Non-operative treatment options for knee osteoarthritis

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Background: Knee osteoarthritis (OA) is a prevalent and debilitating condition for which a wide range of non-surgical treatment options are available. Although there is plethora of literature investigating their safety and efficacy, for many treatment modalities, a consensus has not yet been reached concerning efficacy. Therefore, it is essential for practitioners to understand the risks and benefits of the available treatments for the successful management of knee OA. This study explored the efficacy of non-surgical treatment options for knee OA including: (I) non-steroidal anti-inflammatory drugs (NSAIDs); (II) weight loss; (III) intra-articular injections; (IV) physical therapy; and (V) bracing.

Methods: A comprehensive literature review of studies between 1995 and 2018 was conducted using the electronic databases PubMed and EBSCO Host. Searches were performed using the following terms: total knee arthroplasty (TKA); cyclooxygenase-2 inhibitors; bracing; physical therapy; weight loss; knee; treatment; therapeutics; OA; intra-articular injection; hyaluronic acid; corticosteroid; and alternatives. The initial search yielded 7,882 reports from which 545 relevant studies were identified. After full-text analysis, 43 studies were included for this analysis.

Results: NSAIDs are most effective when used continuously and may be used in conjunction with other forms of treatment for knee OA as they have been shown to provide some pain relief as well as functional improvements. Weight loss is a safe and effective way to improve knee pain, function, and stiffness without adverse effects. However, it can be very challenging for obese patients with knee OA due to their limited mobility and lack of adherence to a low-calorie diet. Intra-articular injections have had mixed results, with findings from recent studies indicating long-term outcomes to be equivocal. Physical therapy leads to significant improvements in pain and function. Decreased compliance with physical therapy is thought to be due to high copayments, pain with activities, lacks of transportation, and high time commitments. Brace modalities have demonstrated significant pain and functional improvements and prolongations of the time to TKA. Additionally, they limit the need for other treatment modalities which are associated with greater risks.

Conclusions: NSAIDs, weight loss, intraarticular injections, and physical therapy have all been shown to be effective non-surgical treatment options for knee OA. However, these options have some limitations, and are best when used in conjunction. Bracing for knee OA is a noninvasive, non-pharmacologic option which can significantly reduce pain and improve function with minimal adverse effects. Therefore, a combination of knee braces along with other non-operative modalities should be one mainstay of treatment in conjunction with other treatment modalities to reduce pain, improve function, stiffness, and mobility in knee OA.

Keywords: Non-operative management; knee osteoarthritis; bracing

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Introduction

Knee osteoarthritis (OA) is a chronic degenerative condition which leads to pain stiffness, and disability and affects almost one-fifth of the American population over the age of 45 years (1). Increased age and body mass index (BMI) are directly correlated with the prevalence of knee OA (2). Obesity is prevalent in approximately 66% of individuals with OA and many patients will report that joint pain prevents them from exercising and losing weight (3). Total knee arthroplasty (TKA) is indicated for advanced OA non-responsive to non-operative treatment, but not all patients are surgical candidates and some prefer not to have surgery. Furthermore, while TKA is a high-successful procedure, patients can still experience post-operative complications (4).

For mild to moderate OA, patients are managed conservatively with one or more non-operative treatment modalities for which there are a wide range of options with varying efficacy. The American Academy of Orthopedic Surgeons (AAOS) recommends strengthening exercises, low impact aerobic exercises, aquatic exercises, weight loss programs, and nonsteroidal anti-inflammatory agents (NSAIDs) (5). However, they did not reach a consensus determination regarding knee bracing, intra-articular corticosteroid injections, or hyaluronate injections due to varying results in the literature.

In order to best provide for our knee OA patients, it is essential for practitioners to understand the risks and benefits of the available treatments for successful management. Therefore, the purpose of this study was to review the non-operative management options for knee OA. Specifically, we evaluated: (I) NSAIDs; (II) weight loss; (III) intra-articular injections; (IV) physical therapy; and (V) bracing.

Methods

A comprehensive literature review was conducted using the electronic databases PubMed and EBSCO Host. All available studies between January 1, 1995 and December 31, 2018 were evaluated. Searches were performed using the following terms: total knee arthroplasty (title), cyclooxygenase-2 inhibitors (title), bracing (title), physical therapy (title), weight loss (title), knee osteoarthritis (title), intra-articular injection (title), hyaluronic acid (title), corticosteroid (title), and alternative (title). It is possible that some studies evaluating the above topics were not included for final analysis, however, for each field, a variety of the current literature is presented to provide at least an overview.

Reports were included if they evaluated clinical post-operative outcomes following TKA, had full-texts available, and were written in the English language. Exclusion criteria were the following: basic science studies, cadaveric studies, animal studies, conference abstracts, conference reviews, editorials, letters to the editor, surveys, case reports, and case series.

An initial literature search was performed by two authors (M DeRogatis, N Sodhi). Abstracts were screened in order to determine if identified articles met the inclusion and exclusion criteria. The full-text of selected articles was then further evaluated. The list of search results was screened for repeat reports by a third author (HK Anis). The references of all included studies were reviewed and determined for eligibility. The initial search yielded 7,882 reports. Through a Title and Abstract review, we identified relevant manuscripts, which were subsequently recovered in full and studied, yielding 545 reports that satisfied the search criteria. After full-text analysis, 43 studies were included in this review (*Figure 1*).

Results

Nonsteroidal anti-inflammatory drugs

In the past two decades, numerous studies have described the use of NSAIDs for knee OA (6-13). Many of these studies have demonstrated that NSAIDs are relatively safe and effective options to reduce pain and to improve function with long-term use. In a large meta-analysis, Puljak *et al.* (7) reviewed 15,337 patients who had a mean duration of OA for 8 years who were treated with celecoxib or a placebo. At an average of 6 months, there was a 12% improvement in the WOMAC pain and function scales without any serious adverse events (*Table 1*). Similarly, Bjordal *et al.* (8) reviewed 10,845 knee OA patients from 23 trials comparing NSAIDs (72%) to a placebo (28%). The mean duration of symptoms prior to intervention was 8 years. At a mean follow up of 13 weeks, VAS pain scores significantly improved by 16% and functional disability was decreased with NSAIDs ($P<0.05$) without any serious events. Additionally, a 6-month multi-center, randomized, double blind trial compared the efficacy of celecoxib (50%) and naproxen (50%) and found Western Ontario and McMasters Universities (WOMAC) pain, stiffness, and function scores improved in both groups (12). One patient developed atrial fibrillation and

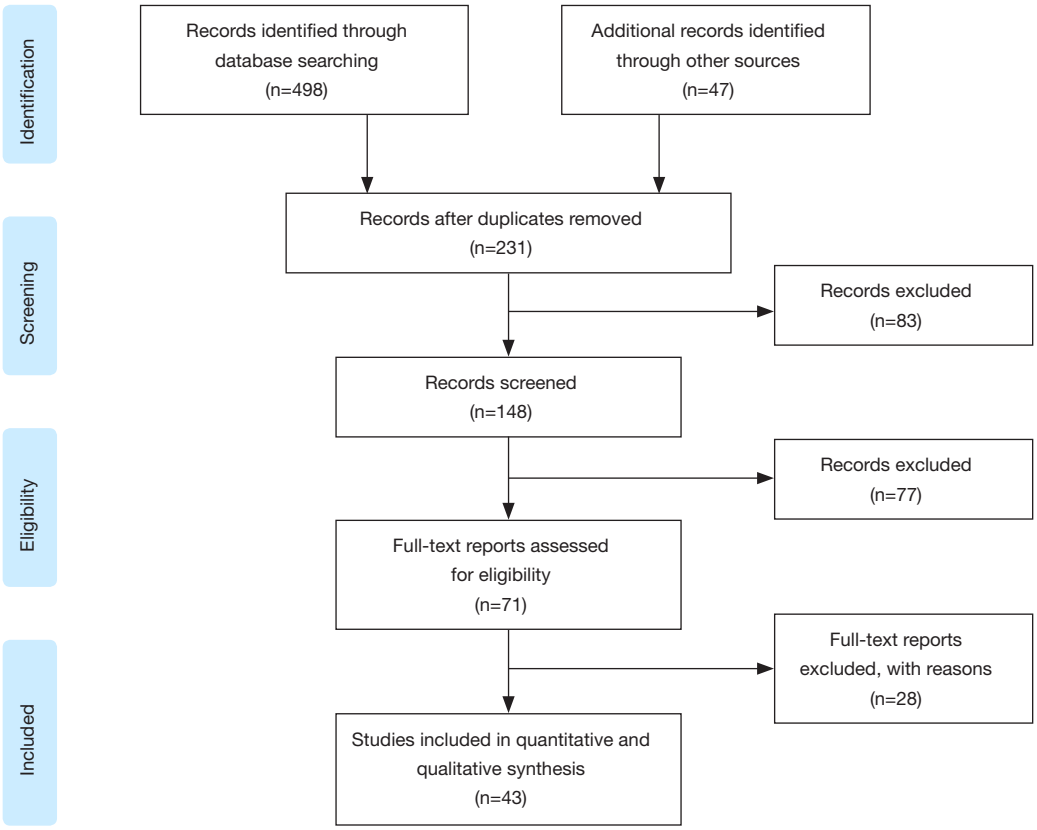

Figure 1 PRISMA diagram for study selection.

another patient suffered anaphylaxis in the celecoxib group. One patient in the naproxen group developed a serious adverse event of thrombocytopenia.

Conversely, Gordo *et al.* (6) retrospectively reviewed 301 knee OA patients treated with ibuprofen, celecoxib, or placebo over 6 weeks. Compared to the placebo groups, VAS pain and total WOMAC scores (measuring pain, stiffness, and function) were not significantly decreased in the treatment groups. Limitations of this study include a small sample size and the possibility of prior chronic use of NSAIDs. There is also literature to suggest that long-term NSAID use lead to renal, gastrointestinal, and cardiovascular adverse effects.

NSAIDs are most effective when used continuously, however, many patients will use them only when they have pain resulting in potentially less than optimal outcomes. They may be used in conjunction with other forms of treatment for knee OA as they have been shown to provide some pain relief as well as functional improvements.

Weight loss

Obesity is a modifiable risk factor for knee OA. It has been shown to improve pain, function, and stiffness with no adverse effects (14-21). There are multiple studies evaluating low energy diets, exercise, or both for the treatment of knee OA. Foy *et al.* (19) studied 2,203 obese diabetic patients with symptomatic knee OA and a mean BMI of 37 kg/m^2 who were randomized into either weight stable (n=1,095) or weight loss (n=1,108) groups for 1 year. Participants in the weight loss group lost 9 kg and reported significantly better WOMAC pain, function, and stiffness scores compared to those in the weight stable group ($P<0.05$) (*Table 2*). Edwards *et al.* (21) studied 24 patients who had a mean BMI of 42 and radiographic evidence of knee OA who underwent bariatric surgery. At one-year follow-up, the average reduction in BMI was 13 kg/m^2 and WOMAC pain, function, and stiffness scores significantly improved when compared to baseline ($P<0.05$).

Similarly, Messier *et al.* (14) studied 316 obese

Table 1 Use of non-steroidal anti-inflammatory medications

Study	Demographics	Δ Pain score	Knee function	Δ Knee stiffness	Complications
Gordo *et al.*, 2017 (6), RCT	N=178 (122 celecoxib *vs.* 56 placebo), mean age (y): 63, f (%): 71, duration of OA (m): 72, follow-up (w): 6	VAS pain—celecoxib: −35, placebo: −28	WOMAC total—celecoxib: 48, placebo: 48		Celecoxib: 3% diarrhea, 3% dyspepsia, 1% abdominal pain. Placebo: 1% diarrhea, 3% dyspepsia, 1% abdominal pain, 3% headache
Gordo *et al.*, 2017 (6), RCT	N=179 (123 ibuprofen 800 mg TID *vs.* 56 placebo), mean age (y): 64, F (%): 72, duration of OA (m): 65, follow-up (w): 6	VAS pain—ibuprofen: −33, placebo: −28	WOMAC total mean—ibuprofen: 48, placebo: 48		Ibuprofen: 1% diarrhea, 5% dyspepsia, 5% abdominal pain, 1% headache. Placebo: 1% diarrhea, 3% dyspepsia, 1% abdominal pain, 3% headache
Puljak *et al.*, 2017 (7), meta-analysis	N=15,337 (9,402 celecoxib 200 mg *vs.* 5,935 placebo), mean age (y): 62, F > M, duration of OA (m): 95, follow-up (w): 24	WOMAC pain—celecoxib: 12% improvement from placebo	WOMAC function—celecoxib: 12% improvement		No serious events
Bjordal *et al.*, 2004 (8), meta-analysis	N=10,845 (7,807 NSAIDs *vs.* 3,038 placebo), mean age (y): 63, duration of OA (m): 98, follow-up (w): 13	VAS pain—16% improvement from placebo	NSAIDs decrease in functional disability Q =40*		9% adverse events
Bensen *et al.*, 1999 (9), multi-centered RCT	405 (202 celecoxib 200 mg *vs.* 203 placebo), duration of OA (m): 120, mean age (y): 62, follow-up (w): 12	WOMAC pain—Celecoxib: 64, placebo: 65. VAS pain at rest—celecoxib: −24, placebo: −18. VAS pain with walking—celecoxib: −27, placebo: −22	WOMAC function—celecoxib: −22, placebo: −13	WOMAC stiffness—Celecoxib: −26, Placebo: −18	
Boswell *et al.*, 2008 (10), RCT	371 (185 celecoxib 200 mg *vs.* 186 placebo), F (%): 70, duration of OA (m): 101, mean age (y): 60 years, follow-up (w): 12	WOMAC pain—celecoxib: −28*, placebo: −22	WOMAC function—celecoxib: −25*, placebo −18		Celecoxib: 3% headache, 3% diarrhea, 3% dyspepsia, 1% hypertension. Placebo: 7% headache, diarrhea 5%, 1% dyspepsia, hypertension <1%
Clegg *et al.* (11), RCT	621 (318 celecoxib 200 mg *vs.* 313 placebo), F (%): 65, duration of OA (m): 118, mean age (y): 59, BMI (kg/m^2): 32, follow-up (w): 24	WOMAC pain—celecoxib: −100, placebo: −86	WOMAC function—celecoxib: −289, placebo: −227	WOMAC stiffness—celecoxib: −42, placebo: −36	1 congestive heart failure, 1 stroke
Essex *et al.* (12), multi-centered RCT	586 (294 celecoxib 200 mg *vs.* 292 naproxen 500 mg BID), F (%): 66, duration of OA (m): 95, mean age (y): 60, follow-up (w): 24	WOMAC pain—celecoxib: −5, naproxen: −5	WOMAC function—celecoxib −15, naproxen: −16	WOMAC stiffness—celecoxib: −2, naproxen: −2	Celecoxib: 1 atrial fibrillation, 1 anaphylaxis. Naproxen: 1 thrombcytopenia
Tannenbaum *et al.* (13), multi-centered RCT	724 (481 celecoxib 200 mg *vs.* 243 placebo), F (%): 68, duration of OA (m): 58, mean age (y): 64 years, follow-up (w): 13, BMI (kg/m^2): 30	WOMAC pain—celecoxib: −3, placebo: −2	WOMAC function—celecoxib: −9, placebo: −6	WOMAC stiffness—celecoxib: −1, placebo: −1	Celecoxib: 15% gastrointestinal events, 1% peripheral edema, <1% chest pain. Placebo: 10% gastrointestinal events, 2% peripheral edema, <1% chest pain
Tannenbaum *et al.* (13), multi-centered RCT	734 (491 lumiracoxib 400 mg *vs.* 243 placebo), F (%): 67, duration of OA (m): 58, mean age (y): 64, follow-up (w): 13, BMI (kg/m^2): 30	WOMAC pain—lumiracoxib: −3, placebo: −2	WOMAC function—lumiracoxib −10, placebo: −6	WOMAC stiffness—lumiracoxib: −1, placebo: −1	Lumiracoxib: 20% gastrointestinal events, 1% peripheral edema, 1% chest pain. Placebo: 10% gastrointestinal events, 2% peripheral edema, <1% chest pain

*, P<0.05. OA, osteoarthritis; RCT, randomized control trial; VAS, visual acuity scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; BMI, body mass index; BID, twice daily; TID, three times daily.

Table 2 Studies evaluating weight loss

Study	Demographics	Δ Weight (kg)	Δ Pain score	Δ Knee function	Δ Knee stiffness	Δ Mobility
Messier *et al.* (14), RCT	N=160 (82 diet, 78 CBT), mean age (y): 69, F (%): 70, follow-up (w): 72, BMI (kg/m^2): 34	Diet: –4*, CBT: –1	WOMAC pain—diet: –1, CBT: –1	WOMAC function—diet: –4, CBT: –3		6 minute walk distance (meters)—diet: 40, CBT –5. Stair climb time (seconds)—diet: –1, CBT: 0
Messier *et al.* (14), RCT	N=158 (80 exercise, 78 CBT), mean age (y): 69, F (%): 71, follow-up (w): 72, BMI (kg/m^2): 34	Exercise: –4, CBT: –1	WOMAC pain—exercise: 0, CBT: –1	WOMAC function—Exercise: –3, CBT: –3		6 minute walk distance (meters)—Exercise: 40*, CBT –5. Stair climb time (seconds)—exercise: –2, CBT: 0
Messier *et al.* (14), RCT	N=154 (76 diet + exercise, 78 CBT), mean age (y): 69, F (%): 71, follow-up (w): 72, BMI (kg/m^2): 34	Diet + Exercise: –4*, CBT: –1	WOMAC pain—diet + Exercise: –6*, CBT: –1	WOMAC function—diet + Exercise: –1*, CBT: –3		6 minute walk distance (meters)—diet + exercise: 40*, CBT –5. Stair climb time (seconds)—diet + exercise: –3*, CBT: 0
Christensen *et al.* (15), RCT	N=80 (40 LED *vs.* 40 CBT), mean age (y): 63, F (%): 89, follow-up (w): 8, BMI (kg/m^2): 36	LED: –11*, CBT: –4	WOMAC pain—LED: –57, CBT: –30	WOMAC function—LED: –253*, CBT: –86	WOMAC stiffness—LED: –23, CBT: –10	
Miller *et al.* (16), RCT	N=87 (44 weight loss *vs.* 43 weight stable), mean age (y): 70, F (%): 62, follow-up (w): 26, BMI (kg/m^2): 34.6	Weight loss: –8*, weight stable: 0	WOMAC pain—weight loss: –2*, weight stable: 0	WOMAC function—weight loss: –8*, weight stable: –2	WOMAC stiffness—weight loss: 0, weight stable: 0	6 minute walk distance (meters)—weight loss: 73*, weight stable: 11. Stair climb time (seconds)—weight loss: –2, weight stable: 1*
Riecke *et al.* (17), RCT	N=192 (96 VLED *vs.* 96 LED), mean age (y): 63, F (%): 81, follow-up (w): 16, BMI (kg/m^2): 37	VLED: –13*, LED: –12*	KOOS pain—VLED: –9*, LED: –11*	KOOS ADLVLED: –11*, LED: –11*		KOOS sports/recreation—VLED: –9*, LED: –8*
Aaboe *et al.* (18), RCT	N=157 LED, mean age (y): 63, F (%): 82, follow-up (w): 16, BMI (kg/m^2): 37	–14*	VAS pain: –13*		Knee flexion: –2%*	Walking speed: –4%*
Foy *et al.* (19), RCT	N=2, 203 (1, 108 weight loss *vs.* 1, 095 weight stable), mean age (y): 59, F (%): 65, follow-up (w): 52, BMI (kg/m^2): 37	Weight loss: –9*, weight stable: –1	WOMAC pain—weight loss: 0.4*, weight stable: 0.1	WOMAC function—weight loss: –3*, weight stable: –1	WOMAC stiffness—weight loss: 0.4, weight stable: 0.3	
A de Luis *et al.* (20), RCT	N=55 LED, mean age (y): 60, F (%): 76, follow-up (w): 12, BMI (kg/m^2): 39	–8*	WOMAC pain: –1. VAS pain: 0	WOMAC function: –5*	WOMAC stiffness: –1*	
Edwards *et al.* (21), RCT	N=24 bariatric surgery, age (y): 18–70, mean Follow-up (w): 52, BMI (kg/m^2): 42	–32 (BMI: –13)*	WOMAC pain: –5*	WOMAC function: –19*	WOMAC stiffness: –3*	

*, P<0.05. LED, low energy diet; CBT, cognitive behavioral therapy; KOOS, knee injury and osteoarthritis outcome score; ADL, function in daily living; VLED, very low energy diet; LED, low energy diet; RCT, randomized control trial; VAS, visual acuity scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; BMI, body mass index.

participants with radiographic evidence of knee OA over 18 months. Participants were randomized into lifestyle changes, diet only, exercise only, or diet plus exercise cohorts. Participants treated with diet plus exercise showed a significant decrease in weight, WOMAC pain and function scores, 6-minute walk distance, and stair climb time compared to a healthy lifestyle control group (P<0.05). Miller and colleagues studied 87 obese individuals randomized to a low energy diet or no diet (16). Participants in the low energy diet lost 8 kg and had significant improvements in WOMAC pain and function scores, along with improvements in 6-minute walk distance and stair climb time when compared to control diets (P<0.05).

Based on the above studies, weight loss is a promising modality for the treatment of knee OA. It is a safe and effective way to improve knee pain, function, and stiffness without serious adverse effects. However, weight loss can be very challenging for obese patients with knee OA due to their limited mobility and lack of adherence to a low-calorie diet. Patients should be educated on alternative methods such as low-calorie diets, medications, and bariatric surgery.

Intra-articular injections

Intra-articular injections for knee OA have been in use for many years, but their efficacy have been questionable in the current literature (22-30). Some patients will experience minimal pain relief, while others have substantial relief for months. Despite inconclusive outcomes, there has been an increasing prevalence in the use of intra-articular injections to treat knee OA often with the aim to postpone a TKA. Corticosteroid and hyaluronic acid (HA) injections are the two main types of intraarticular injections. Corticosteroids take 24 to 48 hours to provide relief and may be repeated every 3 months (24). Patients with uncontrolled diabetes are not good candidates for corticosteroid injections due to the acute rise in serum glucose. HA is a naturally occurring substance in synovial fluid and acts as a shock absorber for the knee, but is decreased in arthritic knees (31). Treatment with HA injections may be repeated every 3 months and can come in a series of three to five injections administered weekly or by a single injection (24).

Jüni and colleagues retrospectively reviewed 27 trials including a total of 1,749 patients treated with either corticosteroid or placebo injections (22). Overall, corticosteroid injections showed significant improvements in pain and function when compared to placebo (P<0.05). The greatest benefits were noticed at 1 to 2 weeks followed by 4 to 6 weeks post-treatment. However, no benefits were noticed at 26 weeks after injection (P>0.05) (*Table 3*).

Askari *et al.* retrospectively reviewed 69 patients treated with corticosteroid injections and 71 patients treated with HA injections (24). There was no difference in pain or stiffness after 3 months in either group (P>0.05), but there was a significant improvement in WOMAC function scores at 3 months (P<0.05). Unlike corticosteroid injections, there was a significant decrease in the VAS pain score with HA at 3 months. Both groups showed a significant decrease in pain at one and two months follow-up (P<0.05). Campos and colleagues prospectively studied the addition of corticosteroid to HA injections versus HA alone in 90 Kellgren-Lawrence stage 3 knees (29). At 4 weeks, VAS pain scores improved by 49% (P<0.05) and WOMAC function scores improved by 43% in patients who received corticosteroid plus HA. There was also significant improvement in pain and function with HA injections. The addition of corticosteroid was superior to HA injections alone for all scores (P<0.05).

The use of corticosteroid injections may be of benefit in the short term, especially when combined with HA. Injections proved to be safe without any reported short term adverse events in the cited studies, however, the long term effects of intraarticular injections remain uncertain.

Physical therapy

Muscle strengthening exercises have led to improved pain and functional outcomes in knee OA patients (32-35). Silva *et al.* (32) randomized 64 patients with knee OA into land or water-based physical therapy cohorts and at 3 months follow-up, both groups reported a reduction in pain (P<0.05). Knee function was only improved in patients treated with hydrotherapy (water-based physical therapy) at final follow up, but improvements in both groups were observed at 9 weeks (P<0.05) (*Table 4*). Similarly, Foley *et al.* (33) randomized 105 patients to be treated with hydrotherapy, gym strengthening exercises, or no therapy and also noted a reduction of pain with hydrotherapy at 6 weeks (P<0.05). A randomized controlled trial including 102 patients with knee OA treated with high-resistance exercise, low-resistance exercise, or no exercise for 8 weeks found that both high-resistance and low-resistance exercises improved knee pain and function when compared to baseline (P<0.05), however, there was no difference between the groups (35).

Physical therapy in the form hydrotherapy, resistance

Table 3 Studies evaluating intra-articular injections

Study	Demographics	Δ Pain score	Δ Knee function	Δ Knee stiffness	Δ Mobility	Adverse events
Jüni *et al.* (22), meta-analysis	N=1, 749 (922 CS, 827 placebo), follow-up (w): 1–26	VAS pain—CS: −3*, placebo: −2	WOMAC function—CS: −2*, placebo: −1			No serious AE
Davis *et al.* (23), ulti-centered RCT	N=151 (75 CS, 76 CRFA), mean age (y): 64, F (%): 67, follow-up (w): 24, BMI (kg/m^2): 30	NRS pain—CS: −1, CRFA: −5*	OKS function—CS: 6, CRFA: 19*			No serious AE
Askari *et al.* (24), RCT	N=140 (69 CS, 71 HA), mean age (y): 58, F (%): 85, follow-up (w): 12	WOMAC pain—CS: −1, HA: −1. VAS pain—CS: −0.6 (P>0.05), HA: −0.8*	WOMAC function—CS: −3*, HA: −2*	WOMAC stiffness—CS: 0, HA: 0		
Gaffney *et al.* (25), RCT	N=84 (42 CS, 42 placebo), mean age (y): 67, F (%): 70, follow-up (w): 6, weight (kg): 77	VAS pain—CS: −15*, placebo: −14*	HAQ function—CS: 0.2*, placebo: 0.2		1 minute walk distance (meters)—CS: 2*, placebo 5*	
Raynauld *et al.* (26), RCT	N=68 (34 CS, 34 placebo), mean age (y): 63, F (%): 68, duration of OA (m): 111, follow-up (w): 104, weight (kg): 85	WOMAC pain—CS: −11*, placebo: −14*	WOMAC function—CS: −11, placebo: −13*	WOMAC stiffness—CS: −12*, placebo: −13*	50−foot walking time (seconds)—CS: 0, placebo: 0. ROM (degrees)—CS: 13, placebo: 0	No serious AE
Jones *et al.* (27), RCT	N=59 (34 CS, 34 placebo), mean age (y): 71, F (%): 63, follow-up (w): 3	VAS pain—CS: −2*, placebo: 0	WOMAC function—CS: −11, placebo: −13	WOMAC stiffness—CS: −12, placebo: −13	50−foot walking time (seconds)—CS: 0, placebo: 0. ROM (degrees)—CS: 13, placebo: 0	
Arden *et al.* (28), RCT	N=150 (79 CS, 71 placebo), mean age (y): 66, F (%): 63, duration of OA (m): 111, follow-up (w): 26, weight (kg): 85	WOMAC pain—CS: −19*, placebo: −75	WOMAC function—CS: −69*, placebo: −219	WOMAC stiffness—CS: −10*, placebo: −34	50−meter walking time (seconds)—CS: 0, placebo −2. Time to climb 10 stairs (seconds)—CS: 0, placebo: −1	
Campos *et al.* (29), RCT	N=90 (45 CS + HA, 45 HA), mean age (y): 62, follow-up (w): 4, BMI (kg/m^2): 30	VAS pain (improvement)—CS + HA: 49%*, HA: 15%*	WOMAC function (improvement)—CS + HA: 43%*, HA: 9%*			
Buyuk *et al.* (30), RCT	N=252 (126 CS-1, 126 CS-2), mean age (y): 69, follow-up (w): 4, BMI (kg/m^2): 26	VAS pain—CS-1: −5*, CS-2: −6*	WOMAC function—CS-1: −33*, CS-2: −33*		No serious AE	

*, P<0.05. CS, corticosteroid; HA, hyaluronic acid; AE, adverse events; BMI, body mass index; RCT, randomized control trial; VAS, visual acuity scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; HAQ, Health Assessment Questionnaire Modified For Lower Limb Function; CRFA, cooled radio frequency ablation; NRS, numeric rating scale; OKS, Oxford knee score.

Table 4 Studies evaluating physical therapy

Study	Demographics	Δ Pain score	Δ Knee function	Δ Knee stiffness	Δ Mobility
Silva *et al.* (32), RCT	N=64 (32 water-based exercise, 32 land-based exercise), mean age (y): 59, weight (kg): 76, follow-up (w): 18	VAS pain—water: –35*, land: –31*	WOMAC total—water: –17, land: –12. Lequesne index—water: –5*, land: –4		50-foot walk test, comfortable pace (seconds)—water: –2*, land: –2*. 50-foot walk test, fast pace (seconds)—water: –1*, land: –1
Foley *et al.* (33), RCT	N=70 (35 water-based exercise, 35 control), mean age (y): 71, F (%): 50, weight (kg): 76, follow-up (w): 24	WOMAC pain—water: –1, control: 1	WOMAC function—water: –1, control: 0	WOMAC stiffness—water: 0, control: 0	
Foley *et al.* (33), RCT	N=70 (35 water-based exercise, 35 gym), mean age (y): 71, F (%): 50, weight (kg): 76, follow-up (w): 24	WOMAC pain—water: –1*, gym: 0	WOMAC function—water: –1, gym: –1	WOMAC stiffness—water: 0, gym: 0	
Foley *et al.* (33), RCT	N=70 (35 gym, 35 control), mean age (y): 71, F (%): 50, weight (kg): 76, follow-up (w): 24	WOMAC pain—gym: –1, control: 1	WOMAC function—gym: –1, control: 0	WOMAC stiffness—gym: 0, control: 0	
Deyle *et al.* (34), RCT	N=69 (33 PT, 36 control), mean age: 61 years, F: 59%, BMI (kg/m^2): 3, follow-up (w): 8	WOMAC total—PT: –584, control: –159			6 minute walk distance (meters)—PT: 56, control: 7
Jan *et al.* (35), RCT	N=84 (34 HR, 50 control), mean age (y): 63, F (%): 59, weight (kg): 63, duration of osteoarthritis (y): 3.4, follow-up (w): 8	WOMAC pain—HR: –4*, control: –1	WOMAC function—HR: –12*, control: –3		Walking time level ground (s)—HR: –3*, control: 0. Walking time stairs (s)—HR: –2*, control: –1
Jan *et al.* (35), RCT	N=84 (34 LR, 50 control), mean age (y): 63, F(%): 59, weight (kg): 62, duration of osteoarthritis (y): 3.2, follow-up (w): 8	WOMAC pain—LR: –3*, control: –1	WOMAC function—LR: –11*, control: –3		Walking time level ground (s)—LR: –4*, control: 0. Walking time stairs (s)—LR: –2, control: –1.4

*, P<0.05. VAS, visual acuity scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; PT, physical therapy; HR, high-resistance strength training; LR, low-resistance strength training.

training, or land-based exercises led to significant improvements in pain and function without any adverse effects. This is another form of a non-pharmacological intervention that is safe and highly effective. Decreased compliance rates of physical therapy are thought to be the result of high copayments, pain with activity, lack of transportation, and time commitment. Therefore, cost issues are a major barrier for usage. Physical therapy programs are varied and therefore patients and physicians should discuss these in order to improve compliance.

Braces

Knee braces are frequently used for knee OA and the American Academy Orthopaedic Surgeons recommends bracing for biomechanical stability (5). Knee malalignment associated with OA can cause significant pain and dysfunction and knee braces have shown to help with stability and function, especially in unicompartmental arthritis (36-42). There are two types of braces that are commonly used for knee OA, an unloader brace and a support brace. An unloader brace relieves pressure from the affected compartment and a support brace provides compression.

Yu *et al.* (37) prospectively studied 204 osteoarthritic knees treated with an unloader brace (n=86), patellofemoral brace (n=50), or no brace (n=68). At 26 weeks there was a significant improvement with bracing compared to no bracing (P<0.05). At 1-year follow-up, pain, activities of daily living (ADLs), 6-minute walk test, and timed up and go (TUG) test were significantly improved in all groups compared to baseline, however, no significant differences were noted between the brace and no brace groups. (*Table 5*).

Kirkley and colleagues performed a randomized controlled trial comparing unloader braces and neoprene sleeves to a control group (38). Significant differences in pain after the 6-minute walk test and 30-second stair-climbing test were reported with the unloader brace when compared to neoprene brace at 6 months (P<0.05). When comparing braced to unbraced patients, there were significant differences in WOMAC function scores (P<0.05).

Chughtai *et al.* (40) randomized 36 patients with Kellgren-Lawrence grades 3 to 4 knee OA to receive either a pneumatic unloader brace with conventional treatment or just conventional treatment. At a follow-up of one year, there were significantly fewer patients who received injections (46% *vs.* 83%, P<0.05) and less subsequent TKAs in the brace group (18% *vs.* 36%, P<0.05).

Imoto *et al.* (43) 100 patients who were randomized to either NMES bracing or control and were evaluated based on a numerical pain scale from 0 to 10, timed up and go (TUG) test, Lequesne index and activities of daily living (ADL) scale. The authors found the NMES cohort to have a statistically significant improvement regarding pain intensity [difference between means: 1.67 (0.31 to 3.02); P=0.01]; Lequesne index [difference between means: 1.98 (0.15 to 3.79); P=0.03]; and ADL scale [difference between means: –11.23 (–19.88 to –2.57); P =0.01] compared to the control cohort. In a smaller case series, Stevens *et al.* (44) also found 80% of patients treated with NMES and exercise to have greater increases in quadriceps strength compared to the contralateral leg treated with exercise only. Cherian *et al.* (45) also evaluated a prospective case-control cohort, and found NMES to help improve quadriceps strength and potentially improve knee functionality in knee OA patients. Other studies have also reported a number of other patient-specific and financial advantages to NMES (46,47).

Based on these data, braces help knee OA patients achieve marked improvements in pain, function, and may prolong their time to a TKA. This is a non-pharmacological treatment option that can improve symptoms and limit the use of other treatment modalities which are associated with greater risks.

Conclusions

Knee OA is a chronic condition that is often challenging to treat for clinicians and confers a substantial burden for affected patients. For clinicians, it is crucial to understand patient goals, insurance coverage, financial status, comorbidities, severity of OA, and the efficacy of treatment options to determine what is most beneficial for the patient. NSAIDs, weight loss, intraarticular injections, and physical therapy have all been shown to be effective non-surgical treatment options for knee OA. Bracing for knee OA is a noninvasive, nonpharmacologic option that can significantly reduce pain and improve function without any adverse effects. Therefore, based on this literature review, knee braces, in combination with other non-operative modalities, should be one mainstay of treatment in conjunction with other treatment modalities to reduce pain, improve function, stiffness, and mobility in knee OA.

Table 5 Studies evaluating braces

Study	Demographics	Δ Pain score	Δ Knee function	Δ Knee stiffness	Δ Mobility	TKA
Brouwer *et al.* (48), multi-centered RCT	N=117 (60 brace, 57 control), F (%): 50, mean age (y): 59, BMI (kg/m^2): 29, duration of OA (m): 70, follow-up (w): 36	VAS pain (difference between groups): −1	HSS function (difference between groups): 3		Walking distance in km (difference between groups): 1*	
Yu *et al.* (37), RCT	N=154 (86 brace TF, 68 control), F (%): 72, mean age (y): 67, BMI (kg/m^2): 32, duration of OA (m): 70, follow-up (w): 52	VAS pain—brace TF: −1*, control: −2*. KOOS pain—brace TF: 8*, control: 13*	KOOS ADL—brace TF: 7*, control: 12*		6 minute walk test (meters)—brace TF: 50*, control: 52*. Timed up and go test (seconds)—brace TF: −3*, control: −2*	
Yu *et al.* (37), RCT	N=118 (50 brace PF, 68 control), F: 78%, mean age (y): 67, BMI (kg/m^2): 32, duration of OA (m): 70, follow-up (w): 52	VAS pain—brace PF: −1*, control: −2*. KOOS pain—brace PF: 10*, control: 13*	KOOS ADL—brace PF: 8*, control: 12*		6 minute walk test (meters)—brace PF: 48*, control: 52*. Timed up and go test (seconds)—brace PF: −2*, control: −2*	
Kirkley *et al.* (38), RCT	N=74 (41 unloader brace, 33 control), F (%): 27, mean age (y): 59, follow-up (w): 26, degrees of varus: 9	WOMAC pain—brace: 43, control: −13	WOMAC function—brace: 157*, control: −7	WOMAC stiffness—brace: +29, control: −8	6 minute walk test (meters)—brace: 30*, control: 26. 30 second stair–climbing test (# stairs)—brace: +11*, control: −5	
Kirkley *et al.* (38), RCT	N=69 (36 neoprene brace, 33 control), F (%): 26, mean age (y): 59, follow-up (w): 26,Degrees of varus: 9	WOMAC pain—brace: 13, control: −13	WOMAC function—brace: 69*, control: −7	WOMAC stiffness—brace: 16, control: −8	6 minute walk test (meters)—brace: 9*, control: 26. 30 second stair–climbing test (# stairs)—brace: 6*, control: −5	
Larsen *et al.* (39), RCT	N=23 (36 unloader brace, 33 control), F (%): 33, mean age (y): 64 years, follow-up (w): 8, weight (kg): 88	KSS pain—brace (moderate OA: 10, low-grade OA: 5)	LEAS—brace (low-grade OA: 1*, moderate OA: 0)	Knee flexion—brace: −3°*, control: 0°		
Chughtai *et al.* (40), RCT	N=36 (11 unloader brace, 25 control), mean age (y): 60, follow-up (w): 52					Patients who underwent TKA—brace: 18%*, control: 36%. Time to TKA (days)—brace: 482, control: 389
Duivenvoorden *et al.* (41), meta-analysis	N=1,356 (unloader brace *vs.* control), follow-up (w): 52	VAS pain (difference between groups): 0	HSS function (difference between groups): 1			

Table 5 (*continued*)

Table 5 (*continued*)

Study	Demographics	Δ Pain score	Δ Knee function	Δ Knee stiffness	Δ Mobility	TKA
Duivenvoorden *et al.* (41), meta-analysis	N=1,356 (unloader brace *vs.* lateral wedge insole), follow-up (w): 52	VAS pain (difference between groups): 0	WOMAC function (difference between groups): 0			
Sattari *et al.* (42), RCT	N=40 (20 unloader brace, 20 control), F (%): 27, mean age (y): 59, follow-up (w): 36	VAS pain—brace: –4*, control: –1			Walking distance (km)—brace: 1*, control: 0	
Sattari *et al.* (42), RCT	N=40 (20 unloader brace, 20 lateral wedge insoles), F (%): 27, mean age (y): 59, follow-up (w): 36	VAS pain—brace: –4*, Insole: –4*			Walking distance (km)—brace: 1*, insole: 0	

*, P<0.05. HSS, hospital for special surgery knee function scale; TF, tibiofemoral osteoarthritis; PF, patellofemoral osteoarthritis; KOOS, knee injury and osteoarthritis outcome score; ADL, activities of daily living; RCT, randomized control trial; LEAS, lower extremity activity scores; KSS, knee society scores for pain; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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Footnote

Conflicts of Interest: MA Mont: AAOS, Cymedica, DJ Orthopaedics, Johnson & Johnson, Journal of Arthroplasty, Journal of Knee Surgery, Microport, National Institutes of Health (NIAMS & NICHD), Ongoing Care Solutions, Orthopedics, Orthosensor, Pacira, Peerwell, Performance Dynamics Inc, Sage, Stryker: IP royalties, Surgical Technologies International, Kolon TissueGene. A Bhave: Cymedica, DJ Orthopaedics, Guardian Inc, On Going Care, Journal of Society of Indian Physiotherapists. M Chughtai: DJ Orthopaedics, Sage Products, Stryker, Peerwell, Reflexion, Astym: Pain consultant. The other authors have no conflicts of interest to declare.

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