



Predictive value of magnetic resonance imaging (MRI) measures for the occurrence of total knee arthroplasty in knee osteoarthritis

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Introduction

The knee is the commonly-affected joint by osteoarthritis (OA) with pain and disability (1). Age- and sex-standardized incidence of knee OA is 240 per 100,000 person-years (2). Recent years, the incidence of OA is increasing progressively because of the ageing population and the epidemic obesity (3). The prevalence of knee OA calculated from data of National Health Interview Survey estimated 14 million persons with symptomatic knee OA in US including 6 million more people between 45 and 65 years old and nearly 2 million people under 45 years old (4).

Structural changes of knee joints with OA involve cartilage, menisci, subchondral bone, ligaments, synovial tissue and muscles (5), while the primary feature is cartilage damage because of bio-mechanical and bio-chemical changes in knee joints (6). Currently the common assessment of OA structural changes is X-ray; however, it can only visualize calcified tissues and mainly evaluate joint space narrowing which proves indirect information of cartilage thickness and meniscal integrity in advanced stages of the disease.

The therapeutic managements for OA include patient education, exercise, weight control, pharmacological treatment (non-steroidal anti-inflammatory drugs, injection of long-acting glucocorticoids or hyaluronic acid) and

surgical treatments. As self-management interventions, muscles strengthening exercises, aerobic exercises and weight reduction, have positive effects for unloading OA knees to reduce pain and disability. For many patients, self-management and pharmacological treatment are commonly combined to manage symptoms effectively (4).

Total knee arthroplasty (TKA)

TKA appears to be an ultimate clinical outcome for many patients of OA at the end stage of the disease (7). TKA has been in clinical use for more than 40 years, and its effectiveness in improving quality of OA patients' life by reducing pain and improving knee function has been validated (8). Actually, precise clinical endpoints of OA are not defined, and indications for TKA include radiographic changes, severe pain, functional disability and social and economic factors. Patient willingness was also associated with the outcome of undergoing TKA (9). While it is generally agreed that the major indication for knee replacement is persistent pain, which is defined as pain that cannot be relieved effectively by at least a six-month course of non-operative treatment, there is no international consensus on the degree of pain as an indication for this surgical treatment. These complex factors should

be considered before surgery decision making by both surgeons and patients.

The increasing number of OA patients promotes the use of TKA worldwide. In terms of reported data of joint registries, there are more than one hundred thousand knee replacements undertaken per year in the UK and the number of knee replacements done in USA has reached seven hundred thousand each year (8,10). OA patients receive knee replacements with an average age of 65, but the number of younger patients undergoing this procedure has been increasing (8).

Although TKA is effective for relieving pain and restoring function of joint, about 15% to 20% of patients are not satisfied for continuing knee pain after undergoing TKA, and the postoperative complications which often cause revision surgery, for instance, infection and prosthesis loosening, should not be ignored (11). With the sustained increasing of length of life, the number of patients requiring revision surgery will increase further.

Cartilage damage is associated with TKA

Data from Osteoarthritis Initiative (OAI) study demonstrated that the proportion of patients with no or only mild radiographic OA (Kellgren-Lawrence radiographic grades 0–2) at baseline undergoing knee replacement within a 5-year period was 28% (12). This result indicates that knees with an end-stage disease have structural damages being not visible on radiographs but seen on magnetic resonance imaging (MRI) (13). Large population-based studies have showed that MRI-detected cartilage damage is highly prevalent in knee joints without evidence of radiographic OA but with pain (14,15).

MRI-based measures of cartilage could be more sensitive imaging biomarkers in regard to OA disease progression, and there have been several studies describing the associations of MRI-assessed cartilage defects with clinically eventual TKA risks. In a longitudinal study of 123 patients (aged over 40) with knee OA (Kellgren-Lawrence radiographic grades 1–3), the rate of tibial cartilage loss over 2 years was an independent predictor of TKA at 4 years (16). An observational study of 4,796 subjects (age 45 to 79 years) demonstrated patients with greater loss of cartilage thickness in the central and medial tibiofemoral compartments were more likely to undergo TKA than controls over 4 years (9). Another observational study of 117 patients (age over 40) with knee OA showed higher total cartilage defect scores were associated with a six-fold

increased risk of TKA over 4 years compared with those with lower scores (17).

The predictive value of cartilage defects for knee OA prognosis is of interest to the scientific community due to its clinical importance of aiding in the decision-making process for surgery. Everhart *et al.* selected 1,319 subjects aged 49–75 years with Kellgren-Lawrence grade 0–3 in the OAI study, and investigated whether baseline full-thickness tibiofemoral cartilage defect or radiographic OA grade would be predictive of TKA over a median of 9 years. This study, similar but not the same as other studies, confirmed that the full-thickness cartilage defect was a strong independent risk factor for TKA [hazard ratio (HR) =2.90] (18). Previous studies included subjects with Kellgren-Lawrence grade 0–4 at baseline, and measured cartilage change quantitatively (9,16) or semi-quantitatively (17). The study by Everhart *et al.* took a slightly different approach, including those without severe radiographic OA and focusing on full-thickness cartilage defects, and confirming that presence of a full-thickness defect was a strong independent risk factor for TKA and the risk of arthroplasty increased with increased total defect size. Although the measurements of volume or thickness of cartilage may be more accurate (9,16), in daily clinical practice the identifying of full-thickness cartilage defect could be more efficient. In addition, this study also described that age, weight, Knee Injury and Osteoarthritis Outcome Score (KOOS) sport/recreation subscale were independently associated with eventual knee replacement surgery.

MRI can be used to assess the whole joint structural changes in 3D fashion, including cartilage damage, meniscal lesions, ligament tear, synovitis, subchondral bone damage, all of which have clinical relevance. Synovial inflammation can occur in both early and end stage of OA, and may be responsible to clinical symptoms (joint pain and swelling) and process of cartilage degradation (19). Subchondral bone marrow lesions, which is identified as a high signal intensity area on water-sensitive MR sequences, are a contributor of pain and linked to rapid loss of cartilage (20). Studies demonstrated that meniscal lesion, bone marrow lesions and synovitis also predicted the outcome of TKA (7). Based on above data, MRI plays an important role in the assessment of knee OA progression not seen in X-rays (14).

Cartilage damage is not isolated. Everhart *et al.* (18) also observed subchondral bone marrow abnormalities, synovial hypertrophy and effusion from MRI images of subjects in their study, but they did not assess the association of these

measures with disease progression.

Underlying mechanisms linking cartilage damage to TKA

This study by Everhart *et al.* provides a more detailed understanding of the prediction of prognosis of OA, but it is also important to understand the possible mechanisms linked cartilage defects with TKA risk. We would concur with the supposing mechanisms, “*full-thickness defects could simply be predictive of future accelerated cartilage loss, leading to progressively worsening symptoms.*” (18). Pain of OA is of multifactorial and complex origin, associating with damaged joint structures, such as subchondral bone and meniscal damages. Cartilage is not a direct source of pain in OA for the absence of innervation of sensory nerve fibres. However, cartilage defect with subchondral bone plate exposure was demonstrated to be linked to knee pain in OA patients. A study has shown a positive relationship between tibiofemoral denuded areas of subchondral bone (dABs) and knee pain, especially when the dABs are located centrally (21). Full-thickness cartilage defects would respond poorly to non-surgical treatments, and this would be another reason why full-thickness cartilage defects were associated with increased risks of TKA.

Targeting cartilage damage to delay TKA

Although this study concluded full-thickness cartilage defects were a major determinant for future knee arthroplasty, we may not encourage surgeons to perform TKA for patients with symptomatic knee OA in the light of presence of full-thickness defects. A systematic, step-by-step conservative treatment strategy should be a primary consideration. However, currently drugs or physiotherapeutics for relieving OA pain just aim to inhibit inflammation, without targeting joint lesions. Although disease-modifying OA drugs (drugs that can reduce symptoms and delay or prevent the disease progression) with protective effect on articular cartilage has entered human clinical trials (22), much work remains to be done in the development of treatments that improve the repair process of damaged cartilage or other joint structures.

Based on the results from the study of Everhart *et al.*, MRI scan may help us establish understanding for the failure of non-operative treatments in patients with mild radiographic OA. For these patients, particularly younger patients, full-thickness cartilage defects should be targeted

to delay or prevent future TKA. Other surgical treatments, such as chondroplasty and debridement, drilling and microfracture, autologous chondrocyte implantation, osteochondral autograft transfer and osteochondral allograft, have been developed to tackle cartilage defects. The critical issue is how to elucidate the indications of different cartilage repair options.

As Everhart *et al.* conceded, a limitation of their study was that younger people (30–45 years old) were not included as the participants. According to authors' opinion, the large majority of subjects of this study should not be appropriate candidates for autologous chondrocyte implantation or a similar procedure for their relatively older age. What we can expect is that the rapid development of emerging technologies has the potential to change the field of cartilage repair and regeneration (23).

Considering that MRI is an expensive technique and often costs a long time for images acquisition and analysis, the authors do not recommend using MRI as part of the initial evaluation for knee OA. However, for young people with knee pain, especially for athletic populations, MRI evaluation should be introduced to detect the possible cartilage damage. In the absence of disease-modifying OA drugs, early detection of knee cartilage damage, especially full-thickness cartilage defect, is very important for prevention or delay of OA disease progression. People with full-thickness cartilage defect are urged to take early exercise and self-management interventions which may led to improvement in cartilage damage and delay the development and progression of knee OA.

Summary

In conclusion, Everhart *et al.* confirmed what we had known from previous studies, and should be commended for the findings that raise our awareness regarding the trend of disease progression in patients with full-thickness cartilage defects. Targeting full-thickness cartilage defects using pharmacological or non-pharmacological therapies could prevent or delay the need of future TKA.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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