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Review

Imaging for osteoarthritis

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ABSTRACT

Osteoarthritis (OA) is a widely prevalent disease worldwide and, with an increasing ageing society, is a challenge for the field of physical and rehabilitation medicine. Technologic advances and implementation of sophisticated post-processing instruments and analytic strategies have resulted in imaging playing a more and more important role in understanding the disease process of OA. Radiography is still the most commonly used imaging modality for establishing an imaging-based diagnosis of OA. The need for an effective non-surgical OA treatment is highly desired, but despite on-going research efforts no disease-modifying OA drugs have been discovered or approved to date. MR imaging-based studies have revealed some of the limitations of radiography. The ability of MR to image all relevant joint tissues within the knee and to visualize cartilage morphology and composition has resulted in MRI playing a key role in understanding the natural history of the disease and in the search for new therapies. Our review will focus on the roles and limitations of radiography and MRI with particular attention to knee OA. The use of other modalities (e.g. ultrasound, nuclear medicine, computed tomography (CT), and CT/MR arthrography) in clinical practice and OA research will also be briefly described. Ultrasound may be useful to evaluate synovial pathology in osteoarthritis, particularly in the hand.

Knee osteoarthritis is a major public health problem that primarily affects the elderly. Almost 10% of the United States population suffers from symptomatic knee osteoarthritis by the age of 60 [S1]. In total, the health care expenditures of this condition have been estimated at US$ 186 billion annually [S2]. Despite this there are no approved interventions that ameliorate structural progression of this disorder.

The increasing importance of imaging in osteoarthritis for diagnosis, prognostication and follow-up is well recognized by both clinicians and osteoarthritis researchers. While conventional radiography is the gold standard imaging technique for the evaluation of known or suspected osteoarthritis in clinical practice and research, it has limitations that have become apparent in the course of large magnetic resonance imaging (MRI)-based knee osteoarthritis studies [1,2]. Pathological changes may be evident in all structures of a joint with osteoarthritis although traditionally researchers have viewed articular cartilage as the central feature and as the primary target for intervention and measurement. Of the commonly employed imaging techniques, only MRI can assess all structures of the joint, including cartilage, meniscus, ligaments, muscle, subarticular bone marrow and synovium, and thus can show the knee as a whole organ three-dimensionally. In addition, it can directly help in the assessment of cartilage morphology and composition. The advantages and limitations of conventional radiography, MRI and other techniques such as ultrasound, nuclear medicine, computed tomography (CT) and CT arthrography in the imaging of osteoarthritis in both clinical practice and research are described in this review article.

1. Conventional radiography

Radiography is the simplest, least expensive and most commonly deployed imaging modality for OA. It enables detection of OA-associated bony features such as osteophytes, subchondral sclerosis and cysts [3]. Radiography can also determine joint space width (JSW), which is a surrogate for cartilage thickness and meniscal integrity in knees, but direct visualization of these articular structures is not possible. Despite this limitation, slowing of radiographically detected joint space narrowing (JSN) remains the only structural end point currently approved by the U.S. Food and Drug Administration to demonstrate efficacy of disease-modifying OA drugs in phase III clinical trials. OA is radiographically defined by the presence of marginal osteophytes

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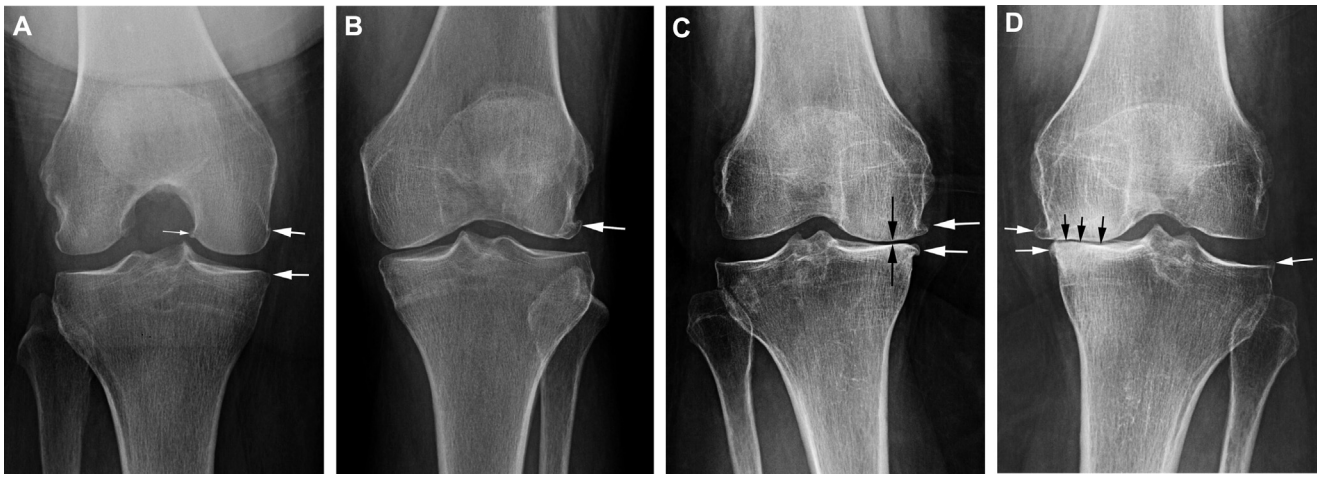

Fig. 1. The Kellgren-Lawrence classification is a composite scale of OA severity taking into account primarily the radiographic OA features of marginal osteophytes and joint space narrowing in the AP radiograph. A. Kellgren-Lawrence grade 1. Minimal, equivocal osteophytes are observed at the medial joint margins (large arrows). Note that, so-called notch osteophytes at the centre of the joint (small arrow) are not considered in the Kellgren-Lawrence scale. B. Kellgren-Lawrence grade 2 is characterized by presence of at least one definite marginal osteophyte (arrow) without evidence of joint space narrowing. C. Kellgren-Lawrence grade 3 knees exhibit signs of definite joint space narrowing (black arrows) and marginal osteophytes (white arrows). The amount of joint space narrowing is not taken into account. D. Kellgren-Lawrence grade 4 is defined by bone-to-bone contact and complete obliteration of the joint space (black arrows). Note definite marginal osteophytes in addition (white arrows).

[S3]. Worsening of JSN is the most commonly used criterion for the assessment of structural OA progression and the total loss of JSW ("bone-on-bone" appearance) is one of the indicators for joint replacement.

We now know cartilage loss is not the only contributor to JSN but that changes in the meniscus such as meniscal extrusion and meniscal substance loss are also causative factors. The lack of sensitivity and specificity of radiography for the detection of OA-associated articular tissue damage, and its poor sensitivity to change longitudinally are other limitations of radiography. Changes in knee positioning can also be problematic in longitudinal studies and can affect the quantitative measurement of various radiographic parameters including JSW. Despite these limitations, radiography is still the gold standard for establishing an imaging-based diagnosis of OA and for assessment of structural modification in clinical trials of knee OA.

1.1. Semiquantitative assessments

The severity of radiographic OA can be assessed with semiquantitative scoring systems. The Kellgren and Lawrence (KL) grading system [4] is a widely accepted scheme for defining radiographic OA based on the presence of a definite osteophyte (grade 2). However, KL grading has its limitations; in particular, KL grade 3 includes all degrees of JSN, regardless of the actual extent. Fig. 1 depicts representative examples of the different KL grades as shown on the AP radiograph. Recently, the so-called atrophic phenotype of knee OA that is characterized by definite joint space narrowing without concomitant osteophyte formation has gained increasing attention as a potential risk factor for more rapid progressive OA, which may be considered a potential adverse event in so-called anti-nerve growth factor (NGF) drug trials, a class of new promising antianalgesic compounds currently under investigation [5]. Although this phenotype is rare, it needs special attention in the research community as it potentially also is a reflection of more rapid disease progression [6]. Fig. 2 shows an example of the atrophic phenotype of radiographic OA.

The Osteoarthritis Research Society International (OARSI) atlas [3] provides image examples for grades for specific features of OA rather than assigning global scores according to definitions like the KL grading system. The atlas grades tibiofemoral JSW and osteophytes separately for each compartment of the knee (medial tibiofemoral, lateral tibiofemoral, and patellofemoral). A recent study using data from the OA Initiative and the OARSI atlas for semiquantitative grading of JSN demonstrated that centralized radiographic reading is important from the point of observer reliability, as even expert readers seem to apply different thresholds for JSN grading [7].

1.2. Quantitative assessments

JSW is the distance between the projected femoral and tibial margins on the anteroposterior radiographic image. Measurements may be performed manually or in a semi-automated fashion using computer software. Quantification using image processing software requires a digital image, whether digitized plain films or images acquired using fully digital modalities such as computed radiography and digital radiography. Minimum JSW is the standard metric, but the use of location-specific JSW has also been reported [S4]. Using software analysis of digital knee radiographic images, measures of location-specific JSW were shown to be comparable with MR imaging in detecting OA progression [8]. Various degrees of responsiveness have been

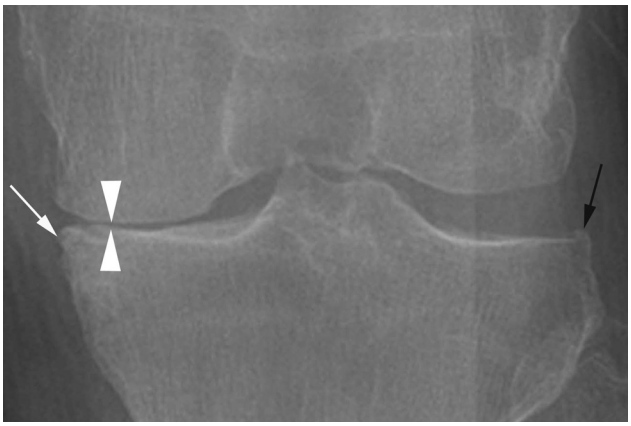

Fig. 2. Kellgren-Lawrence 3 knees with definite joint space narrowing (arrowheads) but only minimal osteophyte formation (arrow) are considered to represent the so-called atrophic phenotype of knee OA. This subtype of radiographic knee OA may be a reflection of more rapid disease progression.