

Early knee osteoarthritis management should first address mechanical joint overload

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Abstract

Early knee osteoarthritis poses a therapeutic dilemma to the musculoskeletal clinician. Despite the recent interest in arthroscopic and injectable regenerative therapies intended to repair or restore a focal target such as cartilage, meniscus, or subchondral bone, none have been shown to slow disease progression. A likely cause of these disappointing treatment outcomes is the failure to address chronic and excessive loading of the knee joint. A growing body of evidence suggests that first-line therapies for early knee osteoarthritis should emphasize unloading the knee joint since any potential therapeutic benefit of regenerative therapies will likely be attenuated by excessive mechanical demand at the knee joint. Minimally invasive medical devices such as patient-specific interpositional implants and extracapsular joint unloading implants are currently in development to address this clinical need.

Early knee osteoarthritis management

The diagnosis of knee osteoarthritis (OA) is based on a combination of radiographic and clinical criteria.¹ Using this standard classification system, identification of patients with early OA proved difficult and studies to address this population were not feasible given the reliance on plain x-rays as the sole imaging tool. Recently, a more comprehensive classification system allowing other methods of structural assessment such as arthroscopy and MRI was proposed to allow identification of patients with early knee OA.² These criteria define early knee OA as the presence of at least two episodes of knee pain lasting 10 or more days in the last year, Kellgren-Lawrence grade of 0, I, or II, and either arthroscopic confirmation of cartilage lesions or magnetic resonance imaging findings demonstrating articular cartilage

degeneration and/or meniscal degeneration, and/or subchondral bone marrow lesions.

Despite the development of these new diagnostic criteria, the patient with early knee OA still poses a therapeutic dilemma to the musculoskeletal clinician. On one hand, traditional nonsurgical OA therapies have limited clinical utility since the treatment effect on disease-specific symptom relief is low.³ Long-term treatment adherence is a concern given the mild and sporadic nature of early knee OA symptoms. On the other hand, consideration for invasive surgeries such as arthroplasty and high tibial osteotomy is unwarranted until the disease progresses to moderate or end-stage, a process that may take years or decades. In the period between initial diagnosis and definitive surgical management, patients may be prescribed numerous nonsurgical management strategies, either alone or concomitantly. Although pharmacological therapy improves knee OA symptoms in many cases, no nonsurgical treatment has been shown to slow disease progression.³ Paradoxically, conservative therapies may actually encourage OA progression in responders since patients may become more physically active, leading to higher peak adduction moments across the knee joint.^{4,7} Over 80% of orthopedic surgeons agreed that better treatment alternatives are needed in younger OA patients in which arthroplasty is not indicated, and over 2 in 3 perceived a treatment gap for early knee OA.⁸ Clearly, the current approach to knee OA treatment, including early knee OA, is often ineffective. Therapies should be targeted to specific disease phases that not only alleviate symptoms, but also address the underlying etiology.

Arthroscopic and injectable regenerative therapies intended to repair or restore a focal target such as cartilage, meniscus, or subchondral bone have demonstrated limited clinical usefulness to date for several reasons. First, early knee OA is not a focal disease but, instead, affects the entire joint including articular cartilage, the menisci, periarticular muscles, ligaments, subchondral bone, and synovial membrane.^{9,10} Second, targeted tissue repair or regeneration likely will not overcome the deleterious effects of chronic biomechanical abnormalities of the knee joint, which is the strongest modifiable risk factor for knee OA development and progression.¹¹⁻¹⁴

Following this logic, a first-line therapy for the patient with early knee OA should focus on chronically unloading the knee joint before any attempts are made at tissue regeneration or repair. Experimental regenerative approaches that involve use of juvenile cartilage, scaffolds and various polymeric matrices are unable to generate normal hyaline cartilage that can adequately integrate with host tissue and sustain physiological biomechanical loads.¹⁵ Additionally, the disorganized structural organ-

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Key words: joint loading, knee, osteoarthritis.

Contributions: LM, JB conceived and designed the research; LM wrote the first draft of the manuscript; EA, JB contributed to the writing of the manuscript; EA, LM, JB agree with manuscript results and conclusions; EA, LM, JB jointly developed the structure and arguments for the paper; EA, LM, JB made critical revisions and approved final version.

Conflict of interests: LM and JB received financial support from Moximed, Inc. (Hayward, CA, USA).

Received for publication: 21 November 2013.
Revision received: 30 January 2014.
Accepted for publication: 10 February 2014.

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Orthopedic Reviews 2014; 6:5188
doi:10.4081/or.2014.5188

ization of the regenerated tissue remains highly susceptible to injury and does not prevent enlargement of the defect in the host cartilage. Consequently, any potential therapeutic benefit of regenerative therapies for early knee OA will likely be attenuated by excessive mechanical demand that exceeds the ability of the joint to repair itself.

Although little direct evidence for the influence of joint loading on the efficacy of regenerative therapies is available, this hypothesis is supported by others.^{11,13,16-18} Mazzuca *et al.*¹⁷ conducted a *post hoc* analysis of a randomized controlled trial investigating the influence of doxycycline or placebo on medial joint narrowing in obese women with knee OA. While doxycycline slowed the rate of medial joint space narrowing by 33% at 30 months, the treatment effect was negated in patients with varus alignment.

Unloading the knee of excessive forces may slow,^{12,19} or potentially reverse,²⁰ OA progression, negating the need for regenerative therapy.²⁰ Nonsurgical treatments such as wedged sole insoles, knee braces, weight loss, and muscular strength training reduce knee joint loading and may alleviate OA symptoms; however, these treatments rarely achieve long-term symptomatic control.³

Two recent systematic reviews of lateral wedged insoles reported no improvement in pain or function when compared to neutral or

no wedge control conditions in patients with medial knee OA.^{21,22} A Cochrane review concluded that there is limited evidence to support the use of knee braces and orthoses in knee OA.²³ A review of 193 randomized controlled trials of exercise interventions concluded that there is low-strength evidence that only a few of the included interventions were effective in controlling knee pain secondary to OA.²⁴

Although aggressive surgical options such as arthroplasty and high tibial osteotomy are rarely considered in this patient population, 4 in 5 orthopedic surgeons would be willing to consider surgery in the early OA patient if the procedure were reversible and recovery was minimal.⁸ Minimally invasive implants that meet these specific requirements are currently in development. Patient-specific interpositional implants inserted into the joint space utilize the concept of functional fixation by use of an implant intended to redistribute joint loading forces in patients with unicompartmental disease. Early generations of this device were plagued by high rates of implant dislocation and revision surgery.²⁵⁻²⁸ Newer generation implants appear to adequately achieve neutral axis correction and alleviate disease-specific symptoms although revision rates of 20% remain a concern.^{29,30} Extra-capsular (non-articular) medial compartment knee load absorber implants fixed to the medial distal femoral cortex and the medial proximal tibial cortex to achieve offloading of the medial compartment are under evaluation.^{31,32} A recent series of patients with Kellgren-Lawrence grade I or II knee OA treated with this joint unloading implant and followed for at least 1 year reported a 70% decrease in WOMAC Pain, a 68% decrease in WOMAC Function, and a 59% decrease in WOMAC Stiffness scores.^{33,34} The premise of these implants is that the device is surgically implanted via a minimally invasive incision, the joint remains fully intact, the procedure is reversible, and the medial knee compartment is unloaded sufficiently to reduce pain and improve joint function. With continued implant refinements and longer term follow-up data suggestive of safety and efficacy, it is plausible that minimally invasive implants intended to redistribute excessive joint loading may become first-line therapies in the patient with early knee OA. Although these intriguing technologies remain in development, their theoretical underpinnings are quite mature.

Conclusions

In conclusion, nonsurgical attempts to alter the course of early OA will likely be futile unless the aberrant biomechanical environment at the knee is first addressed. Arguably, the concerted research effort to identify novel

knee OA treatments should be redirected towards modifying chronic joint overload instead of addressing focal targets such as chondral defects.

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