

Quality of Life in Patients with Knee Osteoarthritis: A Commentary on Nonsurgical and Surgical Treatments

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Abstract: Knee osteoarthritis (OA) has a significant negative impact on health-related quality of life (HRQoL). Identification of therapies that improve HRQoL in patients with knee OA may mitigate the clinical, economic, and social burden of this disease. The purpose of this commentary is to report the impact of knee OA on HRQoL, describe the change in HRQoL attributable to common knee OA interventions, and summarize findings from clinical trials of a promising therapy. Nonsurgical therapies do not reliably modify HRQoL in knee OA patients given their general inability to alleviate physical manifestations of OA. Surgical knee OA interventions generally result in good to excellent patient outcomes. However, there are significant barriers to considering surgery, which limits clinical utility. Therapies that most effectively control OA-related pain with a low risk:benefit ratio will likely have the greatest benefit on HRQoL with greater rates of patient adoption. Initial clinical trial findings suggest that less invasive joint unloading implants hold promise in bridging the therapeutic gap between nonsurgical and surgical treatments for the knee OA patient.

Keywords: Intervention, knee, osteoarthritis, pain, quality of life, unloading.

INTRODUCTION

Chronic musculoskeletal conditions are prevalent worldwide and their impact on the individual is significant. At any given time, 30% of American adults are affected by joint pain, swelling, or limitation of movement [1]. Osteoarthritis (OA), particularly at the knee, is a leading cause of disability in older adults [2] characterized by progressive articular cartilage loss resulting in joint pain and disability [3]. By 2025, the prevalence of knee OA is expected to increase by 40%, largely due to an aging population and the obesity epidemic [1]. The burden of knee OA on individuals, health systems, and social care systems is considered by many as a public health crisis [4].

Limitations in walking, stair climbing, and squatting are common patient complaints that greatly interfere with activities of daily living and recreation. Consequently, most research on knee OA has attempted to quantify the magnitude of physical disability associated with this disease and the impact of various treatments on outcomes such as pain severity and physical functioning. However, the physical manifestations of knee OA have directly impact on other aspects of patient's lives such as social interactions, mental functioning, and sleep quality [5]. Therefore, health-related quality of life (HRQoL) measures are relevant and important adjunct outcomes that help quantify the physical, social, and emotional impact of knee OA and of various OA therapies.

HRQoL is generally considered to comprise five main dimensions including physical functioning, psychological functioning, social functioning, cognitive functioning, and general well-being [6]. Explicit in the framework of HRQoL is the evaluation of functional status as well as patient perceptions of emotional and social functioning and role activities. This concept is critical since patients vary greatly in their responses to identical stressors, such as pain. Not only does HRQoL offer a more holistic approach to quantifying patient experiences compared to isolated, disease-specific outcomes, but HRQoL measures also have direct relevance to clinical practice since they are highly predictive of mortality and health care resource utilization [7-9].

Compared with other chronic diseases, patients with musculoskeletal disorders report among the lowest HRQoL, with knee OA patients reporting lower scores on every HRQoL parameter compared to age-matched norms [10]. Not surprisingly, HRQoL progressively declines in knee OA patients, concomitant with the magnitude of disease progression [11, 12]. Identification of therapies that improve HRQoL in patients with knee OA may mitigate the clinical, economic, and social burden of this disease. The purpose of this commentary was to report the impact of knee OA on HRQoL, describe the change in HRQoL attributable to common knee OA interventions, and summarize findings from clinical trials of a promising therapy.

HRQOL IN KNEE OSTEOARTHRITIS PATIENTS

A large body of evidence substantiates lower HRQoL scores in knee OA patients compared to age-matched norms. Increasing joint pain comorbidity [12] and radiographic

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disease severity [13] are inverse related to HRQoL in knee OA patients. As the disease progresses, HRQoL declines to levels significantly below that of the general population. Desmeules *et al.* [14] reported mean Physical Component Summary (PCS) and Mental Component Summary (MCS) scores from the SF-36 of 28 and 43, respectively, in 197 patients waiting for total knee arthroplasty (TKA); both of these values are well below the 25th percentile compared to age- and gender-matched normative values [15]. Other studies have reported similarly low HRQoL in patients waiting for TKA [11, 16]. Notably, within a group of patients waiting for TKA who already report very low HRQoL, nearly 3 in 4 reported continued worsening in HRQoL during the mean 10-month waiting period before surgery [17]. Even more concerning is that since less than one-third of patients with severe knee OA are willing to undergo arthroplasty [18], it is reasonable to assume that most patients with severe knee OA suffer low HRQoL throughout the remainder of life.

EFFECT OF NONSURGICAL INTERVENTIONS ON HRQOL

The effectiveness of nonsurgical knee OA interventions in alleviating pain and improving joint function is generally unsatisfactory and transient [19]. Concomitant with the lack of meaningful change in self-reported symptoms, HRQoL changes with nonsurgical treatment are modest. Consequently, there is a growing consensus that most nonsurgical knee OA treatments are misguided [19]. Although the etiology of knee OA is multifactorial, chronic aberrant and excessive knee joint loading are arguably the primary risk factors [20, 21]. In general, conservative therapies that fail to address the underlying mechanism of disease have poor efficacy and those that do impact joint loading biomechanics are associated with poor long-term patient adherence.

Regular physical activity, especially low-impact aerobic exercise and quadriceps strengthening programs, are strongly encouraged in the knee OA patient [22]. Despite this recommendation, the evidence supporting physical activity participation on improving HRQoL is limited, variable, and highly dependent on the exercise modality. Bennell and colleagues [23] reported that HRQoL was no different in patients undergoing a 12-week multi-modal physiotherapy program compared to those receiving sham ultrasound. Brosseau and colleagues [24] randomized knee OA patients to walking with behavior intervention, walking with an educational pamphlet, or pamphlet alone. No changes in HRQoL were observed in any of these groups during the 1-year intervention period. Evcik and Sonel [25] reported greater HRQoL improvements with a 3-month group walking program compared to home-based exercise, despite the fact that pain and function scores were similar between the groups. The components of HRQoL attributable for the global HRQoL improvement in the walking group included sleep quality, emotional reactions, physical mobility, and energy. Kao and coworkers [26] reported no changes in HRQoL with self-management consisting of patient education and exercise or usual care for 8 weeks. However, a similar 6-month disease-specific self-management program improved HRQoL 15-20% in domains related to pain and physical function [27]. Tai chi has been reported to modestly

(20%) improve PCS, but not MCS scores [28, 29]. Finally, yoga therapy has consistently been shown to improve physical and emotional HRQoL parameters [30]. Overall, physical activity programs appear to, at best, modestly improve physical domains of HRQoL with minimal impact on the mental domains in knee OA patients. The efficacy of physical activity on HRQoL in patients with knee OA may be limited by the well-known problem of poor adherence to exercise programs in this patient population [31].

Oral analgesic and anti-inflammatory agents are perhaps the most commonly prescribed treatments to alleviate knee OA symptoms with almost 3 in 4 patients reporting regular use [32]. Despite this widespread use, the clinical effectiveness of these agents is limited [33]. Short-term administration of rofecoxib [34], celecoxib [35], and lidocaine patch [35] has yielded variable results on HRQoL. No known studies have examined HRQoL with long-term use of analgesics or non-steroidal anti-inflammatory drugs. The study with the longest follow-up duration reported that analgesic use had no impact on PCS or MCS through 1 year of use [36]. Regular use of these agents has no impact on disease progression and, in fact, they may accelerate OA progression due to higher resulting forces across the knee joint [37-40]. Therefore, their long-term benefit on HRQoL is doubtful.

Lateral wedge insoles and varus- or valgus-knee braces are mainstay first-line treatments in the physician's armamentarium of OA therapies. Although the premise behind redistributing the forces about the knee joint is sound, the clinical utility of these therapies is limited mainly by patient discomfort and resulting poor adherence to therapy. Neither lateral wedge insoles [41-44] nor knee bracing [45, 46] provides demonstrable clinical benefit on knee pain or disease progression. Bennell and colleagues [44] reported that HRQoL was no different in patients with lateral wedge insoles compared to those receiving flat control insoles. Skou and coworkers [47] were able to demonstrate modest HRQoL improvements, but only after excluding the almost 20% of patients who withdrew from the study. Brouwer *et al.* [48] randomized 117 patients with knee OA to a knee brace and standard of care or standard of care alone. These authors reported that the addition of the knee brace had no effect on HRQoL. The totality of evidence on these joint off-loading therapies is not supportive of their use either to relieve symptoms or to improve HRQoL, with patient compliance issues likely limiting the responsiveness of these outcomes.

The use of viscosupplementation in knee OA treatment generally improves HRQoL parameters, although the clinical effects generally subside after 3 to 6 months. Maheu *et al.* [49] reported 27% improvements in PCS, but only 4% improvements in MCS at 24 weeks following hyaluronic acid injection. Most studies of viscosupplements have reported modest changes in selected components of HRQoL (mainly physical), but not in global scores [50]. Although patients may undergo repeat injections in an effort to maintain tolerable pain levels and acceptable HRQoL, the beneficial impact of viscosupplements on HRQoL decreases with repeated injections [51]. Additionally, the changes in functional pain scores with viscosupplementation do not correlate to quality of life scores [50]. Similar to findings

with acetaminophen and NSAIDs, hyaluronic acid injections may actually increase knee joint loading and accelerate joint deterioration due to short-term pain amelioration [37]. Finally, the safety of HA injections has recently been questioned [52]. Overall, hyaluronic acid injections are ineffective in durably increasing HRQoL in the knee OA patient.

EFFECT OF SURGICAL INTERVENTIONS ON HRQOL

Surgical repair of symptomatic knee OA is widely utilized, with over 600,000 cases performed annually in the US [53]. High tibial osteotomy (HTO), unicompartmental knee arthroplasty (UKA), and TKA each reliably restore physical function and alleviate pain [54]. Additionally, the HRQoL improvements observed following these surgeries are similarly impressive. Several studies have reported HRQoL increases of at least 100% through 2 to 7 years following TKA, UKA, or HTO [16, 55-60]. However, some suggest that postoperative HRQoL improvements following TKA are not durable, with declines identified around 3 years post-surgery [61].

A major and often overlooked consideration when evaluating OA therapies is patient willingness to undergo a particular treatment, regardless of therapeutic value. For example, TKA is well-known to substantially improve OA-related pain and function in a cost effective manner [62]. However, less than one-third of TKA candidates are actually willing to undergo the surgery [18], due in large part to lack of confidence in beneficial surgery outcomes and high operative risk due to presence of multiple comorbidities [18]. Additionally, each of these surgical options permanently modifies the knee joint *via* an invasive, irreversible surgical procedure, which may also negatively impact patient willingness to undergo these procedures.

FUTURE DIRECTIONS

For unicompartmental knee OA, the optimal surgery would result in similar safety and effectiveness outcomes as HTO and arthroplasty, but would also enjoy high patient acceptance rates, thereby allowing greater utilization by symptomatic patients. The most common unicompartmental knee OA presentation is medial typically associated with varus alignment. Extra-capsular medial compartment knee load absorber implants that require only two incisions for implant are currently under evaluation (Fig. 1). Three clinical trials have been completed with these implants, with each reporting impressive improvements in HRQoL. The OASYS study (ACTRN12608000451303) treated 30 patients with this knee joint unloading implant. At 3 years, PCS increased from 36 ± 9 at pre-treatment to 52 ± 5 ($p < 0.001$), a value higher than age-matched norms and comparable to values seen following TKA. No changes in MCS were noted (56 ± 8 at baseline and at 3 years). The OAKS study ($n=30$) (ACTRN12609001068257) reported KOOS QOL domain scores improvements from 20 ± 18 to 52 ± 18 ($p < 0.001$) at 1 year. These results were confirmed in the COAST study of 40 patients (ISRCTN63048529), which demonstrated improvements in the KOOS QOL domain 1 year following treatment from 22 ± 15 to 51 ± 23 ($p < 0.001$). Importantly, these KOOS HRQoL changes well exceeded the minimal clinically important difference of 21 points

established for knee OA patients [63] and were at least comparable to HRQoL changes observed with TKA, UKA, and HTO. Larger-scale clinical trials with these joint unloading implants are required, but initial results are promising and suggest utility in improving HRQoL in knee OA patients.

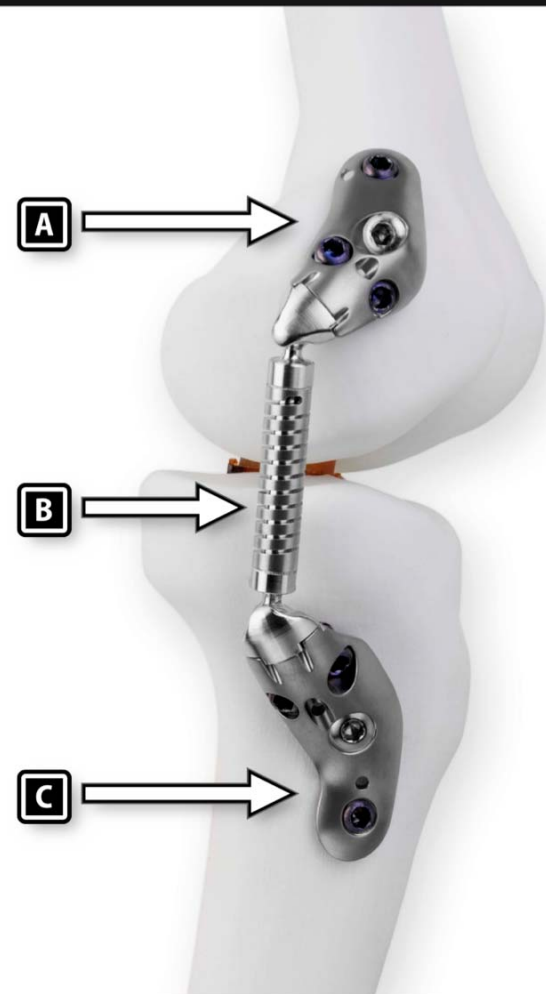


Fig. (1). Medial view of an extra-capsular medial compartment knee load absorber implant. a) femoral base, b) absorber unit, c) tibial base.

CONCLUSIONS

A primary objective of health and medical care is to enhance quality of life, independent of alleviating disease-related symptoms. The evaluation of new therapeutic interventions for knee OA requires a thorough understanding of the impact of a treatment on a patient's physical, social, and psychological status. Therapies for knee OA should ideally decrease pain, improve physical functioning, and increase HRQoL in a safe and durable manner. The failure of nonsurgical therapies to modify HRQoL in knee OA patients is not surprising given their inability to alleviate physical manifestations of OA. Surgical knee OA interventions generally result in good to excellent patient outcomes. However, there are significant barriers to considering surgery, which limits clinical utility. Since the strongest correlate of global measures of HRQoL in the OA patient is pain severity [64], therapies that most effectively control

OA-related pain while imparting no negative consequences (e.g. high cost, side effects, invasive surgery, etc.) will likely have the greatest benefit on HRQoL with greater rates of patient adoption. Less invasive joint unloading implants hold promise in bridging this therapeutic gap for the patient with medial compartment knee OA.

CONFLICT OF INTEREST

LEM and JEB are consultants to Moximed, Inc. (Hayward, CA, USA).

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