19.9 Osteoarthritis 4470 Andrew J. Barr and Philip

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ESSENTIALS Clinical osteoarthritis is a syndrome of joint pain associated with structural deterioration of synovial joints that over time involves the whole joint organ. It is the most common form of arthritis and a leading cause of chronic pain, disability, and socioeconomic burden. Affected individuals report pain (especially on weight bearing) and joint stiffness leading to loss of muscle strength and poor joint func- tion. This results in reduced participation in valued activities, low mood, sleep disturbance, and poor quality of life. Aetiology and pathogenesis The aetiology of joint deterioration, pain, and the interaction of the two remains unclear. Clinical osteoarthritis is associated with a variety of both modifiable and nonmodifiable risk factors including obesity, age, gender, occupational injury, trauma, and genetic predisposition. Obesity is the strongest potentially modifiable risk factor. In early stages of pathogenesis individual tissues may be involved, but typical clinical osteoarthritis involves a complex collection of multitissue joint pathologies characterized by focal and progressive loss of the hyaline articular cartilage with underlying bone changes and secondary synovitis. Biomechanical factors are important in both inci- dence and progression, and together with complex biochemical events promote structural and nociceptive pathology within the synovium and subchondral bone as well as the cartilage. All elements of pain path- ways, including central processes, also play a role in pain perception. Diagnosis The syndrome typically manifests with joint symptoms after the age of 40 years, but the process of structural deterioration of the joint tissues is likely to begin before this. A history of activity-related pain with less than 30 minutes of morning stiffness in the context of the patient’s age, work history, prior injuries, and weight, is usually sufficient to confi- dently diagnose osteoarthritis without need for investigations. Management A holistic assessment is essential to understand the patient’s con- cerns and realistic treatment goals. Information on osteoarthritis should be provided. Treatment consists of a combination of mod- erately effective nonpharmacological (muscle strengthening, in- creased activity and weight loss if needed) and pharmacological (topical and oral

nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids) pain-relieving therapies. No agents are currently licensed as structure-modifying therapies. Joint replacements typically reduce pain, though joint prostheses have a finite life expectancy and revi- sion surgery offers less favourable outcomes. Introduction Osteoarthritis (OA) is the most common arthritis and is a leading cause of global chronic pain, disability, and socioeconomic burden. It affects 8.5 million people in the United Kingdom. In adults above the age of 45 years, radiographic and symptomatic knee osteoarthritis has a prevalence of 19–28% and 7–17%, respectively. The epidemi- ology and natural history differ between joints and individuals. The prevalence of clinical osteoarthritis increases with age and obesity, and it represents a huge personal and health services burden. Defining osteoarthritis and subtypes Clinical osteoarthritis refers to structural deterioration of synovial joints that in early stages may initially involve individual tissues, which in the context of appropriate risk factors may evolve by a complex cascade of biomechanical and biochemical pathologies, into the typical whole joint multitissue pathologies seen in typical painful clinical osteoarthritis. This includes changes to the hyaline articular cartilage, the underlying subchondral bone, the meniscal fibrocartilages (in the knee) and the synovium. The problems with defining osteoarthritis Definitions of osteoarthritis have derived from epidemiological studies and clinical trials where osteoarthritis may be defined using clinical findings (joint symptoms and examination findings) alone, the presence of imaging-assessed pathology, or a combination of the two. Only 50% of knees with radiographic osteoarthritis have symp- toms and activity-related pain of osteoarthritis may occur in a pro-dromal phase before the incidence of radiographic osteoarthritis. Hence in research studies of osteoarthritis, a more specific defin- ition can be achieved by any combination of joint imaging-assessed 19.9 Osteoarthritis Andrew J. Barr and Philip G. Conaghan

19.9 Osteoarthritis 4471 structural pathology (e.g. Kellgren Lawrence grade 2, a definite radio-graphic osteophyte, Table 19.9.1) and clinical findings and laboratory tests (e.g. American College of Rheumatology criteria, Table 19.9.2). While conventional radiography is feasible, it is limited in its utility by its relatively insensitive detection of structural path- ology in tissues other than bone (Fig. 19.9.1). Among individ- uals within the Framingham cohort, the age of 50 years, with no pain and normal knee radiography, 88% of individuals had at least one osteoarthritis tissue lesion in the knee on magnetic resonance imaging (MRI). MRI can visualize the true three-dimensional multitissue joint pathology of osteoarthritis (Fig. 19.9.2) and these MRI-detected structural changes (Table 19.9.3) are more closely associated with patient symptoms. Ultrasound also has the capacity to acquire 3D images and, for example, has been shown to detect many more osteophytes than conventional radiography in hand osteoarthritis. These modern imaging studies highlight that many of our concepts and definitions of osteoarthritis have been based on an inaccurate imaging phenotype. Therefore there is currently no generally agreed-upon ‘gold standard’ for defining cases of osteo- arthritis, and its epidemiology varies according to the definition of clinical osteoarthritis for any specified joint. Early osteoarthritis The concept of early osteoarthritis is imprecisely defined. Incident radiographic osteoarthritis has provided one operational concept of early disease. However, both structural changes and symptoms precede the incidence of radiographic osteoarthritis. As mentioned, at least one structural lesion of knee osteoarthritis is present on MRI of people over 50 years without radiographic osteoarthritis or knee pain. By the time knee radiographic osteoarthritis is detect- able, 10% of knee hyaline articular cartilage is lost. The incidence of knee radiographic osteoarthritis is preceded by prodromal symp-toms of pain on twisting or pivoting and pain on standing by 39 and 25 months respectively. Pain on stair climbing appears to be the first mechanical symptom to manifest among knees with

radiographic osteoarthritis and at risk of this condition. It is very likely that problems such as isolated cartilage de- fects and meniscal tears are early structural lesions that progress to clinical osteoarthritis, though these are not currently classi- fied as early osteoarthritis. Compositional measures using special Table 19.9.1 Kellgren Lawrence grade Kellgren Lawrence grade Features Grade 0 No radiographic features of osteoarthritis Grade 1 Doubtful joint space narrowing Possible osteophytic lipping Grade 2 Possible joint space narrowing Definite osteophytes Grade 3 Multiple osteophytes Definite joint space narrowing Some sclerosis Possible deformity of bone contour Grade 4 Large osteophytes Marked joint space narrowing Severe sclerosis Definite bone deformity Reprinted with permission from Demehri et al. (2015). Conventional and novel imaging modalities in osteoarthritis: current state of the evidence. Curr Opin Rheumatol, 27(3), 295–303. Table 19.9.2 American College of Rheumatology radiological and clinical criteria for osteoarthritis of the knee and hip and hand Hand (clinical) Osteoarthritis if 1, 2, 3, 4 or 1, 2, 3, 5 are present: 1 Hand pain, aching, or stiff ness for most days of previous month 2 Hard tissue enlargement of two or more of ten selected jointsa 3 Swelling in less than three metacarpophalangeal joints 4 Hard tissue enlargement of two or more distal interphalangeal joints 5 Deformity of two or more of ten selected hand jointsa Hip (clinical and radiographic) Osteoarthritis if 1, 2, 3 or 1, 2, 4 or 1, 3, 4 are present: 1 Hip pain for most days of previous month 2 Erythrocyte sedimentation rate of less than 20 mm in the first hour 3 Femoral or acetabular osteophytes on radiographs 4 Hip joint space narrowing on radiographs Knee (clinical) Osteoarthritis if 1, 2, 3, 4 or 1, 2, 5 or 1, 4, 5 are present: 1 Knee pain for most days of previous month 2 Crepitus on active joint motion 3 Morning stiffness lasting 30 min or less 4 Age 38 years or older 5 Bony enlargement of the knee on examination Knee (clinical and radiographic) Osteoarthritis if 1, 2 or 1, 3, 5, 6 or 1, 4, 5, 6 are present: 1 Knee pain for most days of previous month 2 Osteophytes at joint margins on radiographs 3 Synovial fluid typical of osteoarthritis (laboratory) 4 Age 40 years or older 5 Crepitus on active joint motion 6 Morning stiffness lasting 30 minutes or less a Ten selected joints include bilateral second and third interphalangeal proximal joints, second and third proximal interphalangeal joints, and first carpometacarpal joint. Fig. 19.9.1 Radiograph of knee osteoarthritis.

 MRI sequences can demonstrate glycosaminoglycan loss before ‘standard’ MRI can detect morphological changes, so substantial evolution of the concept and alternative definitions of ‘early’ osteo- arthritis are required. Inflammatory osteoarthritis Clinical osteoarthritis is not considered to be a classical inflam- matory arthritis because of features including a relative pau- city of neutrophils in synovial fluid, a lack of subchondral bone erosions, and no evidence of systemic inflammation or features of autoimmunity; these features are used to distinguish osteo- arthritis from the archetypal inflammatory arthritis, rheumatoid arthritis (RA). Clinicians may refer to inflammatory osteoarthritis as the discrete very swollen joints seen in some patients with hand osteoarthritis, but it is likely that there is much more widespread synovitis than is appreciated clinically. Modern imaging with its more accurate detection of synovial hypertrophy and effusion has changed our understanding of the frequency of inflammation in osteoarthritic joints. Using contrast-enhanced MRI, extensive synovitis is preva- lent in most knees (>85%) and hands (68%) with established osteo- arthritis that meet the respective osteoarthritis joint criteria (Table 19.9.2). Erosive osteoarthritis refers to a group of patients with radio- graphic erosions, and the term is often used synonymously with inflammatory osteoarthritis (though not all osteoarthritis inflam- mation is associated with erosions). The overall prevalence of erosive osteoarthritis is unclear, and the prevalence of erosions varies somewhat according to their definition and the imaging modality employed for detection. In two cohorts of women selected for erosive hand radiographic osteoarthritis, erosions were identified in 17–18%,

35%, and 61% of small joints using conventional radiography, ultrasonography, and MRI, respectively. When defined radiographically, erosive hand osteoarthritis appears to have a greater association with obesity, hypertension, dyslipidaemia, and the metabolic syndrome relative to nonerosive hand osteoarthritis. Generalized osteoarthritis An imprecisely defined phenotype is where multiple osteoarth- ritis joints are present in an individual, which may be referred to as generalized or polyarticular osteoarthritis. It is well recog- nized that a history of hand osteoarthritis confers an increased risk of hip and knee osteoarthritis, a history of knee osteoarthritis confers a higher risk of hip osteoarthritis, and vice versa. These associations are independent of confounding factors of age, gender, and body mass index (BMI). Generalized clinical osteoarthritis also confers a greater risk of knee osteoarthritis structural progression. Generalized osteoarthritis has been more frequently observed in women than men and with increasing age, and is associated with poorer function, disability, quality of life, and mortality than osteoarthritis involving fewer joints. Whether generalized osteo- arthritis reflects an accumulation of adverse biomechanical en- vironments in adjacent joints, or load compensation from other joints, or systemic factors such as genetic tendency or obesity, is not well understood. Fig. 19.9.2 MRI-detected multitissue pathologies of knee osteoarthritis. Reprinted by permission from Macmillan Publishers Ltd: Nature Reviews Rheumatology. Wenham CYJ and Conaghan PG (2009). Imaging the painful osteoarthritic knee joint: what have we learned? Volume 5, 149–158, copyright 2009.
Table 19.9.3 The prevalence of MRI-detected tissue lesions in knee osteoarthritis General MTF LTF PF Presence of crepitus 180 (70.5%) 44 (17.3%) 48 (18.7%) 173 (67.9%) Cartilage damage 221 (86.5%) 178 (69.8%) 151 (59.1%) 179 (70.1%) Osteophytes 133 (52.0%) 95 (37.1%) 90 (35.3%) 102 (39.9%) Medial meniscal damage 111 (43.7%) 95 (37.3%) – – Lateral meniscal damage – 30 (11.9%) – Cruciate pathology 23 (9.2%) – – – MCL pathology 48 (18.7%) 48 (18.7%) – – LCL pathology 0 (0%) – 0 (0%) – MCL/LCL, medial and lateral collateral ligaments of the knee; MTF/LTF /PF, medial tibiofemoral/lateral tibiofemoral/patellofemoral Reprinted from Crema MD et al. (2011). The association of magnetic resonance imaging (MRI)-detected structural pathology of the knee with crepitus in a population-based cohort with knee pain: the MoDEKO study. Osteoarthritis and Cartilage, 19(12), 1429–1432. Copyright 2011, with permission from Elsevier.

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