Identifying and Treating Preclinical and Early Osteoarthritis

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KEYWORDS

• Osteoarthritis • Knee pain • Magnetic resonance imaging • Biomarkers

KEY POINTS

- The limited efficacy of current nonsurgical treatments for osteoarthritis (OA) may be due partly to their use at a late point in the evolution of disease when structural deterioration is often advanced; this provides a rationale for identifying persons with early disease or those at high risk.
- Persons at especially high risk of later disease who would be good targets for treatment are those with sports-related major knee injuries, those with anatomic abnormalities of their hips associated with a high rate of later OA, and those from families with an unusually high risk of early disease.
- Chronic knee pain is a harbinger of knee OA.
- Evolving imaging approaches using magnetic resonance imaging hold promise in identifying joints with reversible structural findings that represent early lesions of OA.

INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis. Although prevalence estimates differ depending on the country and how disease is assessed, OA clearly affects millions of persons in the United States and a similar number in Europe. In developing countries it is also the most common form of arthritis. OA prevalence increases with age and with obesity, and the rapidly increasing demand for knee and hip replacements is due in part to the burgeoning population of those with OA because of the aging of the population and increasing rates of obesity. OA is the most common

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cause of mobility disability in the world, and its overall impact as a cause of years lived with disability and limited quality of life is rising.[1]

One of the central reasons for the increase in demand for knee and hip replacements is that medical and rehabilitative treatments for OA are not very effective. There are no treatments that have been shown consistently to delay the structural progression of disease, and none is approved by regulatory agencies for this purpose. Meta-analyses suggest that nonsurgical treatments such as exercise, anti-inflammatory medications, and others all have modest efficacy at best. New more effective treatments for established disease are badly needed.

One major reason why treatments are not delaying joint replacement surgery may be that treatment begins too late in the course of OA to have an effect. Many of the structural findings uncovered in recent comprehensive cohort studies of persons with knee OA have suggested that most persons with disease have advanced structural findings in the knee by the time they are clinically diagnosed, and have frequent knee pain. Varus or valgus malalignment, meniscal damage such as tears, and prevalent cartilage loss are all common features of middle-aged and older persons with new-onset chronic knee pain.[2] Radiographic evidence of OA is a relatively late phenomenon in the structural evolution of this disease. For example, alterations in the shape of the periarticular bones often precede the development of disease by 5 to 10 years radiographically.[3] Abnormalities seen on magnetic resonance imaging (MRI) are present several years before disease development in most cases. Many of these structural changes are not known to be reversible and, to the extent that they drive disease progression, a patient presenting with knee pain is often on the downslope of such a trajectory.

A recent focus on changes in the peripheral and central nervous system that develop as part of osteoarthritic pain suggests that nervous system–related changes have also occurred in many persons by the time they develop the chronic pain of OA. These changes in the nervous system make treatment more challenging and pain more severe than might have occurred had the disease been identified and treated earlier.[4]

Therefore, the rationale for focusing on early OA is that irreversible structural changes may not yet be established and that chronic nervous system sensitization to pain has not yet evolved. To target early OA, the choice might include those with early disease and those at high risk of disease who do not yet have symptoms or early disease.

The evolution of OA from the earliest evidence of joint injury to end-stage disease is shown in **Fig. 1**. Early osteochondral lesions are usually unaccompanied by symptoms in middle-aged and elderly persons. Even meniscal tears, which are common and occur incidentally, are often not associated with knee pain or other symptoms.[5] The initial defect in cartilage or initial meniscal tear or extrusion is followed by a constellation of features including more damage in the initial location leading to asymmetry of the joint and malalignment, bony remodeling, and damage to adjacent tissues.[6] For example, an incidental meniscal tear puts a knee at high risk of adjacent cartilage damage and of meniscal extrusion. There is tissue loss between the 2 bones and narrowing of the joint on that side, initially to a subtle degree that is not visible on the radiograph. First symptoms occur only after this process is far advanced, and are mild and intermittent. The patient usually does not seek care until symptoms including pain are more troublesome or frequent. By the time symptoms are present, roughly 80% of knees have clinically important frontal plane malalignment (varus or valgus) and even knees without frontal plane malalignment often have patellofemoral malalignment. This malalignment increases stress or focal loading across the affected region of the joint. Cartilage loss and/or meniscal damage is the rule.[7]