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ORIGINAL ARTICLE

Hand Osteoarthritis: An Update on Therapy

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ABSTRACT

Objectives: This literature review aims to summarize and discuss the most novel clinical studies relevant to the treatment of hand osteoarthritis.

Materials and methods: A comprehensive search using Medline and PubMed was performed. Results were restricted to the period between January 2008 and May 2014, and included randomized controlled trials and reviews. The bibliographies of articles retrieved through this search were searched manually for additional relevant references.

Results: The latest methods of nerve mobilization, splinting, exercise, and other diverse nonpharmacological treatments have led to significant functional and symptomatic improvements. Topical nonsteroidal antiinflammatory drugs' clinical beneficence was reinforced and corticosteroid injections were shown to be superior to hyaluronic acid injections. Other pharmacological therapies, such as Hylan injections and synergistic drugs, also showed promise. Antitumor necrosis factor was suggested to play role as a potential disease-modifying agent. Surgical procedures such as arthroscopic debridement, synovectomy of the trapeziometacarpal joint, and early tendon arthroplasty were promising with long-term benefits when used as early interventions.

Conclusion: Recent studies show that emerging therapies may play role in the clinical setting as an upgrade over current practices, and that earlier surgical interventions should be considered in the management process.

Keywords: Hand; medical; osteoarthritis; surgery; therapy.

Symptomatic hand osteoarthritis (OA) is a disease beginning in middle age, with increased prevalence in the elderly. It is found in about 13% of males and 26% of females above the age of 70, with a relatively stable prevalence thereafter. The most commonly affected joints are the distal interphalangeal and the proximal interphalangeal (PIP), followed by the base of thumb joint. In virtually all hand joints, the prevalence of symptomatic OA is higher in females than in males, with the overall odds ratio being three to one in terms of the total number of joints involved,[1] thus implying a hormonal influence on the prevalence of hand OA. Other known risk factors include obesity[2] -despite the fact that the hand joints are not weight bearing-, a positive family history, with a relative risk of two in patients with affected siblings,[3] hyperglycemia,[4] higher maximal grip strength,[5] and previous digital fractures.[6]

Usual symptoms of hand OA are pain on usage and only mild stiffness in the morning or after a period of inactivity.[7] The pain is usually of a gradual onset with decreased function of the affected joint(s).[8] This usually affects one joint or a couple of joints a time. Symptoms target characteristic sites: distal interphalangeal, PIP, thumb base, index, and metacarpophalangeal joints and are commonly present intermittently. Functional impairment may be as severe as that in rheumatoid arthritis, hence careful assessment and monitoring of function should be carried out using validated outcome measures.[7]

Bony enlargements such as Bouchard's nodes on the PIP joints and Heberden's nodes on the

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distal interphalangeal are commonly found in hand OA. These nodes can be painful at their onset, but non-tender thereafter.[8] They are useful clinical markers for the diagnosis of hand OA, especially when utilized in combination with other characteristics of the disease.[7]

The differential diagnosis for hand OA is broad and includes psoriatic arthritis, rheumatoid arthritis, gout, and hemochromatosis. A combination of clinical features, such as age, sex, joint distribution, bone swelling, radiographic changes, and laboratory findings should be considered to reach a conclusive diagnosis.[7]

Plain radiographs are the current gold standard for morphological assessment of hand OA, whereby classical features such osteophytes, joint space narrowing, subchondral bone sclerosis and cysts are regularly seen. Blood tests are not necessary for the diagnosis of hand OA, but can be useful to exclude other inflammatory arthropathies in patients with marked inflammatory signs and/or symptoms, particularly those involving unusual sites.[8]

Management of hand OA has been classically directed towards improving symptomatology and functionality of affected patients. Classical therapies have been well documented in recommendations by organizations such as the American College of Rheumatology and the European League Against Rheumatism. However, no disease-modifying agent has been identified, yet the search is ongoing. Thus, in this literature review, we aimed to summarize and discuss the most novel clinical studies relevant to the treatment of hand OA.

MATERIALS AND METHODS

The search was carried out in two databases: Medline and PubMed. Articles were restricted to those published within the time period from January 2008 to May 2014 this review aimed to highlight the novel nonpharmacological, pharmacological, and surgical treatments within this period specifically.

Inclusion criteria were as follows; patients with hand OA according to clinical and/or radiographic criteria, randomized controlled trials (RCT) or reviews, study population ≥25, all types of relevant nonpharmacological, pharmacological, and surgical interventions, and English language. Studies deemed by the authors to be not relevant and/or of low quality based on thorough assessment of the studies were excluded.

Keywords used in the Medline search engine were hand, hand joints, osteoarthritis [Diet Therapy, Drug Therapy, Prevention & Control, Radiotherapy, Rehabilitation, Surgery, Therapy]. Hand and hand joints were joined by the Boolean operator OR and subsequently with osteoarthritis [Diet Therapy, Drug Therapy, Prevention & Control, Radiotherapy, Rehabilitation, Surgery, Therapy] by the Boolean operator AND. This was followed by a search using the PubMed search engine, with the following keywords: (((Hand) OR Hand joints) AND Osteoarthritis)) AND ((Treatment OR Therapy))).

Medline generated 252 potentially relevant results, and of these, 39 were included based on the inclusion/exclusion criteria listed above. On the other hand, PubMed generated 242 results, and from these, only three were found to be additionally relevant to the 39 previously chosen from the Medline search. (Duplicate results were chosen only once.)

The bibliographies of articles retrieved through this search were searched manually for additionally relevant references, which were used in the 'Epidemiology of Hand Osteoarthritis' and 'Clinical Presentation and Diagnosis' sections only. Eight articles were retrieved accordingly.

RESULTS

Therapy for hand OA can be divided into three broad categories: nonpharmacological, pharmacological, and surgical therapy (Table 1). Nonpharmacological therapy includes physiotherapeutic exercises, local heat application, splint, and others. The search for disease-modifying therapies has been unsuccessful, thus pharmacological therapies target mainly pain relief and function amelioration. Surgery is classically resorted to when more conservative treatment fails.

In a study evaluating the effect of Kaltenborn manual therapy on sensory and motor function in elderly patients with secondary carpometacarpal

Table 1. Recently studied treatment options for managing hand osteoarthritis

Nonpharmacological	Pharmacological	Surgical
Kaltenborn manual therapy[9]	Topical NSAIDs[27-29]	Volar ligament reconstruction[45]
Radial nerve mobilization[10,11]	Arnica gel[30]	Metacarpal osteotomy[45]
Maitland's passive accessory mobilization[12]	Topical analgesic + paraffin bath therapy[31]	Carpometacarpal arthrodesis[45]
Joint mobilization + neural mobilization + exercise[13]	Intraarticular corticosteroid injections[32-35]	Joint replacement[45]
Custom-made splinting[17,18]	Intraarticular hyaluronic acid injections[36,37]	Trapeziectomy[45]
Splinting + exercise[19]	Intraarticular hylan injections[38,39]	Trapeziectomy with tendon interposition[45]
Balneotherapy + magnetotherapy[20]	Chondroitin 4 and 6 sulfate[40]	Trapeziectomy with ligament reconstruction[45]
Paraffin bath therapy[22]	Infliximab (TNF inhibitor)[41]	Trapeziectomy with ligament reconstruction and tendon interposition[45,46]
Leech therapy[23]	Adalimumab (TNF inhibitor)[42]	
	CRx-102 (dipyridamole + low-dose prednisolone)[43]	
	0.5% Sodium salicylate[44]	

NSAID: Nonsteroidal antiinflammatory drugs; TNF: Tumor necrosis factor.

(CMC) OA, it was shown that the pain pressure threshold in the CMC joint and scaphoid bone areas was increased, however grip strength was not improved. The tip and tripod pinch strength were unchanged as well.[9] Two trials studying the effect of radial nerve mobilization on patients with thumb CMC OA found it to have hypoalgesic effects on the same[10] and contralateral hand,[11] indicating bilateral hypoalgesic effects of the practice. In addition, tip pinch strength and tripod pinch strength both improved in the same hand.[10] In a double-blind RCT, Maitland's passive accessory mobilization of the thumb led to increased pain pressure threshold in the trapeziometacarpal (TM) joint, but did not improve tip, tripod pinch, or grip strength.[12] A combination of joint mobilization, neural mobilization, and exercise was shown to improve pain levels after two months of treatment in patients with hand OA, but it had limited effect on improving pressure pain thresholds, as well as pinch and grip strengths.[13]

A number of guidelines recommend splinting for base-of-thumb OA, yet no evidence of efficacy exists. A randomized trial showed that wearing a splint improved pain and disability after 12 months, but not at one month, in patients with base-of-thumb OA.[14] Using a splint during activities of daily living for patients with TM OA was shown to improve pain but not function, grip strength, pinch strength, or dexterity.[15] In addition, use of assistive technology including splints and other devices was shown to be well tolerated and useful in improving activity performance and overall patient satisfaction.[16] Usually, a client-centered approach is preferred, and two trials reinforced that by showing that a custom-made splint decreases pain slightly more than a prefabricated one.[17,18]

Although the European League Against Rheumatism already recommends combining splinting and exercise, a comparative study reinforces that by demonstrating that when splinting and an exercise regimen are added to a joint protection program, they yield a superiorly improved pain, stiffness, grip force, and daily activities when compared to the joint protection program only.[19]

It was proven in a single-blind, follow-up RCT that balneotherapy combined with magnetotherapy was superior to magnetotherapy alone in improving pain and function as well as the quality of life in patients with hand OA. Specifically, using thermal water is probably more effective at 38 °C than at 36 °C, since use of the former improved the pinch strength of the right hand and Health Assessment Questionnaire parameters significantly, including in the long term, whereas the latter's use did not.[20] Within balneotherapy, the use of sulphurous spa water alone was shown to be more effective than that of warm tap water exclusively in the reduction of pain in patients with hand OA.[21] Another

single-blind RCT showed that paraffin bath therapy in patients with bilateral hand OA was successful in reducing stiffness and pain at rest and during activities of daily living. As well, range of motion was enhanced in one hand, and muscle strength was better maintained as compared to the control group.[22]

Since leech therapy is known to be useful for knee OA, its effectiveness in TM OA was investigated in an RCT, which compared the results of a single treatment with two or three locally applied leeches with that of a 30-day course of topical diclofenac, twice a day, in two different groups. Leech therapy was superior in enhancing pain relief, and a single course was shown to be effective in relieving pain and improving disability and quality of life for a minimum of two months.[23]

An RCT indicated that magnetic and copper bracelets have no benefit for managing pain, stiffness, and physical function in OA.[24] Similarly, no role for diacerein, an interleukin-1 and metalloprotease inhibitor, has been shown in improving hand OA symptomatology.[25] Even though vitamin K has bone and cartilage effects and an association with radiographic OA has been shown, an RCT showed that there was no significant effect of vitamin K on radiographic hand OA. However, some benefit in joint space narrowing was shown in subjects who were vitamin K insufficient initially, and later attained sufficient levels,[26] suggesting a role for vitamin K in hand OA pathogenesis.

Nonsteroidal antiinflammatory drugs (NSAIDs) have a prominent role in the treatment of OA in general. They have been successful in improving symptomatology, yet they are notorious for their dose and age-related gastrointestinal, cardiovascular, and renal adverse effects, especially in older patients and those with other comorbidities. In an attempt to avoid these effects, topical NSAIDs have been recommended by the European League Against Rheumatism, since they have shown an efficacy similar to oral NSAIDs and an adverse effect profile similar to placebo, with the exception of application site reactions. As of 2010, the only topical NSAID approved in the United States for the treatment of hand OA is diclofenac sodium 1% gel.[27]

In a double-blind RCT, the efficacy and safety of diclofenac sodium 1% gel was determined in patients with primary hand OA.[28] It was found that its application four times daily for eight weeks significantly decreased pain intensity scores by more than 42%, total Australian/Canadian OA Hand Index score by at least 35%, and global rating of disease by 36-40%. Other secondary outcomes, such as onset of efficacy in the first two weeks and its durability for eight weeks, generally supported the above primary outcomes. Application-site paresthesia was the most common treatment-related adverse effect. No gastrointestinal bleeding, ulcers, or cardiac events were seen. In an analysis of pooled data from five RCTs, diclofenac sodium 1% gel treatment was demonstrated to be well tolerated and to have similar adverse effects when comparing patients with hand OA above and below 65 years and when comparing those with/without comorbid hypertension, type 2 diabetes, or cerebrovascular or cardiovascular disease.[29]

Some patients have demonstrated intolerance to the standard pain treatments of hand OA. A well-designed, double-blind RCT showed that the use of a proprietary arnica gel, of which its pharmacologically active ingredients are helenalin and dihydrohelenalin, was similar to the ibuprofen gel in terms of improving hand functional capacity, pain intensity, number of painful joints, duration and severity of morning stiffness, and paracetamol consumption. Hence, this arnica gel can be considered as an alternative to ibuprofen gel for short-term use in hand OA.[30]

Topical analgesics can also be of benefit, when used in unconventional ways. An RCT showed that the use of a topical analgesic, containing menthol along with chondroitin and glucosamine, mixed with paraffin (80% wax with 20% analgesic), produces significantly increased pain relief at rest and during movement, when compared to paraffin baths alone, as well as improved hand function, after 12 sessions.[31]

Steroid injections are used to decrease pain and inflammation with consequent function improvement. They do not, however, cure the disease. A review of intra-articular (IA) corticosteroid injections into the TM joint of patients with hand OA looked at the longevity of their benefit. From a total of 83 patients, it was found that two-thirds were improved at two months, with almost half having a three-month

improvement. One sixth of the patients had a six-month benefit, with some still improving two years after the injection. The efficacy of the injection was not related to OA severity, and patients with previous injections had reduced duration of benefit.[32] A similar review determined that from a total of 41 patients undergoing a single injection, 76% reported pain relief lasting an average of four weeks. 76% continued to have pain after a median follow-up of three years, yet 59% were satisfied with the outcome. Only 28% of the patients had undergone surgery.[33] Based on the above reviews, corticosteroid injections are recommended in TM joint OA of all degrees,[32] and provide only short-term pain relief.[33]

In a study of intramuscular methylprednisolone injection, it was seen that the parenteral corticosteroids were successful in significantly reducing symptoms. However, when ultrasound images were compared before and after, no significant reduction was found in synovial inflammation.[34] In a double-blind RCT of patients with hand OA, it was shown that short-term low-dose oral prednisolone is not an effective analgesic treatment.[35]

Intra-articular hyaluronic acid injections have been shown to be useful; however, it is essential to compare their efficacy to that of IA corticosteroid injections. In a randomized, open-label, evaluator-blinded clinical study, 40 females with stage II or III TM joint OA received either 20 mg triamcinolone acetonide once or three injections of 5 mg sodium hyaluronate at one-week intervals. Even though it was detected that both were effective in improving pain and grip strength in TM joint OA, patients receiving the corticosteroid injections had better pain relief and enhancement of hand function.[36]

As well, a review concluded that, until now, there seems to be no benefit for IA hyaluronic acid injections over corticosteroid injections, and maybe even placebo treatment, for the management of symptomatic OA.[37]

Hyaluronic acid was chemically cross-linked to form hylan molecules. This was done in an attempt to increase average molecular weight and, subsequently, viscosity and half-life in the joint, leading to a better efficacy. An RCT evaluated the efficacy of IA Hylan G-F 20 injection in patients with bilateral TM OA. Hands of the patients were divided to Hylan G-F 20 and saline-injection receiving groups. Significant improvements were detected in function, visual analog scale (VAS) pain, and pinch strength at 24 weeks in the Hylan G-F 20 group.[38]

The placebo effect might partly explain the above results. To investigate that, as well as compare its effect with that of a corticosteroid injection, a prospective, double-blind RCT was conducted.[39] No statistically significant differences among hylan, steroid, and placebo injections were found for most of the outcome measure, such as pain at any time, symptoms at 26 weeks, Disabilities of the Arm, Shoulder, and Hand scores, and range of motion. However, due to the durable pain relief, improvement in symptoms, and enhanced grip strength compared to the pre-injection state, hylan injections do have a role in the management of TM OA.

A double-blind RCT studied the effects of highly purified chondroitin 4 and 6 sulfate treatment in patients with symptomatic hand OA. Patients' global assessment of hand pain, hand function, duration of morning stiffness, and investigator's global impression of treatment efficacy were all in favor of chondroitin sulfate group. Grip strength, acetaminophen consumption, and safety end points were not significantly improved though.[40]

The search for an accepted disease-modifying agent for hand OA has not been successful yet. While pilot studies have suggested such a role for infliximab, a tumor necrosis factor inhibitor, no well-designed RCTs exist to better evaluate this in patients with hand OA (give some references about pilot studies). A different study demonstrated that treatment of rheumatoid arthritis patients with infliximab decreased incident secondary OA in the PIP joints, independent of decrease in inflammation. This suggests that this antitumor necrosis factor drug may work via pathways other than suppression of inflammation.[41]

Adalimumab, another tumor necrosis factor inhibitor, reduces disease progression in rheumatoid and psoriatic arthritis. Its effect on controlling progression of structural damage in erosive hand OA was studied in an RCT.[42] Overall, no effect for adalimumab was seen, as the disease remained similarly active in the placebo group and adalimumab group. It was realized, though, that soft tissue swelling at

baseline is the strongest predictor of erosive progression. And when disease progression was studied in that group, adalimumab turned out to significantly slow the progression of joint damage compared to placebo.

A new synergistic drug candidate CRx-102, a combination of dipyridamole and low dose prednisolone, was assessed for its efficacy and safety in patients with hand OA in a blinded, RCT.[43] It was demonstrated to lower Australian/Canadian OA Hand Index pain, joint pain VAS, and patient global VAS, when compared to placebo. Headache was the most common adverse event, with a 52% occurrence, compared to placebo with 15%.

Many patients with hand OA have areas of tender subcutaneous thickening in the forearm and upper scapular region. An RCT showed that injecting 0.5% sodium salicylate into the forearm and then into the upper scapular region a week later, in those specific areas, lead to a significantly improved pain, tenderness, and VAS score when compared to placebo.[44]

Surgery is usually considered as the last resort for the treatment of hand OA, after more conservative therapy has failed. Eight most commonly performed surgical procedures are volar ligament reconstruction, metacarpal osteotomy, CMC arthrodesis, joint replacement, trapeziectomy, trapeziectomy with tendon interposition, trapeziectomy with ligament reconstruction, and trapeziectomy with ligament reconstruction and tendon interposition.[45]

Based on two independent reviews, it was concluded that no surgical procedure could be considered superior to another.[45,46] However, trapeziectomy with ligament reconstruction and tendon interposition[45,46] and CMC arthrodesis were associated with higher complication rates, with CMC arthrodesis associated as well with a higher frequency of repeat surgeries. One of the reviews did note that total joint prosthesis might have better short-term results than trapeziectomy with ligament reconstruction and tendon interposition.[45] Due to the improved implant design and refinement of surgical indications, a different review supported adding basal joint implant arthroplasty to the surgical treatment options.[47]

A controlled clinical trial investigated whether arthroscopic debridement and synovectomy of the TM joint would improve outcomes in patients with stage I and stage II TM OA.[48] It was detected that compared to traditional, conservative treatment, this procedure improved pain scores, functional scores, subjective outcome, and pinch strength.

Primary prevention of hand OA can be started in young adulthood (middle adult?) to reduce the development of radiographically defined OA at mid-life. In a study evaluating the durability of a tendon arthroplasty procedure in a young population (<55 years), no deterioration in the strength and mobility of the operated thumbs was found over a long-term follow-up of 86 months.[49] In addition, there was a significant improvement in tip pinch strength, grip strength, and range of motion. The durability of the improvements from this surgery might be an encouragement for early, proactive intervention, to reduce the possibility of future, multiple surgeries.

DISCUSSION

A continuously growing repertoire of nonpharmacological solutions is emerging with many showing excellent promise. The latest methods ranging from neurodynamic mobilization of the radial nerve, to base-of-thumb splinting, to combining balneotherapy with magnetotherapy, and to leech therapy are greatly diverse and have demonstrated improved pain levels, stiffness, mobility, strength, and daily activities. Greater potential exists by combining the different options, which will probably be evaluated in future studies. As for pharmacological therapies, topical NSAIDs are highly popular because of a therapeutic profile similar to oral NSAIDs and an adverse effect profile comparable to that of placebo. Other topical therapies, with similar results, also exist, such as arnica gel. Corticosteroid injections have mainly shown short-term gains with decreasing effectiveness with subsequent injections. However, they are still more effective than hyaluronic acid injections and likely as effective as hylan injections. The latter two options remain important, though, since they avoid the rises in blood sugars of patients with

diabetes and the cutaneous and ligamentous side effects that may occur with multiple corticosteroid injections, thus making them a safer option. Potential disease modifying agents, such as infliximab and adalimumab, are currently being evaluated with no conclusive benefits as of yet. Other pharmacological therapies such as chondroitin 4 and 6 sulfate injections, CRx-102, and sodium salicylate injections have shown positive results. As for the classical last resort, surgery, no difference has been detected between the different types of procedures. Early, proactive surgical interventions, such as arthroscopic debridement and synovectomy of the TM joint and early tendon arthroplasty, should be considered in selected cases, as they can provide long-term improvements with fewer surgeries in the future, thus challenging the classical nonpharmacological, pharmacological, and lastly surgical sequence of therapy.

In comparison to the 2012 guidelines recommended by the American College of Rheumatology for the use of nonpharmacological and pharmacological therapies in OA of the hand, we see that the latest studies provide additional options to help treat patients. Concerning nonpharmacological recommendations, which are limited to evaluation of activities of daily living, joint protection techniques, provision of assistive devices, use of thermal modalities, and provision of splints for TM joint OA, there is no mention of therapies such as Kaltenborn manual therapy, radial nerve mobilization, Maitland's passive accessory mobilization, custom-made splinting, balneotherapy, magnetotherapy, and paraffin bath therapy.[50]

As for pharmacological recommendations, these are limited to the use of topical capsaicin, topical NSAIDs, and oral NSAIDs, with advice against the use of intraarticular therapies, despite evidence for their significant benefit presented in many recent trials. There is no mention of arnica gel, use of chondroitin 4 and 6 sulfate, infliximab, adalimumab, CRx-102, or sodium salicylate.[50] This can be partly attributed to the modest effect that some of these therapies have; however, it is our belief that the greater the number of treatment modalities the patient is provided with, the better his chances at improvement of pain and functionality, and thus better overall management.

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REFERENCES

1. Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: The Framingham Study. Am J Epidemiol 2002;156:1021-7.
2. Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol 1996;23:1221-6.
3. Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol 1996;23:1221-6.
4. Cimmino MA, Cutolo M. Plasma glucose concentration in symptomatic osteoarthritis: a clinical and epidemiological survey. Clin Exp Rheumatol 1990;8:251-7.
5. Zhang Y, Hannan MT, Chaisson CE, McAlindon TE, Evans SR, Aliabadi P, et al. Bone mineral density and risk of incident and progressive radiographic knee osteoarthritis in women: the Framingham Study. J Rheumatol 2000;27:1032-7.
6. Jones G, Cooley HM, Stankovich JM. A cross sectional study of the association between sex, smoking, and other lifestyle factors and osteoarthritis of the hand. J Rheumatol 2002;29:1719-24.
7. Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. Ann Rheum Dis 2009;68:8-17.
8. Glass GG. Osteoarthritis. Dis Mon 2006;52:343-62.
9. Villafañe JH, Silva GB, Diaz-Parreño SA, Fernandez-Carnero J. Hypoalgesic and motor effects of kaltenborn mobilization on elderly patients with secondary thumb carpometacarpal osteoarthritis: a randomized controlled trial. J Manipulative Physiol Ther 2011;34:547-56.
10. Villafañe JH, Silva GB, Bishop MD, Fernandez-Carnero J. Radial nerve mobilization decreases pain sensitivity and improves motor performance in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. Arch Phys Med Rehabil 2012;93:396-403.
11. Villafañe JH, Bishop MD, Fernández-de-Las-Peñas C, Langford D. Radial nerve mobilisation had bilateral sensory effects in people with thumb carpometacarpal osteoarthritis: a randomised trial. J Physiother 2013;59:25-30.

12. Villafañe JH, Silva GB, Fernandez-Carnero J. Effect of thumb joint mobilization on pressure pain threshold in elderly patients with thumb carpometacarpal osteoarthritis. J Manipulative Physiol Ther 2012;35:110-20.
13. Villafañe JH, Cleland JA, Fernández-de-Las-Peñas C. The effectiveness of a manual therapy and exercise protocol in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. J Orthop Sports Phys Ther 2013;43:204-13.
14. Rannou F, Dimet J, Boutron I, Baron G, Fayad F, Macé Y, et al. Splint for base-of-thumb osteoarthritis: a randomized trial. Ann Intern Med 2009;150:661-9.
15. Gomes Carreira AC, Jones A, Natour J. Assessment of the effectiveness of a functional splint for osteoarthritis of the trapeziometacarpal joint on the dominant hand: a randomized controlled study. J Rehabil Med 2010;42:469-74.
16. Kjeken I, Darre S, Smedslund G, Hagen KB, Nossum R. Effect of assistive technology in hand osteoarthritis: a randomised controlled trial. Ann Rheum Dis 2011;70:1447-52.
17. Sillem H, Backman CL, Miller WC, Li LC. Comparison of two carpometacarpal stabilizing splints for individuals with thumb osteoarthritis. J Hand Ther 2011;24:216-25.
18. Bani MA, Arazpour M, Kashani RV, Mousavi ME, Hutchins SW. Comparison of custom-made and prefabricated neoprene splinting in patients with the first carpometacarpal joint osteoarthritis. Disabil Rehabil Assist Technol 2013;8:232-7.
19. Boustedt C, Nordenskiöld U, Lundgren Nilsson A. Effects of a hand-joint protection programme with an addition of splinting and exercise: one year follow-up. Clin Rheumatol 2009;28:793-9.
20. Horváth K, Kulisch Á, Németh A, Bender T. Evaluation of the effect of balneotherapy in patients with osteoarthritis of the hands: a randomized controlled single-blind follow-up study. Clin Rehabil 2012;26:431-41.
21. Kovács C, Pecze M, Tihanyi Á, Kovács L, Balogh S, Bender T. The effect of sulphurous water in patients with osteoarthritis of hand. Double-blind, randomized, controlled follow-up study. Clin Rheumatol 2012;31:1437-42.
22. Dilek B, Gözüm M, Şahin E, Baydar M, Ergör G, El O, et al. Efficacy of paraffin bath therapy in hand osteoarthritis: a single-blinded randomized controlled trial. Arch Phys Med Rehabil 2013;94:642-9.
23. Michalsen A, Lüdtke R, Cesur O, Afra D, Musial F, Baecker M, et al. Effectiveness of leech therapy in women with symptomatic arthrosis of the first carpometacarpal joint: a randomized controlled trial. Pain 2008;137:452-9.
24. Richmond SJ, Brown SR, Campion PD, Porter AJ, Moffett JA, Jackson DA, et al. Therapeutic effects of magnetic and copper bracelets in osteoarthritis: a randomised placebo-controlled crossover trial. Complement Ther Med 2009;17:249-56.
25. Shin K, Kim JW, Moon KW, Yang JA, Lee EY, Song YW, et al. The efficacy of diacerein in hand osteoarthritis: a double-blind, randomized, placebo-controlled study. Clin Ther 2013;35:431-9.
26. Neogi T, Felson DT, Sarno R, Booth SL. Vitamin K in hand osteoarthritis: results from a randomised clinical trial. Ann Rheum Dis 2008;67:1570-3.
27. Barthel HR, Axford-Gatley RA. Topical nonsteroidal anti-inflammatory drugs for osteoarthritis. Postgrad Med 2010;122:98-106.
28. Altman RD, Dreiser RL, Fisher CL, Chase WF, Dreher DS, Zacher J. Diclofenac sodium gel in patients with primary hand osteoarthritis: a randomized, double-blind, placebo-controlled trial. J Rheumatol 2009;36:1991-9.
29. Baraf HS, Gold MS, Petruschke RA, Wieman MS. Tolerability of topical diclofenac sodium 1% gel for osteoarthritis in seniors and patients with comorbidities. Am J Geriatr Pharmacother 2012;10:47-60.
30. Ross SM. Osteoarthritis: a proprietary Arnica gel is found to be as effective as ibuprofen gel in osteoarthritis of the hands. Holist Nurs Pract 2008;22:237-9.
31. Myrer JW, Johnson AW, Mitchell UH, Measom GJ, Fellingham GW. Topical analgesic added to paraffin enhances paraffin bath treatment of individuals with hand osteoarthritis. Disabil Rehabil 2011;33:467-74.
32. Swindells MG, Logan AJ, Armstrong DJ, Chan P, Burke FD, Lindau TR. The benefit of radiologically-guided steroid injections for trapeziometacarpal osteoarthritis. Ann R Coll Surg Engl 2010;92:680-4.
33. Maarse W, Watts AC, Bain GI. Medium-term outcome following intra-articular corticosteroid injection in first CMC joint arthritis using fluoroscopy. Hand Surg 2009;14:99-104.
34. Keen HI, Wakefield RJ, Hensor EM, Emery P, Conaghan PG. Response of symptoms and synovitis to intra-muscular methylprednisolone in osteoarthritis of the hand: an ultrasonographic study. Rheumatology (Oxford) 2010;49:1093-100.
35. Wenham CY, Hensor EM, Grainger AJ, Hodgson R, Balamoody S, Doré CJ, et al. A randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for treating painful hand osteoarthritis. Rheumatology (Oxford) 2012;51:2286-94.
36. Bahadir C, Onal B, Dayan VY, Gürer N. Comparison of therapeutic effects of sodium hyaluronate and corticosteroid injections on trapeziometacarpal joint osteoarthritis. Clin Rheumatol 2009;28:529-33.
37. Moran SL, Duymaz A, Karabekmez FE. The efficacy of hyaluronic acid in the treatment of osteoarthritis of the trapeziometacarpal joint. J Hand Surg Am 2009;34:942-4.
38. Figen Ayhan F, Ustün N. The evaluation of efficacy and tolerability of Hylan G-F 20 in bilateral thumb base osteoarthritis: 6 months follow-up. Clin Rheumatol 2009;28:535-41.
39. Heyworth BE, Lee JH, Kim PD, Lipton CB, Strauch RJ, Rosenwasser MP. Hylan versus corticosteroid

versus placebo for treatment of basal joint arthritis: a prospective, randomized, double-blinded clinical trial. J Hand Surg Am 2008;33:40-8.
40. Gabay C, Medinger-Sadowski C, Gascon D, Kolo F, Finckh A. Symptomatic effects of chondroitin 4 and chondroitin 6 sulfate on hand osteoarthritis: a randomized, double-blind, placebo-controlled clinical trial at a single center. Arthritis Rheum 2011;63:3383-91.
41. Güler-Yüksel M, Allaart CF, Watt I, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, van Schaardenburg D, et al. Treatment with TNF-α inhibitor infliximab might reduce hand osteoarthritis in patients with rheumatoid arthritis. Osteoarthritis Cartilage 2010;18:1256-62.
42. Verbruggen G, Wittoek R, Vander Cruyssen B, Elewaut D. Tumour necrosis factor blockade for the treatment of erosive osteoarthritis of the interphalangeal finger joints: a double blind, randomised trial on structure modification. Ann Rheum Dis 2012;71:891-8.
43. Kvien TK, Fjeld E, Slatkowsky-Christensen B, Nichols M, Zhang Y, Prøven A, et al. Efficacy and safety of a novel synergistic drug candidate, CRx-102, in hand osteoarthritis. Ann Rheum Dis 2008;67:942-8.
44. Smith AS, Doré CJ, Dennis L, Julius A, Mackworth-Young CG. A randomised controlled trial of subcutaneous sodium salicylate therapy for osteoarthritis of the thumb. Postgrad Med J 2010;86:341-5.
45. Vermeulen GM, Slijper H, Feitz R, Hovius SE, Moojen TM, Selles RW. Surgical management of primary thumb carpometacarpal osteoarthritis: a systematic review. J Hand Surg Am 2011;36:157-69.
46. Wajon A, Carr E, Edmunds I, Ada L. Surgery for thumb (trapeziometacarpal joint) osteoarthritis. Cochrane Database Syst Rev 2009;4:4631.
47. Badia A. Total joint arthroplasty for the arthritic thumb carpometacarpal joint. Am J Orthop (Belle Mead NJ) 2008;37:4-7.
48. Furia JP. Arthroscopic debridement and synovectomy for treating basal joint arthritis. Arthroscopy 2010;26:34-40.
49. Wollstein R, Watson HK, Martin RT, Taieb A, Pankonin D, Carlson L. Long-term durability of tendon arthroplasty with excision of the trapezium in stage 1 osteoarthritis of the thumb CMC joint. Ann Plast Surg 2009;62:358-60.
50. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken) 2012;64:465-74.