SMART Approach

Personalizing the Management of Knee Osteoarthritis

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1. Introduction

Knee osteoarthritis (OA) is common, debilitating, and heterogeneous in clinical presentation, making a personalized approach essential. In 2020, an estimated 595 million people globally (7% of the population) live with OA with the knee being affected in ~50% of cases.[1,2] From 1990 to 2020, OA ranked as the 14th highest cause of age-adjusted years lived with disability.[2] In addition to considerable economic impact[1], knee OA profoundly affects quality of life, through functional impairment and pain.[3] Clinically, knee osteoarthritis presents as pain, particularly with weight bearing, and stiffness in the morning or with prolonged sitting that improves within 30 minutes.[4] Randomized clinical trials have shown that multiple treatments are efficacious, including physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs), duloxetine, joint injections, and joint replacement.[4] However, there is considerable heterogeneity in clinical presentation, impact, and course of knee OA.[5-9] Moreover, the current "trial-and-error" management of knee OA focuses primarily on joint pathology, neglecting amplifying pain processing in the nervous system and psychosocial mechanisms. Personalizing treatment selection by identifying relevant mechanisms in each patient and incorporating treatments that address these mechanisms holds promise for improvement of knee OA management.

2. Key Points

- Although historically defined by cartilage degeneration, knee osteoarthritis pain and functional impairment only moderately correlate with radiographic findings.
- Heterogeneity at the level of the joint, nervous system, cognition, coping strategies and social determinants of health influence knee pain and functional impairment.
- The degree of amplifying pain processing may explain some heterogeneity in clinical presentation.
- Identifying mechanistically-relevant heterogeneity through surveys, quantitative sensory testing, wearable devices, and noninvasive imaging shows promise but requires further research.

3. Background and State of the Science

Knee osteoarthritis is characterized by micro- and macroscopic joint tissue injury, maladaptive repair responses, and complex anatomic and physiological changes associated with cartilage degradation, bone remodeling, osteophyte formation, and inflammation, ultimately leading to "joint failure" which *can* lead to pain and disability.[10] Implicit in this definition is that even with structural evidence of joint failure, patients experience a range of pain and functional impairment. Radiographic osteoarthritis only moderately correlates with these outcomes. It is likely that this heterogeneity arises from variation at multiple mechanistic levels. Complexity at the level of the joint contributes to patient-to-patient heterogeneity, including the degree and pattern of cartilage degeneration, synovial inflammation, and bone marrow lesions.[11-13] Amplified pain processing in the pain-sensing nervous system is associated with worse pain and functional impairment.[14,15] Large observational studies have identified population heterogeneity in pain amplification using quantitative sensory tests.[16,17] Cognitive and affective factors including expectations about pain and treatment responses[18], pain catastrophizing[19,20], fear of movement[20-22], depression[20], and anxiety[20] contribute to knee pain, functional impairment, and treatment responses. Social function and interaction also impact pain and impairment.[23,24] Socioeconomic factors associated with worse pain and functional impairment include educational attainment, economic status, and racialized identity.[20]

Abbreviations used in this paper: OA, osteoarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; PT, physical therapy.

Keywords: chronic pain, musculoskeletal pain, pain management, knee osteoarthritis

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Although many conceptualize knee osteoarthritis as a joint-level disease with pain and functional impairment as a consequence, it is likely that the biopsychosocial factors play key roles in the joint pathophysiology with positive feedback loops worsening joint pathophysiology. For example, worse pain is associated with worse ambulatory function which is associated with worse radiological outcomes.[4] These complex loops have implications for treatment as well. Physical therapy (PT) is a first-line treatment for knee OA thought to maintain function and improve outcomes.[4] However, like many knee OA treatments, only a subset of patients benefit.[25,26] Additionally, knee pain can limit participation in PT with worse outcomes in those who drop out early in a treatment course.[27-29] One might predict that weight loss would improve pain by reducing joint load and affecting structural aspects of the joint. However, a large prospective study found that pain sensitization and depression were improved rather than radiographically-identified joint lesions.[30] The success of joint replacement also appears to depend not only on joint degenerative change but also on biopsychosocial factors outside the joint, including immune, neurobiological, psychological, and social factors.[31-34] Although current research strongly implicates "whole-person" biopsychosocial factors in knee osteoarthritis, the relative importance of each factor for a given patient and whether tailored treatment plans based on comprehensive biopsychosocial assessments are superior to current practice requires further research.

4. Current practice: "How I do it"

For a given patient presenting with knee osteoarthritis, it becomes important to assess biopsychosocial factors comprehensively in addition to joint assessments. Joint assessments should rule out inflammatory arthritis, crystalline arthritis, and soft tissue lesions.[4] Comprehensive "whole-person" assessments are routinely done with any new patient. However, it is important to specifically assess for common comorbidities that contribute to the varied presentation of knee OA, including mood disorders and obesity for example. Patient-reported outcomes can be used to assess multiple biopsychosocial domains, even in a busy clinical environment. Computerized multidomain assessments can be administered prior to the clinical encounter in the waiting room, be reviewed by clinicians prior the visit, and guide treatment discussions. Although objective measures of pain amplification may play a future role, currently pain sensitization may be assessed by history (e.g. multiple pain comorbidities, widespread pain), exam (e.g. "pain out of proportion" to palpation or exam maneuver), or even pain characteristics. For example, knee OA patients who report neuropathic pain quality, e.g. "burning" or "tingling," on the PainDETECT questionnaire had neurobiological evidence of pain amplification which was associated with worse outcomes after knee replacement.[35] Therefore, in patients without pain sensitization, joint-focused treatments may be sufficient, such as conventional PT or NSAIDs. If these fail, then more invasive treatments may be considered, including injections and knee replacement. However, in those with evidence of pain sensitization, duloxetine may be considered prior to invasive treatments.

5. Future Directions

Comprehensive biopsychosocial data will be increasingly available and actionable for the management of knee osteoarthritis. Research tools include noninvasive imaging of both the joint and nervous system[36-38], wearable devices to track activity and physiologic responses[39,40], and objective sensory assessments to identify sensitization.[15,41] Large prospective datasets, such as the Acute to Chronic Pain Signatures study, will help focus attention on pathophysiologic heterogeneity relevant to important clinical outcomes, like chronic pain after joint replacement.[42] It is also likely that learning health systems will integrate some of these comprehensive assessments and, through data analytics, provide decision support to clinicians and patients considering invasive treatments for knee osteoarthritis.[43] Overall, the research reviewed above highlighting biopsychosocial heterogeneity in knee OA helps explain variation seen in the clinic between patients with apparently similar looking knee imaging. Comprehensive assessments can help clinicians and patients choose treatments that are likely to help them. Future work will provide greater certainty in these predictions, truly personalizing knee OA management.

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