02 (-0.02, 0.05)	1.00 (0.97, 1.03)	0.02 (-0.01, 0.06)	1.02 (0.98, 1.05)	0.02 (-0.01, 0.06)
Standing upright	1.02 (0.99, 1.05)	-0.01 (-0.04, 0.03)	1.02 (0.99, 1.06)	0.00 (-0.03, 0.03)	1.03 (0.99, 1.07)	0.00 (-0.03, 0.04)
Pain score	1.01 (0.98, 1.04)	-0.01 (-0.05, 0.02)	1.01 (0.98, 1.04)	-0.01 (-0.05, 0.02)	1.01 (0.97, 1.04)	-0.01 (-0.05, 0.03)
Function limitation score	1.03 (1.00, 1.06)	-0.03 (-0.07, 0.01)	**1.03 (1.00, 1.06)**	-0.03 (-0.07, 0.00)	1.02 (0.98, 1.06)	-0.03 (-0.07, 0.02)
Total WOMAC score	1.02 (0.99, 1.05)	-0.01 (-0.05, 0.03)	1.02 (0.99, 1.06)	-0.01 (-0.05, 0.02)	1.02 (0.98, 1.06)	0.02 (-0.06, 0.02)

Bold denotes p-value<0.05

Multivariable 1- adjusted for age, sex, BMI, knee extension strength

Multivariable 2 – further adjusted for presence of medial tibiofemoral BMLs, cartilage defects, and suprapatellar effusion.

Hurdle model was used to report the association of PTE abnormalities and present/absent and intensity of the outcomes compared with participants without PTE abnormalities. Change over 10.7 years is the estimated change in outcomes over 10.7 years associated with PTE abnormalities.

Table 3. Associations of baseline PTE abnormalities and presence of baseline BMLs, increase in BML size >52mm^2 over 10.7 years, and baseline infrapatellar fat pad area.

	Univariable	Multivariable 1	Multivariable 2
Baseline presence of BML (n=647) (RR (95%CI))			
Tibial	**1.58 (1.24, 2.01)**	**1.41 (1.10, 1.80)**	1.27 (0.99, 1.62)
Femoral	**1.79 (1.35, 2.39)**	**1.68 (1.25, 2.24)**	**1.46 (1.12, 1.90)**
Patellar	1.21 (0.86, 1.71)	1.25 (0.88, 1.77)	1.17 (0.89, 1.55)
Increase in BML size >52mm^2 over 10.7 years (n=489) (RR (95%CI))			
Tibial	**1.94 (1.43, 2.63)**	**1.94 (1.42, 2.65)**	**1.52 (1.12, 2.05)**
Femoral	1.19 (0.81, 1.73)	1.14 (0.78, 1.67)	1.04 (0.74, 1.48)
Patellar	1.67 (0.91, 3.04)	1.64 (0.91, 2.95)	1.27 (0.73, 2.22)
Baseline Infrapatellar fat pad area (n=961) (β (95% CI))	-0.03 (-0.21, 0.16)	**-0.20 (-0.35, -0.05)**	**-0.27 (-0.47, -0.06)**

Bold denotes p-value<0.05

Multivariable 1– adjusted for age, sex, and BMI. Baseline infrapatellar fat pad were also adjusted for interaction of age and sex.

Multivariable 2– baseline presence of BMLs and BML size change >52mm^2 over 10.7 years were further adjusted for baseline cartilage defects, and baseline BMLs for change in BML size. Baseline infrapatellar fat pad were further adjusted for cartilage defects and BMLs.

Baseline BML and increase in BML size were assessed using log binomial model. Baseline IPFP were assessed using linear regression.

Table 4. Association of baseline PTE abnormalities and baseline cartilage defects, improved/worsening of cartilage defects over 2.7 years, cartilage volume over 10.7 years and TKR incident over 13.3 years.

	Univariable	Multivariable 1	Multivariable 2
Baseline cartilage defects (n=961) (RR (95% CI))			
Tibial	**1.73 (1.28, 2.34)**	**1.47 (1.09, 1.97)**	**1.70 (1.16, 2.47)**
Femoral	**1.44 (1.12, 1.85)**	**1.28 (1.01, 1.64)**	1.14 (0.84, 1.55)
Patellar	1.15 (0.96, 1.38)	1.07 (0.90, 1.29)	0.97 (0.77, 1.21)
Worsening of cartilage defects over 2.7 years (n=419) (RR (95% CI))			
Tibial	0.94 (0.60, 1.47)	0.90 (0.56, 1.44)	0.81 (0.51, 1.29)
Femoral	1.27 (0.96, 1.67)	1.20 (0.90, 1.59)	1.12 (0.83, 1.51)
Patellar	0.76 (0.48, 1.22)	0.78 (0.49, 1.25)	0.80 (0.50, 1.29)
Change in cartilage volume over 10.7 years (n=481) (β (95% CI))			
Medial tibial	**-42.39 (-83.71, -1.07)**	**-42.18 (-83.50, -0.87)**	-39.40 (-81.79, 3.00)
Lateral tibial	-25.44 (-176.99, 126.12)	-24.12 (-175.67, 127.42)	-15.61 (-171.48, 140.25)
Tibial	-213.27 (-466.07, 39.52)	-211.10 (-463.86, 41.66)	-186.22 (-446.04, 73.61)
Patellar	-58.49 (-198.51, 81.53)	-58.33 (-198.34, 81.69)	-47.53 (-192.54, 97.48)
Total knee replacement surgery over 13.3 years (n=961) (RR (95% CI))			
Right knee (n=40)	1.55 (0.78, 3.10)	1.42 (0.71, 2.85)	1.61 (0.64, 4.05)
Left knee (n=42)	1.42 (0.71, 2.83)	1.23 (0.63, 2.40)	0.91 (0.36, 2.29)
Any TKR (n=65)	1.37 (0.79, 2.37)	1.22 (0.71, 2.10)	1.01 (0.49, 2.08)

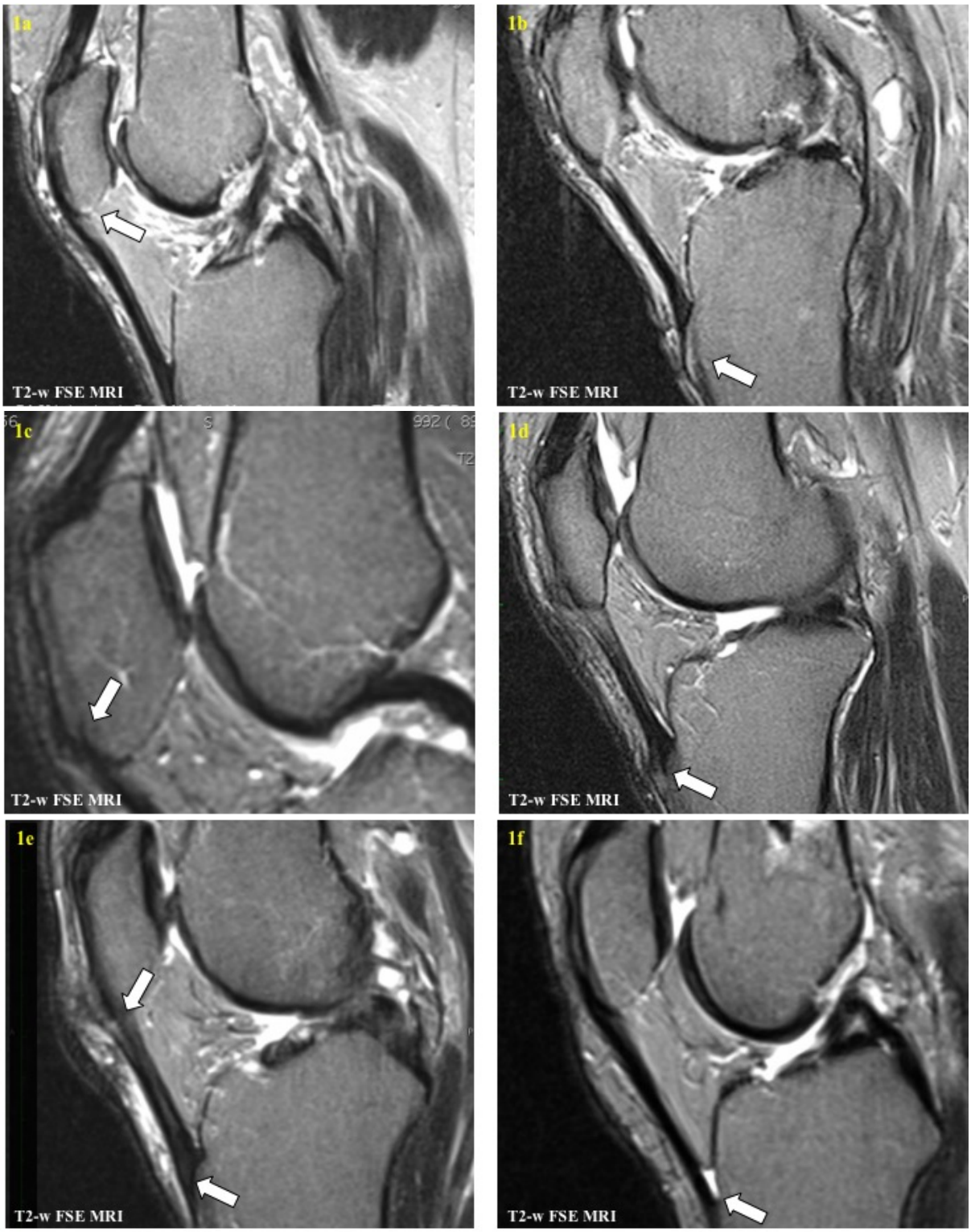
Multivariable 1– adjusted for age, sex, and BMI

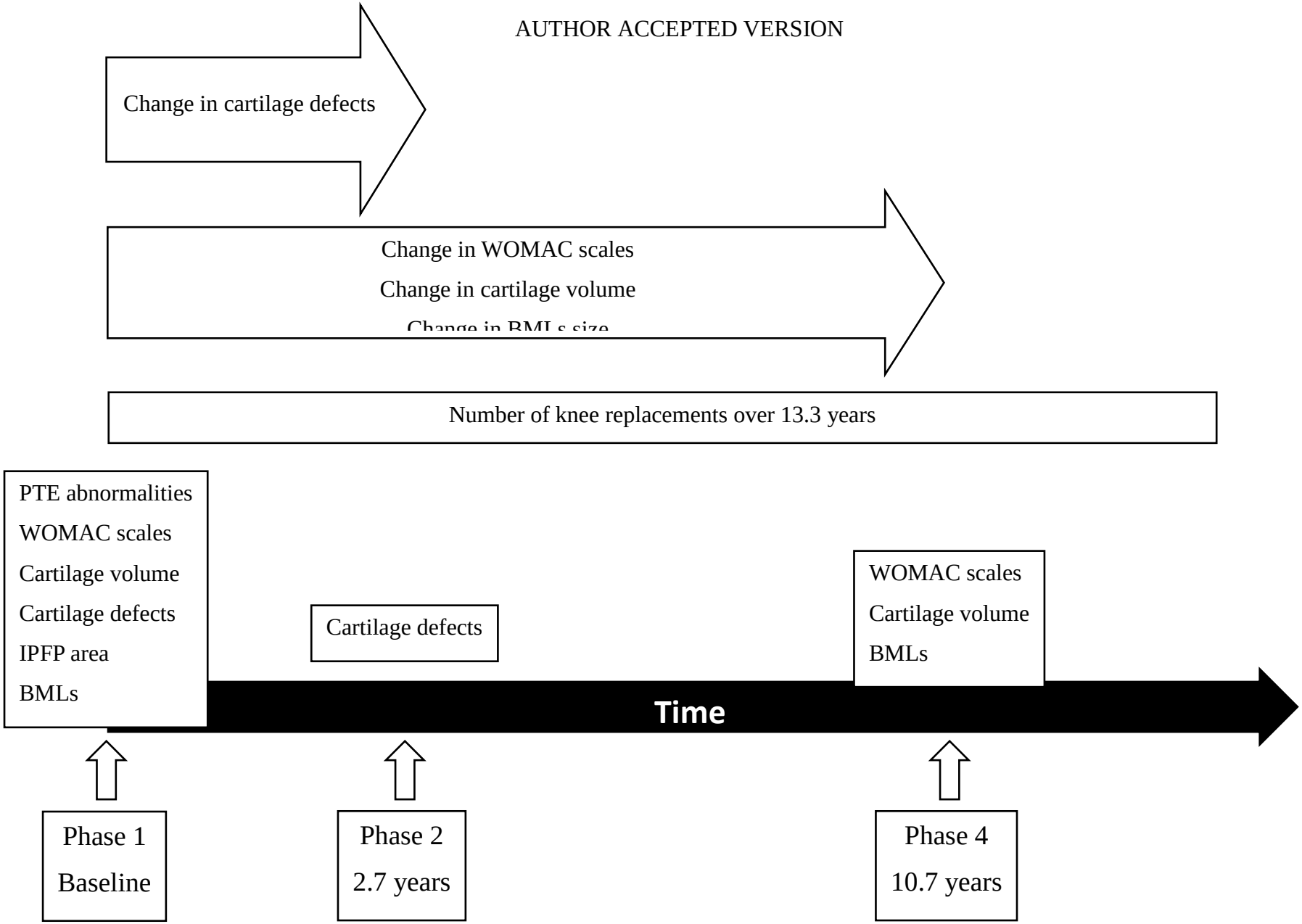
Multivariable 2– baseline cartilage defects were further adjusted for BMLs. Worsening of cartilage defect, change in cartilage volume loss, and TKR were further adjusted for baseline BMLs and cartilage defects. Baseline and worsening of cartilage defects were assessed using log binomial regression. Change in cartilage volume were assessed using mixed model; β-coefficient represents $1mm^3$ change in cartilage volume over 2.7 years for those with PTE abnormalities compared to those without PTE abnormalities. Incident of TKR were assessed using log binomial regression.

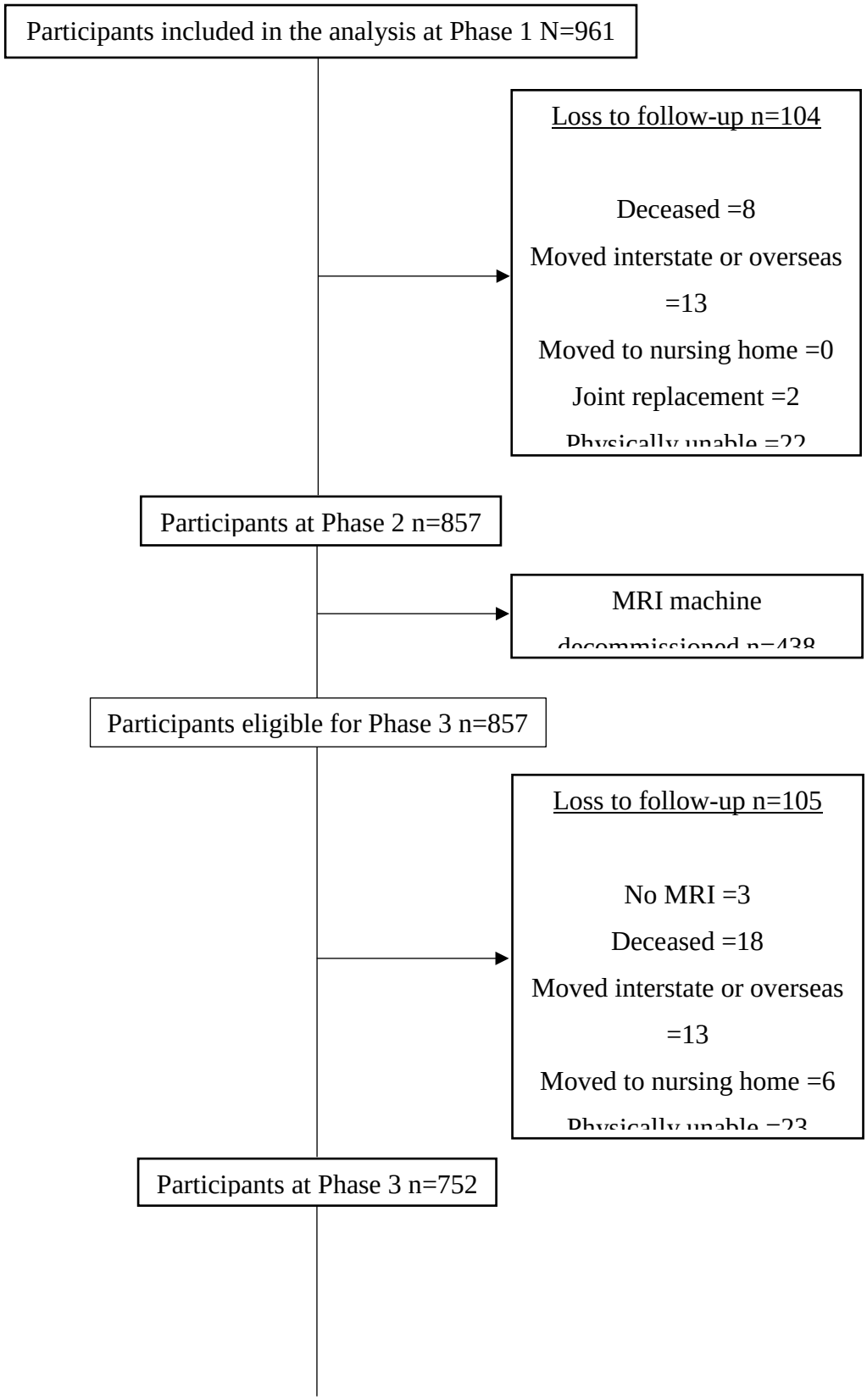
Figure 1. Patellar tendon and enthesis (PTE) abnormalities measured on T2-w FSE MRI, indicated by white arrows. 1a shows bone signal (increased signal intensity) at the proximal end of PTE and 1b shows bone signal (increased signal intensity with black band) at the distal end of PTE. 1c shows bone erosion at the proximal end of PTE and 1d shows bone erosion at the distal end of PTE. 1e shows proximal and distal tendon signal, while 1f shows presence of deep infrapatellar bursae between the tibia, distal PTE and infrapatellar fat pad. Note: Tendon signal abnormalities and deep infrapatellar bursa were ubiquitous abnormalities and thus were not included in the scoring system for PTE abnormalities

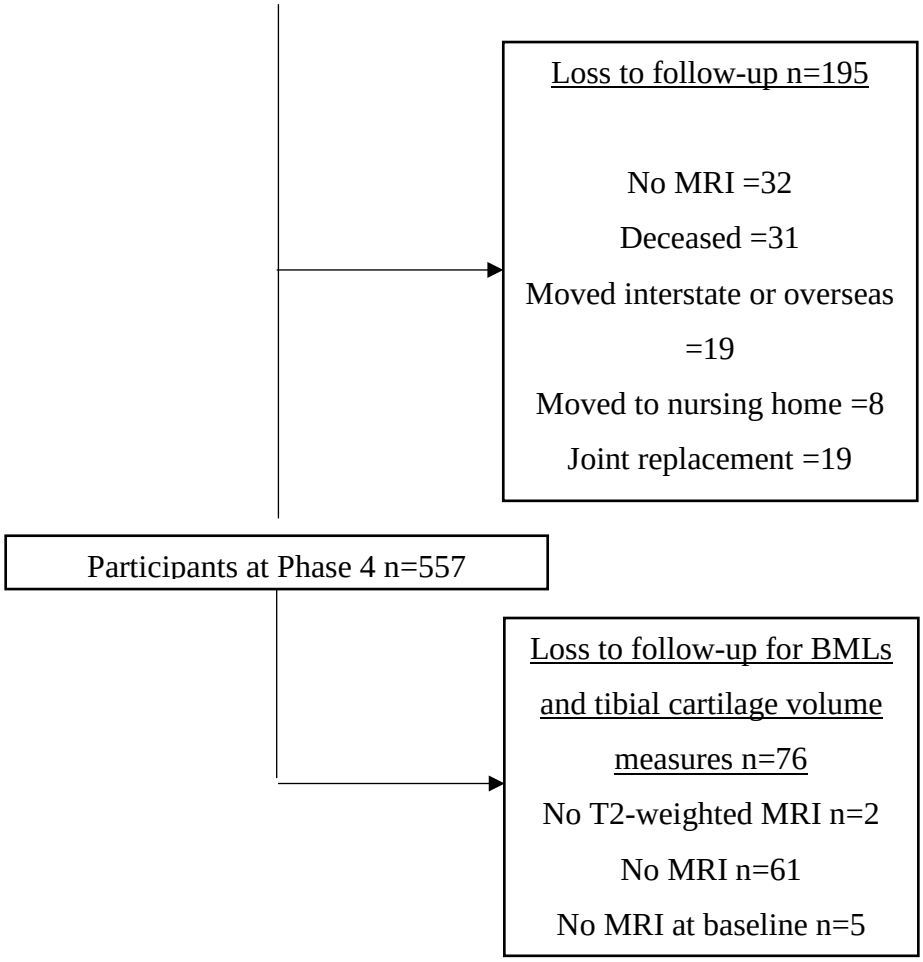
Figure 2. Study time line.

Figure 3. Flow of study participants. n=number of participants included in the analysis.


1a
T2-w FSE MRI
1b
T2-w FSE MRI
1c
T2-w FSE MRI
1d
T2-w FSE MRI
1e
T2-w FSE MRI
1f
T2-w FSE MRI


Change in cartilage defects
Change in WOMAC scales
Change in cartilage volume
Change in BMLs size
Number of knee replacements over 13.3 years
PTE abnormalities
WOMAC scales
Cartilage volume
Cartilage defects
IPFP area
BMLs
Cartilage defects
WOMAC scales
Cartilage volume
BMLs
Time
Phase 1
Baseline
Phase 2
2.7 years
Phase 4
10.7 years


Participants included in the analysis at Phase 1 N=961
Loss to follow-up n=104
Deceased =8
Moved interstate or overseas =13
Moved to nursing home =0
Joint replacement =2
Physically unable =22
Participants at Phase 2 n=857
MRI machine
Participants eligible for Phase 3 n=857
Loss to follow-up n=105
No MRI =3
Deceased =18
Moved interstate or overseas =13
Moved to nursing home =6
Physically unable =23
Participants at Phase 3 n=752


Loss to follow-up n=195
No MRI =32
Deceased =31
Moved interstate or overseas =19
Moved to nursing home =8
Joint replacement =19
Participants at Phase 4 n=557
Loss to follow-up for BMLs and tibial cartilage volume measures n=76
No T2-weighted MRI n=2
No MRI n=61
No MRI at baseline n=5

Supplementary table.

Table 5. The demographic differences between participants included and excluded (without MRI scans (n=116) and artefacts at PTE sites (n=21)) in this study analysis at baseline.

	Participants with MRI (n=961)	Participant without MRI (n=137)	p-value
Age	62.9 (7.4)	64.1 (8.2)	0.086
Female sex (%)	51	53	0.732
BMI (kg/m^2)	27.7 (4.7)	28.9 (5.1)	0.006
Knee Extension (kg)	30.2 (11.2)	28.3 (10.9)	0.060
Radiographic OA (%)	59	60	0.878

Mean(SD) except for percentages.