

Imaging the painful osteoarthritic knee joint: what have we learned?

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SUMMARY

Pain in the peripheral joints is an increasingly common problem, resulting in significant patient disability and health-care expenditure. Osteoarthritis (OA), a syndrome of joint pain with associated structural changes, is the most prevalent joint disease, yet the etiology of pain in OA is not entirely clear. Traditional assessment of the structure–pain relationship in knee OA has relied on conventional radiography, which has several limitations, not least the discrepancy between symptoms and radiographic findings. MRI has the capability to visualize all the structures within the knee joint, and there is a growing body of work using MRI to examine the correlation between structural findings and symptoms. In large cohort studies, synovial hypertrophy, synovial effusions, and abnormalities in the subchondral bone have been associated with knee pain. Advances in our understanding of the etiology of pain in OA will assist in the identification of further targets for treatment of this common and painful disease.

KEYWORDS joint pain, MRI, osteoarthritis, radiography

REVIEW CRITERIA

Data for this Review was identified using textbooks and searches on Pubmed with an unrestricted time frame. Articles were identified using the search terms “osteoarthritis”, “magnetic resonance imaging”, “radiograph”, “pain” and “joint pain” in various combinations. Additional references were found by searching the bibliographies of pertinent references and previous reviews.

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Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the prevalence of joint pain and its clinical impact.
- 2 Identify limitations of plain x-rays in the diagnosis of osteoarthritis (OA).
- 3 Specify common findings on MRI among patients with knee OA.
- 4 Describe the correlation between findings on MRI and knee symptoms.

Competing interests

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INTRODUCTION

Pain in the peripheral joints is an increasing problem. According to a 1998 epidemiological study, approximately 16% of the adult population of the UK have joint pain lasting more than 1 week over the course of a 1-month period, in more than three joints.¹ The prevalence of persistent musculoskeletal pain, joint swelling or stiffness in people aged 55 years or over has been reported at 40%, and increases with age.² Furthermore, the likelihood of an individual suffering disability due to joint pain also rises with age, with 60% of women and 40% of men over the age of 75 years reporting this condition.¹ Although each painful joint has a considerable effect on a person's functional ability, the overall effect is substantially increased when more than one joint is involved.² For example, individuals

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with musculoskeletal disease involvement of the feet, knee(s), hip and back are 60 times more likely to experience functional difficulty than individuals with just one painful joint.²

Osteoarthritis (OA) is characterized by joint pain, inactivity-related stiffness, impaired social role and reduced quality of life. Although there is no strict definition for OA, classification criteria for OA of the hand, hip and knee are available from the American College of Rheumatology, based on clinical, laboratory and radiographic findings.³ As a syndrome of joint pain with associated radiographic structural abnormalities, OA is the most prevalent joint disease and a major cause of disability.^{4,5} Murphy and colleagues have reported that almost half of US adults will have symptomatic knee OA by the age of 85 years, with the highest risk among obese individuals.⁶ OA is also the most common reason for undergoing total hip or total knee joint replacement. There was a 53% increase in the number of total knee joint replacements performed in the US between 2000 and 2004,⁷ and, as the population ages and hospital charges increase, the economic implications are huge. In 2004, the US annual national bill for hospital charges for the 226,000 hip and 431,000 knee replacements that were performed was \$26 billion.⁷ If current trends continue, nearly 600,000 hip replacements and 1.4 million knee replacements will be performed in the year 2015.⁷

Although pain is undoubtedly the most important presenting feature in the clinical syndrome of OA, the causes of nociceptive pain in the peripheral joints are still not entirely clear. The pathology of OA involves the whole joint in a biomechanically driven process that includes meniscal damage and extrusion, as well as focal and progressive hyaline articular cartilage loss with changes in the subchondral bone, including the development of marginal osteophytes and increased bony sclerosis. This is accompanied by synovial inflammation, lax ligaments and muscle weakness.⁵ Interestingly, although healthy cartilage is aneural, a report has suggested that nerve and vascular ingrowth occurs in damaged areas of OA cartilage.⁸ Although the causes of the joint pain are unclear, candidate sources of the pain, such as the subchondral bone or the synovium, have been proposed.^{9–11}

The use of imaging modalities, especially MRI, is providing new insights into the OA phenotype and the potential tissue origins of pain in joint disease beyond the understanding provided by traditional radiography. As it is becoming clearer that OA affects the whole joint, MRI has become

invaluable for improving our understanding of the disease, owing to its capability to visualize all the structures of a joint, including subchondral bone and soft tissue, thereby allowing us to fully analyze the structure–pain relationship. Most imaging studies of joint pain have evaluated knee OA; accordingly, this will be the main focus of this article, which will discuss what these studies have told us about the relationship between the symptoms of OA, including pain, and the associated imaging-detected structural changes in OA. Studies that have evaluated other painful joints will also be discussed where appropriate.

OBSTACLES IN STUDYING THE STRUCTURE–PAIN RELATIONSHIPS IN OA

Studying the structure–pain relationship in OA is not easy. Accurate quantification and description of pain can be difficult. Pain has been defined by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage”.¹² People with OA describe their pain using a variety of terms, including ‘dull ache’ and ‘sharp stabbing pain’, and there is a wide range of reported pain severity. The pain can be indistinguishable from stiffness, and is usually worse with prolonged weight-bearing. Furthermore, the episodic nature of pain makes detecting its association with structural changes difficult. Accordingly, studies that specify the duration and frequency of pain might influence the study results. The pain measure chosen, and how patient-reported outcomes are applied, will also influence results, as will confounders of reporting (e.g. depression). The most commonly used OA-specific pain outcome measures include the pain subscale of the Western Ontario and McMaster University Index (WOMAC) for the hip and knee, and the Australian/Canadian Hand Osteoarthritis Index (AUSCAN) for the hand.^{13,14} Generic self-reported pain measures that might be used in OA include a visual analog pain scale (VAS) or Likert scale, or questionnaires such as the McGill pain questionnaire.^{15,16} There has been no consistency in the use of these tools across studies, with some using OA-specific measures and some using generic, self-reported pain measures, but where possible in this Review the pain tool employed in a given study has been described.

Measuring and quantifying structural abnormalities is also difficult. Many conventional radiography studies of the knee have only imaged the tibiofemoral and not the patellofemoral joint.

MRI studies are complex and have a new range of variables, including different sequences and magnet strength. Quantification of MRI findings is improving, however, and most of the improvements are related to allowing for a good level of accuracy and reliability in measurements of cartilage volume and thickness.¹⁷ Currently, however, there are no well-validated quantitative measures for assessing non-cartilage features, although a number of semi-quantitative scores have been designed for evaluating knee MRI findings, for example the Boston Leeds Osteoarthritis Knee Score (BLOKS), the Whole Organ MRI Score (WORMS) and the Knee Osteoarthritis Score (KOSS).^{18–21} Each of these measurement tools divide the knee into various anatomical subregions, and use categorical scales to describe the extent of a number of multiple pathological features within these subregions. However, only limited data exist on the performance metrics of these tools. The reliability of these methods is often reported, and validity has been reported for BLOKS bone marrow lesion (BML) score.¹⁸

EXTRA-ARTICULAR CAUSES OF KNEE PAIN

Periarticular pathologies, including anserine bursitis, iliotibial band syndrome and semi-membranosus–tibial collateral ligament bursitis, in patients with radiographic OA are more common in those patients with pain than in those without pain.²² In addition to periarticular pathology, structures external to the knee joint might give rise to pain in and around the knees. Pain as a result of periarticular pathology can be referred to as a ‘non-articular condition’, and can include pain from the back, hip, bursitides, lower limbs (e.g. peripheral vascular disease), and widespread body pain.²³ Not accounting for potential periarticular conditions might partly explain the discordance between radiographic OA and pain in epidemiological studies, as well as the variance in WOMAC scores in studies of knee pain and OA.²³

RADIOGRAPHY OF KNEE OA

The Kellgren–Lawrence (K/L) grading system remains the most widely used tool for quantifying radiographic OA pathology.²⁴ The system assesses osteophytes, joint space width and the presence of subchondral bone sclerosis. Not all patients with knee pain demonstrate radiographic OA. Although radiographic OA has been shown to be more common in patients with painful knees rather than non-painful knees (53% versus 17%),

half of the subjects who report knee pain and who are at or above the age when OA starts to become common (about 55 years), have no definite radiographic evidence of OA.²⁵ A 2008 literature review reported that the proportion of patients with knee pain found to have radiographic OA ranged from 15% to 76%.²⁶ The reason for this lack of consistency across the data might be partly due to studies not using X-ray views of all three compartments of the knee; however, even when all compartments are imaged, the highest proportion of people with pain who have radiographic knee OA is 76%.²⁷ This finding is similar to those from a population-based group of 819 adults with knee pain; 777 of the patients’ data for all three X-rays views were available, and 68% of these had evidence of radiographic OA.²⁸ Earlier radiographic studies of OA might have underestimated the contribution of structural pathology to pain and disability by excluding the patellofemoral joint.²⁹ Duncan and colleagues²⁸ demonstrated that the use of a posteroanterior view alone identifies around only half of the cases of radiographic OA in patients with knee pain; this increased to 87% with two views, and 98% when all three views (posteroanterior, supine skyline and supine lateral) were used.

Although the likelihood of a patient experiencing knee pain generally increases with the severity of radiographic OA, there is substantial discordance between radiographic changes, clinical symptoms and the degree of disability experienced by patients.^{24,27,30–32} In a study of over 6,000 patients, around half of those with radiographic K/L scores of 2–4 reported knee pain.³⁰ The level of disability experienced by patients with knee OA has been shown to correlate more accurately with their age and psychological involvement than with their radiographic scores.³² Nonetheless, in a 2007 study of over 700 patients with knee pain, of whom 68% had radiographic OA, the presence of radiographic OA (as defined by the K/L score) was consistently associated with the severity of pain, stiffness and physical function.³³ The study used the WOMAC index and the graded chronic pain scale to measure pain.³³

With regard to individual radiographic, pathological features, the presence of osteophytes has been shown to be associated with the occurrence of knee pain.^{29,34,35} The association of joint space narrowing with pain is, however, inconsistent.^{34,35} This might be because we now recognize from MRI studies that joint space narrowing reflects a number of pathologies, including meniscal



Figure 1 Medial tibial bone marrow lesion and macerated medial meniscus. Coronal short-tau inversion recovery sequence of the knee, demonstrating a medial tibial bone marrow lesion (long arrow), a normal lateral meniscus and a macerated medial meniscus (short arrow).



Figure 2 Medial articular cartilage loss and bone marrow lesions. T₁-weighted coronal fat-suppressed image of the knee, demonstrating medial articular cartilage loss (long arrow) and tibial and femoral bone marrow lesion (short arrows).

degeneration and extrusion, as well as hyaline cartilage loss.³⁶

MRI-DETECTED OA ABNORMALITIES AND THEIR ASSOCIATION WITH SYMPTOMS

An increasing number of studies are documenting the frequency of the occurrence of multiple structural abnormalities in OA joints, which indicates that OA involves the whole organ.^{37–41} Generally, MRI abnormalities are seen more frequently with increasing K/L grade;³⁷ a study of 54 patients with OA confirmed the increased likelihood of the presence of MRI-detected structural changes as the radiological OA grade, measured by the K/L score, increased.⁴² All patients with a K/L score of 4 demonstrated synovial thickening, effusion, subchondral lesions, osteophytes and cartilage erosions on MRI.⁴²

Patients with normal radiography findings and no knee symptoms might also have MRI-detected structural changes. In a study of 25 patients with no knee pain, 55% demonstrated a small knee effusion on MRI, with a further 11% having a moderate effusion.¹⁰ In another report of 30 women with a mean age of 45 years, no knee symptoms and a normal X-ray, 35% demonstrated the presence of BMLs and 50% demonstrated cartilage defects on MRI.³⁸ In a further study of women from a community-based cohort with normal radiographs and no knee pain, cartilage

defects were again common, and this group had a lower incidence of BMLs (only 14%).³⁷ A similar incidence of BMLs was found in a cohort of 170 healthy adult women with no clinical knee OA, of whom 13% had BMLs.⁴³

Subchondral bone marrow changes

MRI allows the evaluation of subchondral bone, which is a richly innervated structure that is considered to be important in the occurrence of pain and the structural progression of OA.^{9,44} The most common MRI-detected subchondral bone abnormality represents a high-signal area on fat-suppressed T₂-weighted or short-tau inversion recovery sequences, and has been referred to as a subarticular bone marrow abnormality,²¹ bone marrow edema-like lesion⁴⁵ or a BML (Figures 1 and 2).⁹ For the purpose of this article, these subchondral bone abnormalities will be collectively termed BMLs. BMLs detected on MRI are not diagnostic for OA and have been seen in a range of conditions, including trauma, transient osteoporosis and rheumatoid arthritis; furthermore, they represent different disease-specific pathological processes.^{44,46} Three small MRI studies have correlated the histology of tibial plateau bone with the site of these BMLs in OA patients.^{47–49} In the larger of these studies, which involved 16 patients, abnormal tissue was seen in half the sites corresponding to BMLs, which

consisted of marrow necrosis, fibrosis and bony trabecular abnormalities.⁴⁷ Subchondral ingrowth of fibrovascular tissue has been demonstrated at the exact anatomical location of the BMLs identified on MRI.⁴⁹ Similar findings have been described in the osteoarthritic hip joint.⁵⁰

Felson and colleagues⁹ studied 401 patients with radiographic knee OA, of whom 50 had no knee pain (assessed using WOMAC). The incidence of BMLs increased as the radiographic K/L grade increased. The presence of BMLs on T₂-weighted MRI was seen in 78% of patients with painful knees, compared with 30% of the non-painful group ($P < 0.001$). Larger BMLs were present in 36% of patients with knee pain, compared with just 2% of those without pain. A further study demonstrated that larger BMLs ($> 1 \text{ cm}^2$) were more common in painful than non-painful knees; however, the frequency of BMLs were similar in the painful and non-painful groups.³⁸

Importantly, not all studies have shown an association between BMLs and pain. Kornaat and colleagues⁵¹ reported that, in 205 people, of whom 35% had symptomatic OA and 50% had radiographic OA, BMLs were not associated with pain. The reason for this lack of consistency among the data might be that the cohort inclusion criteria differed between the Kornaat study and the Felson study—only half the patients in the Kornaat study had radiographic OA, patients with a K/L score of 4 were excluded from MRI, and only one third had symptoms in the knee joint.

One of the issues in discerning the importance of changes in size of pathological features is whether change greater than measurement error is reported—this remains a confounder for many MRI studies. Felson and colleagues⁵² have studied whether BMLs that are actively enlarging are associated with new-onset knee pain. Knee pain was defined as pain on most days of the previous month. All study patients had no knee pain at baseline, and cases were defined as patients that developed knee pain by 15 months' follow-up. Changes in BMLs were evaluated using WORMS on a compartment-specific basis. Enlarged BMLs were noted in 49% of cases compared with 26% of controls ($P < 0.001$). The development of new BMLs was more common in case knees than control knees.⁵² In a community cohort of initially asymptomatic people, Davies-Tuck and colleagues⁵³ have also demonstrated that the development of new BMLs is associated with the development of knee pain (odds ratio [OR] 4.2).

The above findings, however, were not replicated in a similar study of 182 people, in whom changes in BMLs over a 2-year period were not associated with the severity of WOMAC score at the study end point.⁴⁵ Again this might be due to differences in cohort inclusion criteria: in the latter study, knees with a K/L score of 4 were excluded and 40% of subjects had knee pain at baseline, whereas in the two previously described studies,^{52,53} all subjects were pain free at baseline.

Bone attrition

Bone attrition is thought to represent remodeling of the subchondral bone.⁵⁴ On MRI, bone attrition is represented by a flattening or depression of the articular bone cortex, and is commonly seen in conjunction with BMLs and effusions.³⁹ Typically seen in advanced OA, it might occur in milder OA and earlier in the disease course than previously thought.⁵⁴

Bone attrition has been associated with knee pain, assessed by a VAS in patients with confirmed radiographic OA.⁴⁰ It has also been shown to be related to pain, as assessed by a self-reported pain questionnaire, in knees without radiographic OA.³⁹ In the latter study, definite bone attrition was seen in 28% of painful knees and 10% of painless knees ($P < 0.0001$).

Osteophytes

Although marginal osteophytes might be visualized better with conventional radiography than with MRI, central osteophytes are more easily detected on MRI^{55,56} (Figures 3 and 4) and have been demonstrated in 15% of patients referred for knee MRI who were not necessarily thought to have OA.⁵⁵ A small study of 44 asymptomatic people demonstrated that 25% had osteophytes detected by MRI, of which three-quarters had no evidence of osteophytes on radiography.⁵⁷ A larger community group of over 200 older patients (mean age 63 years) with knee pain, as assessed by WOMAC, demonstrated that 13% had osteophytes detected by MRI.⁵⁸

MRI studies to investigate the association between osteophytes and pain have shown conflicting results. A positive correlation was demonstrated between the presence of patellofemoral osteophytes and knee pain (OR 2.25) in a group of 200 patients, of whom a third had symptomatic knee OA.⁵¹ In this study, knee pain was defined as pain or stiffness on most days in the previous month.⁵¹ In a large study, which included 371 younger patients (mean age 45 years)

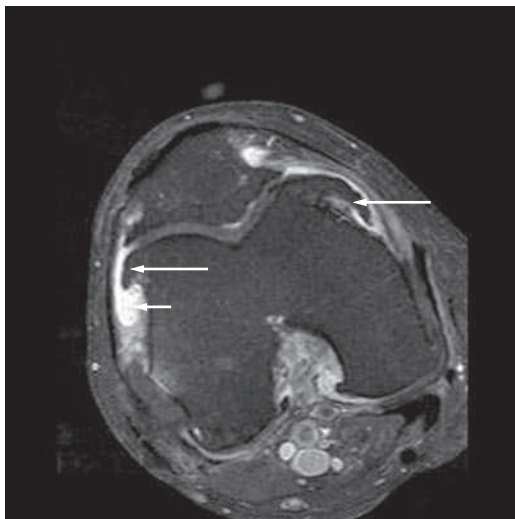


Figure 3 Large osteophytes and synovitis. T₁-weighted axial fat-suppressed image of the knee with contrast enhancement, demonstrating large osteophytes (long arrows) on the anterior margins of the femur (medial and lateral) and synovitis (short arrow) in the medial and lateral recesses.



Figure 4 Synovitis in suprapatellar pouch and osteophytes. T₁-weighted sagittal fat-suppressed image of the knee with contrast enhancement, demonstrating synovitis in the suprapatellar pouch (long arrow) and multiple osteophytes (short arrows).

of whom a third had knee pain (as assessed using a self-reported pain questionnaire), the presence of osteophytes were also significantly associated with knee pain (OR 2.51), even after adjustment for BMI and chondral defects.⁵⁹ By contrast, a study of a community-based cohort of 500 older people, of whom half had knee pain, reported no association between the presence of osteophytes and knee pain as assessed by WOMAC.⁵⁸ Another study

examined the association between increased signal intensity of osteophytes detected by MRI—which could be a BML within an osteophyte—and knee pain in 200 people with confirmed radiographic OA, and found there to be no link.⁶⁰

Synovitis and joint effusion

Joint effusion is best detected on fat-suppressed proton-density or T₂-weighted fast-spin echo MRI sequences (see Figures 3 and 4).⁶¹ It is possible to calculate the volume of joint effusions using semi-automated volume analysis.⁶² In a group of 100 patients with severe X-ray changes (K/L score ≥ 3), 80% had a moderate or large effusion detected by MRI.¹⁰

Synovitis is common in OA, and is present from the earliest stages of the disease.^{63–65} Synovial hypertrophy, which is seen on MRI in patients with OA, has been correlated with microscopic synovial inflammation.^{65,66} Quantitative MRI markers of synovitis include synovial membrane thickness, synovial fluid volume^{18,67} and the rate of synovial enhancement after intravenous injection of a contrast agent.⁶⁸ The use of intravenous contrast agents is the gold standard for assessing synovitis, as it can be difficult to accurately detect without their use. However, it is possible to be accurate in the quantification of synovial membrane thickness without using contrast.⁶⁷ Nonetheless, owing to emerging concerns over their potential toxicity in patients with severe renal impairment⁶⁹ and other issues regarding the feasibility of their use, such as expense, contrast agents are not used in many MRI studies.

The association between synovitis and pain was examined in a study of 450 people, 85% of whom had knee pain and the majority of whom had radiographic OA.¹⁰ All patients presented with painful knee symptoms on the majority of days during the previous 4 weeks, and pain was assessed using a VAS. Participants were evaluated on the basis of the association between their knee symptoms and effusions, popliteal cysts and synovial thickening on MRI. Intravenous contrast agents were not used. The frequency of effusions (moderate or large) and synovial hypertrophy, as assessed by a single observer as either present or absent at three sites in the knee, was significantly higher in painful knees compared to those without pain ($P < 0.001$).¹⁰ The mean pain score in those with synovial thickening was significantly higher than in those without synovial thickening (47 versus 28, $P = 0.006$), even after adjustment for effusion size and radiographic severity of OA.¹⁰

Further work by the same authors, again without using intravenous contrast agents, examined the temporal relationship between synovitis and pain, as assessed by VAS for knee symptoms during the previous week.¹¹ Baseline synovitis did not correlate with baseline pain levels, but there was a correlation between the change in synovitis score, assessed by a single observer as either present or absent at three sites, and the change in pain score, assessed by VAS ($P < 0.001$, $r = 0.21$).¹¹

Cartilage abnormalities

MRI can provide accurate and reproducible data on a series of cartilage measures (Figure 2), such as volume, thickness and denuded cartilage area.⁷⁰ Reliable measurements of cartilage change can also be recorded for longitudinal and cross-sectional studies with the use of MRI.⁷⁰ Cartilage defects range from focal blistering and surface irregularities to deep ulceration and full-thickness cartilage wear with exposure of subchondral bone.⁷¹ These defects are highly prevalent in MRI studies of OA knees, and tend to progress in patients with symptomatic OA.⁷¹

Different techniques, such as delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), T_2 and $T_{1\rho}$ mapping, can provide information on the composition and structure of the cartilage matrix.^{72–74} However, there is limited evidence of correlations between these measures and clinical symptoms, although a study of knee pain in patients postmeniscectomy demonstrated that a change in the dGEMRIC index might correlate with knee symptoms.⁷⁴ Other work has demonstrated that the dGEMRIC index might correlate with pain and the severity of hip dysplasia, suggesting that it might be a sensitive measure of early OA in the hip.⁷⁵ Two studies have attempted to correlate T_2 and $T_{1\rho}$ mapping techniques with symptoms in OA knees, assessed using WOMAC, one of which found a significant positive correlation.^{72,73}

Reduced cartilage volume has been associated with WOMAC-assessed knee pain in MRI studies,^{76,77} although this association is generally not a strong one and is not true in all studies.⁷⁸ As cartilage should be aneural, the source of pain is unclear. Studies have demonstrated that the articular cartilage becomes thinner, both by loss of the articular surface and by advancing ossification at the endochondral junction.⁷⁹ Angiogenesis is required for endochondral ossification, thereby offering a mechanism for introducing sensory nerves into the aneural cartilage.^{8,79}

Meniscal abnormalities

MRI is seen as the best noninvasive test for assessing meniscal pathology.⁶¹ Meniscal tears and meniscal extrusion (when the meniscus is partially or totally luxated from the tibial plateau) are very common in OA (Figure 1). The frequency of MRI-detected meniscal tears increases as the K/L grade increases.⁸⁰ A study of over 250 people with radiographic knee OA demonstrated that MRI evidence of meniscal malposition or damage, as assessed by the WOMS score, is associated with cartilage loss ($P < 0.0001$) over a 30-month period.³⁶

A study of a group of 140 people with radiographic OA and symptoms, including knee pain reported in the previous week and measured on a VAS, detected an association between meniscal tears and increased pain (coefficient of regression, $r = 1.99$);⁴⁰ however, only the joint compartment with the highest WOMS score was included in this analysis. Other studies have found that pain and function is no different between OA patients with or without meniscal tears. Bhattacharyya and colleagues⁸⁰ imaged 154 people with clinical knee OA, and defined meniscal tears as those extending to an articular surface. With regard to pain or WOMAC score, no significant difference was observed between the OA patients with and without a medial or lateral meniscal tear. As 91% of the OA group had a meniscal tear, the numbers in the comparison group might have been too small to detect a difference.⁸⁰

Further work in a cohort of over 300 asymptomatic people found no direct association between meniscal damage and the development of knee symptoms over a 15-month period.⁸¹ Knee symptoms were defined as pain, aching or stiffness on most days in the previous month, and meniscal damage was assessed using the WOMS. Meniscal damage was highly associated with the presence of OA at baseline; however, when OA occurrence was taken into account, there was limited evidence that meniscal damage directly caused later symptoms.⁸¹ Other work has also found no association between meniscal tears and pain.⁵¹

Ligament tears

The association between anterior cruciate ligament (ACL) tears and subsequent development and progression of radiographic OA is well described. The incidence of ACL changes seen in MRI studies of OA patients is high, with the occurrence of complete ACL tear occurring in around 20% of patients.^{82,83} Analysis of a large cohort of 265 female patients with symptomatic knee OA

demonstrated that ACL tears were not associated with worse pain or disability when compared to subjects without ACL tears;⁸³ neither was there any association with progression of pain during the 30-month follow-up.⁸³

Multiple MRI-detected abnormalities and their relationship with OA symptoms

Few studies have reported MRI-detected structural abnormalities of the knee in individuals with painful knees without a diagnosis of OA. A multivariate analysis of a cross-sectional cohort of 500 randomly selected people, with a mean age of 63 years, half of whom had WOMAC-assessed knee pain, reported a significant association between knee pain and medial–tibial chondral defects (OR 2.32) and BMLs (OR 1.44).⁵⁸ Pain was not associated with radiographic knee OA.⁵⁸ The same authors have carried out a further study of 370 younger patients (median age 45 years), of whom 130 had knee pain.⁵⁹ Half of these patients had a parent who had undergone knee replacement for OA, and half were randomly selected. Knee pain, assessed using a self-reported pain questionnaire, was significantly associated with femoral (OR 1.5) and patellar (OR 1.36) chondral defects, and osteophytes seen on MRI (OR 2.51). This study was not able to assess BMLs or effusions.⁵⁹

Several studies have analyzed the relationship between multiple MRI pathologies and joint symptoms in people with confirmed radiographic OA. Link and colleagues⁴¹ assessed 50 patients with confirmed radiographic knee OA and reported a significant association between WOMAC score and cartilage lesions on MRI. BMLs increased with K/L score, but this was not significantly associated with the WOMAC score. A report of 143 patients with confirmed radiographic OA and knee pain (measured on a VAS) showed that the severity of pain was positively correlated with MRI findings of bone attrition, BMLs, meniscal tears and synovitis/effusion (graded using a semi-quantitative scoring system).⁴⁰ There was a weak but significant association between presence of osteophytes and changes in cartilage morphology and pain.⁴⁰

Other studies have demonstrated the association between pain, BML and cartilage defects in people with radiographic OA.³⁸ Painful knees with radiographic OA demonstrated more frequent and more severe abnormalities on MRI than did knees without radiographic change. Abnormalities included defects of cartilage (severe defect in 67% versus 14%), meniscal tears ($P=0.001$),

osteophytes, subchondral cysts, sclerosis, joint effusion and synovitis ($P<0.001$).³⁷

CONCLUSIONS

The improvement in phenotyping that has occurred as a result of using MRI in OA studies has allowed us to gain a much wider knowledge of the different structures in the knee joint that are involved in OA, but has also raised many important questions. What is a structure-modifying therapy: an agent that modifies only a single pathology? When does OA begin: with the presence of structural abnormalities of cartilage or subchondral bone, or with the onset of symptoms? Novel MRI techniques might help us detect subtle changes in cartilage before macroscopic defects occur, further challenging our definitions of when OA begins, but offering exciting therapeutic potential. Although MRI has improved our understanding of structural OA, it has not yet been widely incorporated into the study of the weight-bearing or biomechanical loading component of OA.

More importantly, the improved picture of OA provided by MRI allows us to think about peripheral sources of pain in this disease. As discussed in this Review, abnormalities in the synovium and subchondral bone—both richly innervated structures—seem to be the pathologies most consistently associated with knee pain. These might represent targets for developing novel symptomatic treatment options for OA.

KEY POINTS

- Osteoarthritis (OA) is the most common joint disease and a major cause of joint pain, disability and health-care expenditure
- Traditional imaging for diagnosing OA has relied upon radiography, but there are discrepancies between clinical symptoms and radiographic findings
- As OA is now seen as a whole-organ joint disease, MRI is increasingly important in giving insight into the structures affected in OA, especially in symptomatic patients with normal radiographic findings
- The cause of pain in OA is unclear, but MRI studies of the structure–pain relationship have suggested the importance of subchondral bone and the synovium; these are targets for ongoing research
- The importance of extra-articular sources of joint pain and the psychosocial factors contributing to pain should not be ignored

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Competing interests

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