

Rehabilitation in knee osteoarthritis patients in 2020. Narrative review

Florin Ovidiu Fugaru¹, Adina Kamal², Diana Kamal³, Diana Trașcă⁴, Kamal Constantin Kamal⁵,
Magdalena Rodica Trăistaru⁶

¹ PhD Student, University of Medicine and Pharmacy of Craiova, Romania

² Department of Clinical Nursing-Internal Medicine, University of Medicine and Pharmacy of Craiova, Romania

³ Department of Physical and Rehabilitation Medicine, Sama Medical Center, Craiova, Romania

⁴ Department of Internal Medicine, University of Medicine and Pharmacy of Craiova, Romania

⁵ Department of Family Medicine, University of Medicine and Pharmacy of Craiova, Romania

⁶ Department of Physical and Rehabilitation Medicine, University of Medicine and Pharmacy of Craiova, Romania

Abstract

There are a multitude and variety of treatment options available for patients with knee osteoarthritis, which can be overwhelming for rehabilitation and physiotherapy healthcare professionals.

The basis of the 2020 review of rehabilitation in KOA patients was performed by our team selecting systematic reviews from Medline via Ovid, PubMed, CINAHL and Google Scholar in regard to trends and recommendations in rehabilitation / physical therapy programs in people diagnosed with KOA.

In our descriptive research, we used combinations of “osteoarthritis” and “knee”, “rehabilitation” “physical therapy”, “exercises”, “kinetic program”, “balneotherapy”, yielding a total of 965 publications. This was reduced to just 62 papers after the removal of publications dealing with clinical trials, imaging, biomechanics, biomarkers and genetics, medications, knee replacement, which are dealt with elsewhere in this rich medical literature.

The objective of our study is to assess and review the effectiveness of current available rehabilitation options for knee osteoarthritis to guide all practitioners in physical medicine and rehabilitation, for ensuring that the care they provide is safe and aligns with best practices.

Keywords: knee osteoarthritis, rehabilitation, physical therapy, exercises, kinetic program, balneotherapy.

Introduction

One of the most common subjects in the medical literature worldwide is osteoarthritis (OA) – the most prevalent chronic degenerative musculoskeletal and joint disorder, defined as the deterioration of cartilage in joints, which results in stiffness, pain and impaired movement (Lau et al., 2021), disability and decreased quality of life (Vos et al., 2012). Its definitions refer to epidemiological, pathogenic, clinical, imaging and functional data. According to this aspect, the management of OA requires a major interest in the medical fields, especially in rehabilitation and physiotherapy. Moreover, it is unanimously recognized that OA has no cure, and self-management with exercise and physical activity is a main strategy in the complex management of OA patients (Quicke et al., 2020).

Knee osteoarthritis (KOA) is the most common OA localization (Teo et al., 2020).

The dynamic process of modernization of electric and physical modalities used in physical medicine and rehabilitation characterizes the last years. Over the last few years, systematic reviews (SRs) with or without meta-analyses (MAs) have been widely used in resolving questions in various compartments of KOA management. According to the Joanna Briggs Institute (JBI), scoping reviews are useful for effectively and rigorously examining emerging evidence (Peters et al., 2020). Research mentioned in these SRs has focused especially on determining the underlying mechanisms, the health benefits of exercise and physical activity, mediation of knee state, and less on the role of physiotherapy in KOA. So, we consider that a multidisciplinary team who believes

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Address for correspondence: University of Medicine and Pharmacy of Craiova, No 2-4, Petru Rareș Str., Craiova, 200349, Romania

E-mail: kamalconstantin@gmail.com

Corresponding author: Kamal Constantin Kamal; e-mail: kamalconstantin@gmail.com

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that KOA patients should be informed by updated evidence from systemic reviews on the effectiveness of all physical therapies indicated for these patients is necessary.

We performed, to our knowledge, the first Romanian narrative overview of systematic review articles to comprehensively analyze various rehabilitation (kinetic and physiotherapeutic) programs in KOA. Based on the available English language documents published only in 2020 in four important databases - Medline via Ovid, PubMed, CINAHL and Google Scholar, we aimed to assess and perform a narrative summary of the effectiveness of all physical, kinetic and alternative interventions for KOA, in the complex management of this disease. The mentioned systematic literature reviews were hand-researched. We performed our search strategy using combinations of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords - "osteoarthritis" and "knee", "rehabilitation" "physical therapy", "exercises", "kinetic program", "balneotherapy", yielding a total of 965 publications (Fig. 1). This was reduced to 62 papers, abstracts and full texts. All studied SRs are based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and included randomized controlled trials (RCTs).

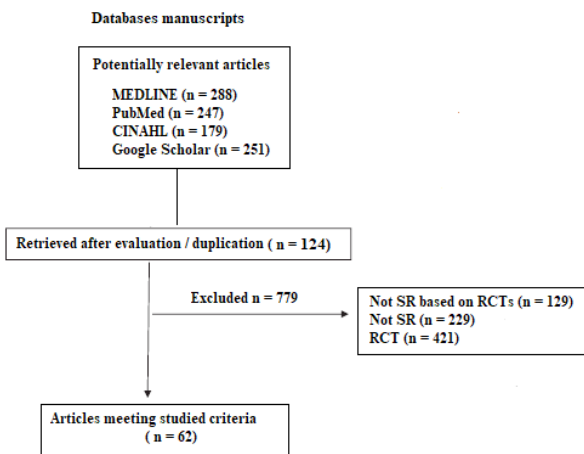


Fig. 1 – Flowchart of our narrative review

Initial literature search was performed by FOF and screening for relevance was performed by all authors, based on the authors' clinical and research expertise in the field of KOA rehabilitation. Here, we will review the current state of KOA rehabilitation in this field from a biological, clinical, and functional perspective and in terms of outcomes for pain, knee physical function and quality of life after the rehabilitation program.

Knee osteoarthritis definitions

The knee is identified as one of the most commonly affected joints in OA, being followed by the hand and hip. Described as a complex multifactorial and polygenetic disease involving structural and functional alterations of the entire joint (articular cartilage, menisci, subchondral bone, capsule, synovium, ligaments, and periarticular muscles) (Byra & Czernicki, 2020) and one of the

leading contributors to global chronic disability, KOA is characterized by joint pain and stiffness leading to functional limitations and loss in participation and quality of life (Zhou et al., 2020).

The prevalence of KOA is increasing worldwide, has an enormous health care impact, and entails a high cost to society. Although it is most prevalent in the elderly population (>65 years old, more than 70% of this population has symptomatic KOA) (Zhang et al, 2020), particularly overweight elderly people, and in persons with traumatic joint injuries (Smith, 2020), there is an increasing trend of young adults (under 55 years old) being diagnosed with KOA, estimated to affect one in eight adults. KOA now represents one of the major causes of disability worldwide, with reduced mobility of the entire population, women being twice as affected compared to men (Lau et al., 2021).

Complete diagnosis

Before considering rehabilitation for knee osteoarthritis, a complete assessment (pathogenic, clinical, paraclinical and functional evaluation) is needed, both for the joint and the patient as a whole.

The knee is a complex joint, with mechanical and biological functionalities that can be difficult to separate. The cellular and molecular events from chondrocytes which lead to KOA signs and symptoms are neither well understood nor easily measurable (Kanamoto et al., 2020).

The pathogenesis of OA disease is unclear, but studies have indicated several factors which include: articular cartilage degeneration (partial-thickness and full-thickness focal cartilage defects seem to contribute equally to the development of new cartilage damage in knee OA), subchondral bone thickening, osteophyte formation, synovium inflammation (synovitis), degradation of ligaments and menisci, and joint capsule hypertrophy (Smith, 2020). The complex morphological and pathogenic knee disturbances cause clinical symptoms – various types of pain (dull or sharp, intermittent or persistent), crepitation, swelling, stiffness, muscle weakness (especially quadriceps), instability and a decline in range of motion due to pathogenic conditions that block normal synchronous movement; all these symptoms and signs decrease physical function and quality of life (Kawabata et al., 2020). Weight-bearing activities that involve large knee flexion are biomechanically and physiologically more challenging than level walking and are thought to be the first mobility limitation observed in KOA patients. End-stage KOA results in severe pain and remarkably limited functional activities (Hislop et al., 2020).

Among contributors to global disability, osteoarthritis is among the three most disabling conditions, having a remarkable public health impact in developed countries (1).

Today, complete diagnosis of KOA is established due to imaging investigations. The imaging hallmark of OA is plain film X-ray (for changes in subchondral bone). Early bone changes - bone marrow lesions - are detected by MRI exam. The whole-organ MRI scoring method (WORMS) is used in MRI for OA, assessing damage, providing a detailed analysis of the joint (Sandhar et al., 2020). Direct visualization of the cartilage phenotype, using 3D

transport-based morphometry, defining predictive KOA, and possible diagnosis made at a potentially reversible stage will be very important in the future (Kundu et al., 2020).

Functional evaluation is important and represents one of the six domains that are mandatory in the assessment of KOA, including pain, physical function, quality of life, patient's global assessment of the target joint and adverse events including mortality and/or joint structure, depending on the intervention tested (Smith et al., 2019). Gait analysis is included as a target outcome measure in KOA patients, considering that gait is the essential function of the lower limbs (Sandhar et al., 2020). Functional examination is undertaken according to a standard evaluation form based on the International Classification of Functioning, Disability and Health (ICF) model (1) (Vongsirinavat et al., 2020).

After complete diagnosis of KOA patients, it is important to mention the KOA phenotypes to better understand the individual patient's need. Until now, six distinct KOA phenotypes have been identified through a synthesis of 24 individual studies: chronic pain, inflammatory, metabolic syndrome, bone and cartilage metabolism, mechanical overload and minimal joint disease phenotypes. Also, the research of OA phenotypes is only beginning; this aspect permits to individualize treatment options and rehabilitation treatment protocols (Primorac et al., 2020).

Optimal rehabilitation program in KOA

OA is a progressive disorder, with different degrees of severity, which requires long-term management with various treatment options over the course of the disease. The goals of treatment are to reduce symptoms and ultimately slow disease progression, which may in turn reduce the impact of OA on patient's mobility and quality of life, with a consequent reduction in healthcare resource needs.

Improvement or compensation of impaired movement function remains key to the management of KOA and is the basic principle in the ESCEO algorithm (Economic Aspects of Osteoporosis and Osteoarthritis algorithm), which provides advice for treatment prioritization and possible combination (Whittaker et al., 2020).

Several professional recommendations for KOA care (EULAR - European League Against Rheumatism, ACR - American College of Rheumatology, OARSI - Osteoarthritis Research Society International) highlight the role of non-pharmacological and non-surgical approaches including education, and weight reduction, kinetic programs (aerobics, muscle strengthening and water-based exercises - recommended first-line treatment for people with KOA), and orthotic devices, heat and cooling packing, neuromuscular electrical stimulation and other electric interventions (for example transcutaneous electrical nerve stimulation, ultrasound and low-level laser therapy), acupuncture and spa therapy (Kolasinski et al., 2020; Holden et al., 2020).

It is important to take into consideration adapting all rehabilitation programs to comorbid populations, exercise behavior change, community-based self-management education and technology support,

including alternative, low-cost, flexible delivery options, from online self-directed guides to low-tech phone contact and self-help program books and tool kits (Arden et al., 2021), as it is mentioned in several available updated guidelines for the management of KOA (Kolasinski et al., 2020).

These interventions can reduce pain and improve physical function in patients with KOA, in accordance with studies, reviews and meta-analyses published so far (Ferreira et al., 2018), with a seven-year-old remark that exercise is a key factor for managing OA (Nelson et al., 2014). The management of KOA depends on the severity of its clinical symptoms. Patients with mild KOA benefit from non-pharmacological interventions and topical non-steroidal anti-inflammatory drugs - NSAIDs. In moderate to severe cases, treatment and rehabilitation modalities include exercise, knee braces, walking aids, oral NSAIDs and surgery. Alternative treatment modalities to alleviate KOA symptoms are in high demand, because oral NSAIDs are often associated with cardiovascular diseases, kidney injury, gastrointestinal bleeding. Furthermore, rehabilitation measures may control the neuropathic pain components in KOA, especially in patients with minor bone and joint changes but with a high level of this symptom refractory to classical analgesic pharmacological treatment (Kanamoto et al., 2020; Peprah & Argáez, 2020; Rocha et al., 2020).

Pharmacotherapy measures

All rehabilitation team members have to know the recommended pharmacological measures for KOA patients. Relatively low-grade inflammation is present in the majority of OA patients, characterized by synovitis and a pro-inflammatory/ catabolic state of chondrocytes. So, non-steroidal anti-inflammatory drugs (NSAIDs), analgesic agents with topical and oral administration, and intra-articular injection of corticosteroids are indicated to control the inflammatory joint process and pain status (Nelson et al., 2014).

Recent studies have focused on new intra-articular injections of various agents which facilitate the delivery of growth factors, cytokines and morphogens, all of which have proven chondroprotective, anabolic, anti-inflammatory and immunomodulatory properties: hyaluronic acid, platelet-rich plasma, and plasma rich in growth factor articular injection, ozone therapy, prolotherapy, intra-articular botulinum toxin administration. These newer injectable therapies have safer side effect profiles (Billesberger et al., 2020; Tang et al., 2020), and research efforts to find the most effective injection therapy for knee OA continue, without a real standardization of the testing protocol (Saltzman et al., 2020).

In the last decade, the new pharmacological treatment has been focused on macrophages as key mediators in OA-associated inflammation and mesenchymal stem cells (MSCs), which have been predominantly tested with the aim to repair cartilage, in order to produce anti-inflammatory mediators and induce reparative properties in a paracrine manner (van den Bosch, 2020).

Also, multiple research groups have published their results regarding the possible protective effects of

metformin on OA development (structural damage and progression) (van den Bosch, 2020), and there is evidence in recent SRs (Ma W et al., 2020) that curcuminoids relieve the symptoms of patients suffering from KOA.

In general, pharmaceutical treatment does not promote clinically important effects in time regarding improvements in pain and function. On the contrary, exercise and physical therapy show high-quality evidence of optimal effects for patients with KOA - significant reduction of pain, improved function and quality of life (Whittaker et al., 2020).

Education and dietary intake

Today, all medical literature mentions the importance of effective education of KOA patients for optimal management. All members of the rehabilitation team, including physiotherapists, provide information and advice regarding weight loss (Sprouse et al., 2020), pain medications, physical and kinetic measures, and behavior modification techniques which influence patients' experiences of KOA, aimed at learning to live and control this disorder. Care may be improved when KOA patients are fully informed about all their treatment options, as it is mentioned in a last year review (Teo et al., 2020).

Weight management and knee joint health are two educational objectives in KOA patient management. Patients with KOA who maintain an appropriate body weight can potentially slow progression of the disease, due to greater reductions in knee compression forces (Sprouse et al., 2020).

In a review by van den Bosch, it is mentioned that dietary intake and composition likely represent an important factor that lowers the threshold for OA development. So, future OA-preventing strategies may include an adapted diet, in accordance with the gastrointestinal microbiome so sensitive to therapeutic interventions (van den Bosch, 2020). Diet is very important for people with mild to severe knee OA, which are at a high risk of sarcopenia. Several recent studies have indicated physical activity, protein supplementation in daily nutrition and protein-based diet interventions as adequate methods to improve muscle mass, muscle strength, and functional outcomes, and to reduce pain in older adults with KOA (these persons are at a high risk of sarcopenia) (Liao et al., 2020; Lo et al., 2020).

In accordance with the electronic development of our society in recent years, education tools are currently adapted. So, podcasts (portable digital audio files) have become a powerful medium and an indispensable tool in higher education for disseminating research findings, providing continuing medical education for healthcare professionals and educating patients about self-managing their condition. These podcasts promote the dialogue between them using this increasingly popular platform (Mobasheri & Costello, 2021).

In their article, Karasavvidis A. and colleagues mentioned the importance of education in KOA, even in pandemic conditions. Education on OA management along with information about physical exercises and weight loss by virtual visits to the physician could reinforce the effectiveness of exercise and weight loss programs when implemented simultaneously. The results were promising

in WOMAC pain scores and IL-6 levels (Karasavvidis et al., 2020).

Today, all researchers agree with the cost-effective or cost-saving dimension of education or diet with a kinetic program, comparatively with the well mentioned aspect that education interventions were not cost-effective compared to usual care or placebo at conventional willingness-to-pay thresholds in 2020 medical databases (Mazzei et al., 2020).

Physiotherapy

The term physiotherapy was used for any supervised, physiotherapist-led, non-invasive treatment (mobilizations and massage / manual therapy, application of ice and heat, diathermy, electrotherapy modalities) (3).

In the Romanian Physiotherapy High School, it is considered that therapy with physical agents is recommended to assist kinetic programs in the management of KOA patients.

All studied SRs mentioned that physical agents improve pain and function, increase the strength of the knee extensors, and include: thermal interventions (locally applied heat / paraffin or cold), electrical (transcutaneous electrical nerve stimulation - TENS, neuromuscular electrical stimulation - NMES, interferential current therapy - ICT), electromagnetic (pulsed electromagnetic field - PEMF, classical magnet therapy) and phototherapeutic procedures (shortwave diathermy therapy - SDT, iontophoresis, low-level laser therapy - LLLT, non-selective chromotherapy with Bioptron), extracorporeal shock wave therapy (ESWT), acupuncture (Bierma-Zeinstra et al., 2020).

The effects of various physical therapies on temporal summation and conditioned pain modulation in KOA patients with chronic musculoskeletal pain are mentioned in a systematic review and meta-analysis (Arribas-Romano et al., 2020).

So, we consider that patients with chronic pain and KOA really benefit from the process of central sensitization after physical therapy, based on various types of electrical and magnetic procedures. The most effective therapeutic modalities for KOA seem to be magnet therapy and ultrasound, and cold therapy. It is not yet known which physical resources promote the greatest improvement in clinical variables when added to exercise therapy. Probably, multimodal strategies are optimal to control / reduce the signs and symptoms of KOA (Chen AT et al., 2020).

Choosing a physical agent in the rehabilitation program for a patient with KOA depends on the equipment, the experience of the team and the particularities of the patient. After examining the published reviews in 2020 for the physical therapy of patients with KOA, we can determine the following:

- TENS – a non-pharmacological pain-reduction intervention in KOA patients is efficient (in order to best control pain and maximize functional status, *12-15 sessions over 4-6 weeks*, measured using instruments such as the visual analog scale or the Western Ontario and McMaster Universities Arthritis Index scale and *it lasts about 2 weeks*) in all patients, but with special genotyped COMT and EDNRA genes implicated in central and peripheral pain pathways. The pathogenic theories for TENS pain control are mentioned in a recent systematic

review: the gait control theory of pain and activation of endogenous opioids for nociceptive pain mechanisms, the increasing of neural drive and diminishing the excitatory effect upon removal, providing increased afferent stimuli interpreted by the central nervous system as excitatory resulting in the facilitation of inhibited motor neuron pools (Lee et al., 2020). When TENS is applied in conjunction with exercise, the results are better. TENS after exercise was proved to be more effective in increasing function and reducing disability in knee OA patients (Shamsi et al., 2020). Other researchers mentioned that TENS was not beneficial for KOA, but in small size studies with variable controls (Kolasinski et al., 2020).

- NMES - produces high muscle force at a relatively low intensity; it occurs non-selectively with regard to the type of motor unit and synchrony, and it preferentially activates type II fibers as compared with voluntary muscle contraction (Gregory & Bickel, 2005). In 2020, an interesting review was performed to provide guidelines - standardized clinical treatment parameters for neuromuscular electrical stimulation (frequency of at least 50 Hz and no more than 75 Hz with a pulse duration between 200 and 400 μ s, and a treatment duration of 20 mins) - by researching its efficacy in improving muscle strength and decreasing pain in patients with knee osteoarthritis (Novak et al., 2020). Conventional NMES can train both quadriceps and hamstring at the same time if electrodes are placed on both muscles. A higher intensity NMES is more effective but causes discomfort. In rehabilitation, electrical stimulation of quadriceps and hamstring is preferred, which are alternate and intermittent during hybrid training system, a technique to combine the application of electrical stimulation and volitional contractions (Gregory & Bickel, 2005).

- ICT – despite its widespread use, information about it is limited, and the heterogeneity across studies and methodological limitations prevent conclusive statements regarding analgesic efficacy. There is a lack of ICT specific research compared with TENS. Classically, four electrodes were placed around the affected knee joint, the intensity adopted by the stimulator was kept at a level considered strong but comfortable, throughout the treatment (Whittaker et al., 2021).

- PEMF therapy - the effects on KOA patients are still unclear, because the underlying mechanism of action of PEMFs in OA is not entirely understood; probably, the clinical results may be explained through a significant reduction in some of the most relevant pro-inflammatory cytokines in human chondrocytes; today, PEMFs are effective in preventing OA development and progression and have beneficial effects on pain, stiffness, and physical function in patients with OA. Duration of treatment may not be a critical factor in pain management. Further studies are required to confirm the effects of PEMF therapy on QOL (Yang et al., 2020).

- LLLT – is an effective modality for short-term pain relief, function improvement and disability control in patients with chronic KOA, as mentioned in the systematic reviews (Ganjeh et al., 2020).

- ESWT using medium energetic density is an effective treatment for improving pain and functionality in patients

with KOA (Avendano-Coy et al., 2020). The conclusion of last year reviews mentioned the efficacy and safety of ESWT for KOA; physical measure was efficacious and safe for reducing pain and improving knee function (in terms of the Western Ontario and McMaster Universities Osteoarthritis Index at 4-12 weeks), without increasing the risk of adverse effects (Wei et al., 2020; Ma H et al., 2020).

- acupuncture - is one of the most popular treatment modalities to control KOA symptoms; it has similar mechanisms to relieve pain without serious adverse effects like TENS. Electroacupuncture (a combination of acupuncture and transcutaneous electrical nerve stimulation) and laser acupuncture (a form of low-level laser therapy) have become popular treatments for KOA and are associated with a low risk of adverse reactions (Wu SY et al., 2020).

There is little evidence to support the use of thermal packs (used at the same time as stretching during painful episodes) or ice packs (for managing acute episodes) or alternation between heat and cold therapies. However, due to the fact that they are accessible and affordable for most patients, thermal modalities are included in OA treatment guidelines for managing pain (Whittaker et al., 2021)

Kinetic program in KOA patients

More recent reviews have pointed out the complex and complete role of therapeutic exercise (TE) in the management of KOA patients. Physical exercise appears to be the most effective therapy for controlling symptoms and can delay disease progression and thus the need for joint replacement. Exercise therapy may be recommended as a relatively safe intervention in all KOA patients (Niemeijer et al., 2020) and has beneficial effects on physical and psychosocial health in people with multimorbidities (Bricca et al., 2020). After their investigation about the role of physical activity as a conservative treatment for older KOA people, the authors of SRs mentioned that active exercise and sport are effective to improve pain and physical function; for validating the use of physical activity to control stiffness, quality of life, and dynamic balance, further studies are required (Zampogna et al., 2020).

a) The pathogenic impact of TE in KOA patients

In their review, Dalle and Koppo presented the evidence so far that describes the involvement of inflammatory signaling in pathology-related muscle wasting in KOA patients. More exactly, this disease induces morphological changes in skeletal muscle tissue in end-stage patients, including neurogenic muscular atrophy and muscle fiber degeneration. Because the changes in systemic and muscle inflammation are connected to changes in muscle molecular signaling (anabolic, catabolic, oxidative stress, etc.), muscle mass and muscle strength, it is important to include physical activity as a modulating variable when studying muscle function (Dalle & Koppo, 2020).

In 2020, Smith explained the beneficial effect of TE on the skeletal system and its role as an adjuvant to cartilage regeneration therapy. TE decreases immune cell production of osteoclastogenic cytokines and increases the production of anti-osteoclastogenic cytokines (Smith, 2020).

Other authors consider that there was no decrease in systemic inflammation markers (interleukin-6, tumor necrosis factor-alpha) and small to moderate changes in

markers of cardiovascular health (heart rate, systolic and diastolic blood pressure) occurred when KOA patients performed aerobic exercise (Schulz et al., 2020).

Some authors observed that resistance exercise training exerted benefits on lean mass or muscle hypertrophy in patients with OA, whereas others indicated no significant effects of strength training exercise on muscle mass and muscle volume. Controlling the decline in muscle mass, a risk factor for KOA, allows limiting KOA progression (Aguiar et al., 2016).

Muscle strength exercise training (MSET) is effective in increasing lean mass and muscle size in older adults with OA. Clinicians should incorporate MSET into their management of patients at risk of low muscle mass to maximize health status, particularly for older individuals with OA (Liao et al., 2020).

Knee sagittal dynamic joint stiffness may be a potentially modifiable risk factor for patellofemoral cartilage damage worsening over 2 years (Haj-Mirzaian et al., 2020). So, novel insights into kinetic programs in KOA take into consideration the prevention of patellofemoral cartilage loss through maintenance of adequate extensor/flexor muscle balance in the knee joint.

Combining exercise and cognitive behavior therapy seems to be an effective method to reduce KOA pain, even though it is based on a small number of studies. Although it is known that KOA chronic pain can result in brain structural and organizational changes, and patients' pain level, emotional status, and perception of their condition might be negatively altered, further studies are needed to reveal any differences when each intervention is applied separately (Pitsillides et al., 2021).

Although the taping technique did not produce better results in mobility and functioning improvement over non-specific knee taping, it had a higher patient-reported subjective value for symptom attenuation and experienced mobility enhancement. The pathogenic support for this functional improvement would be the neurophysiological effects due to the irritation of skin receptors and sensory neurons evoked by the tapes attached to the knee skin. The elastic taping, which applies appropriate tension along the tape and places the target muscle in a stretched position, may improve mechanoreceptors and proprioceptive input causing central inhibition of nociceptive transmission and hence modulation of pain, in line with the gate control theory of pain (Banerjee & Johnson, 2020).

b) Clinical and functional effects of TE in KOA patients

- Pain

Until now, it has been established that TE may be effective in reducing pain in people with knee OA and neutral alignment. The reviews and meta-analyses of randomized controlled trials (RCTs) of TE interventions in people with KOA provide strong evidence of, on average, small-to-medium effects on pain and function compared to non-exercise controls. These results depend on some factors, named moderators, such as socio-demographics (age), clinical assessment findings (the presence of comorbidity – obesity, cardiac problems, vascular lower limb disease), or biomechanical factors (joint malalignment) (Quicke et al., 2020). Future research is

needed to increase statistical power for moderator analyses before drawing firm conclusions about how TE controls pain in different clinical subgroups of KOA patients.

The effect size on pain is variable. Strength training or exercise therapy alone showed a small effect size on pain compared to the moderate effect of exercise therapy plus manual mobilization. In the short term, non-weight-bearing hip and knee strengthening exercises were recommended to reduce pain in people with knee osteoarthritis (Hislop et al., 2020).

A systematic search conducted in seven databases concluded that stationary cycling exercise relieves pain and improves sport function in KOA patients, but may not be as clinically effective for improving stiffness, daily activity, and quality of life (Luan et al., 2020).

Resistance training improves pain and physical function in knee osteoarthritis. Greater improvements in pain tend to be associated with higher functional levels. Large effect sizes were associated with 24 total sessions and 8- to 12-week duration. No optimal number of repetitions, maximum strength, or frequency of sets or repetitions was found. The most common regimen was a 30- to 60-minute session of 2 to 3 sets of 8 to 12 repetitions with an initial resistance of 50% to 60% of maximum resistance that progressed over 3 sessions per week for 24 weeks (Turner et al., 2020).

Pain in KOA patients has a multidimensional aspect, so various types of physical therapy are available and applied. One of these is kinesiology taping. When comparing the therapeutic effects between physical therapy (PT) combined with kinesio-taping (KT) and PT alone in knee osteoarthritis treatment, the authors of a systematic review established that PT combined with KT provided a better therapeutic effect regarding pain reduction and functional improvement in patients with knee osteoarthritis (Lin et al., 2020). The results could last at least six weeks after initial treatments.

Xie and colleagues conducted a systematic review and meta-analysis to assess the effect of internet-based rehabilitation programs on pain and physical function in patients with knee OA. The results showed that internet-based rehabilitation programs could improve pain, but not physical function for KOA patients (Xie SH et al., 2021).

- Muscle strength

Pain was considered to be a limiting factor for physical function (strength and range of motion), and a pain–weakness–pain vicious circle would be formed in the progression of KOA. Most of the exercise programs had a significantly positive outcome result in both criteria (pain and muscle strength), but mainly for pain relief (Rocha et al., 2020). So, the common denominator in all articles that performed muscle strengthening, regardless of the kinetic protocols used, is the improvement of pain.

A physical method for increasing the muscular strength of the quadriceps for patients with painful KOA is blood-flow restriction (BFR). Because quadriceps strengthening requires heavy resistance that can increase knee pain, BFR (which involves placing a pneumatic cuff proximal to the muscle to limit blood flow during exercise; based on brief periods of vascular occlusion which cause muscle hypertrophy and increased strength) may be a low-load

alternative to increase quadriceps strength in people with pain KOA, as concluded by Cant and colleagues (Cant et al., 2020).

An ideal kinetic program for the treatment of pain and muscle strength in KOA patients would include isometric and quadriceps femoris and crural ischial muscle isotonic strengthening exercises, especially quadriceps isotonic strengthening, crural and gastrocnemius ischial muscle dynamic stretching and other proprioception and balance exercises. The duration of the intervention was very variable (Rocha et al., 2020).

- *Joint instability*

While in general, previous reports of common exercise treatment of age-related OA showed functional improvements, exercise therapy focusing on knee joint stabilization tended to be effective for patients with knee OA and many instability episodes. So, prior to exercise therapy for knee joint instability, evaluation of muscle strength and knee joint instability, and appropriate treatment protocols (education, medication, physical therapy), may improve the treatment for knee joint instability.

One review conducted after searches in three databases concluded that exercise therapy focusing on joint instability, including muscle maintenance and strength training, and specific training targeting knee instability have no additional beneficial effects on knee joint instability (Kawabata et al., 2020).

- *Proprioceptive acuity and motor control*

Theoretically, osteoarthritis may lead to a decrease of proprioceptive function and sensory input, thus affecting patients' ability to maintain balance. There is a lot of evidence of the effects of cognitive tasks on motor performance in patients with knee conditions (Abdallat et al., 2020). Alterations in neuromuscular control of the knee joint are common in knee osteoarthritis, but there have been conflicting results in terms of proprioceptive deficit in osteoarthritic knees. Studies comparing proprioception in osteoarthritic and healthy knees of an age-matched control group using thresholds to detect passive motion or joint position sense tests were reviewed in 2020 and published in 2021 (Lee et al., 2021). The conclusion was that the knee proprioceptive acuity of patients with KOA was poorer than that of patients with unaffected knees.

Quadriceps weakness is also a risk factor for early-onset post-traumatic knee osteoarthritis (PTOA). Identifying the strength, control and timing of muscle force deficits in accordance with neural adaptations in the PTOA population justifies targeted rehabilitation strategies and optimal recovery based on adapted kinetic measures (Tayfur et al., 2021).

A review of studies on how exercise affects measures of pain processing and motor function in KOA concluded that following an exercise program (range 5-12 weeks), there were no statistically significant changes in pressure pain threshold, temporal pain summation and voluntary quadriceps muscle activation (Hall et al., 2020).

In 2020, Xie C and colleagues reported a higher methodological quality and more rigorous reporting quality for the effects of Otago exercise on falls and balance in patients suffering from OA (Xie C et al., 2020).

A narrative review was aimed at investigating the

effectiveness of virtual reality (VR) in the rehabilitation of elderly patients with knee or hip osteoarthritis, but the conclusion was that effectiveness of VR-based rehabilitation is unclear and not sufficient to create clinical guidelines, although interventions based on VR are promising in view of postural and proprioception training and pain management (Byra & Czernicki, 2020).

- *Quality of life*

Worldwide, the benefit of physical activity on function and quality of life is recognized (QOL) in osteoarthritis patients. How the relief of pain has a direct favorable impact on QOL will be mentioned here, as well as other conclusions of review studies for QOL, besides the ones mentioned before, in the *Pain* subchapter. A systematic review included in the study randomized controlled trials investigating the effect of adding hip exercises to quadriceps exercises in KOA people on pain, function and QOL (Hislop et al., 2019). The conclusion was that this addition resulted in greater improvements in patient-reported pain, walking and QOL.

Zampogna et al. reported no significant differences in improvements in pain, physical function, and QOL between aquatic and land-based exercise; when analyzing sports, such as Baduanjin, Tai Chi, or yoga, all the studies presented significant improvements in pain, stiffness, physical function, and QOL after the rehabilitation program (Zampogna et al., 2020).

A systematic review examined the effects of technology-supported exercise programs on knee pain, physical function, and QOL of individuals with KOA and/or chronic knee pain. The technology types and program features that were associated with health values were identified, so this kind of delivering the exercise programs appears to offer benefits (Chen et al., 2021).

c) *The TE types indicated in KOA*

The unanimously accepted definition of TE is - a physical activity that involves repetitive voluntary contractions of limb, back, or abdominal muscles that are of sufficient force to maintain or improve physical conditioning (Smith, 2020); it is planned, structured, repetitive and purposeful for the improvement or maintenance of a specific health condition. TE has great potential to reduce pain and improve muscular strength, balance, and range of motion in individuals with osteoarthritis (Bielecki & Tadi, 2021). Dosing parameters are needed to ensure the best practice guidelines for knee osteoarthritis. Exercise is associated with better outcomes (pain perception, knee function recovery, mobility, improvement of the movable degree of the knee joint, quadriceps strength and adverse events: increase of pain or disease activity, various dysfunctions of the knee joint) when supervised (Chen L et al., 2020).

Evidence exists to support the utilization of various forms of exercise.

Both traditional (for example – strengthening, resistance and endurance, flexibility, aerobic / walking and proprioceptive based exercises / balance training) and non-traditional exercises (for example - mind-body exercise, Tai Chi, yoga, and aquatic exercise) have been shown to be effective in the management of KOA (Li R et al., 2020).

Land-based exercise and strength training are recommended as core treatments for all patients with KOA. Exercises were performed to enhance muscle strength, mainly the gluteus medius, maximus and quadriceps. Various procedures are mentioned for use of loads, repetitions and implementations of loads over time. The maximum load was defined before the first treatment session and, when necessary, reviewed at the end of each week (Hislop et al., 2020). The recent systematic review of Hislop AC and colleagues demonstrated greater gains in quadriceps strength with high-intensity compared to low-intensity resistance training in people with KOA, associated with greater improvements in symptoms and disability. Strengthening of the upper leg muscles is thought to be one of the factors involved in reducing pain associated with knee OA. The benefits often last less than one year because people often fail to maintain exercises in the long term (Li R et al., 2020).

In general, lower impact activities (walking, swimming, biking, yoga) are preferred over higher impact activities (running, jumping) in order to lessen pain with exercise. Weight-bearing strength training, non-weight-bearing strength training, and aerobic exercise have all been shown to be effective for short-term pain relief in knee OA, with non-weight-bearing strength training being the most effective (Shamsi et al., 2020).

Resistance training exercises involve muscle actions that are concentric and eccentric. Concentric actions are vital in stair ascent, standing up, and rising from a chair. Eccentric exercise actions, essential in daily activities, such as descent, squatting or sitting into a chair, are characterized by low energy cost, high force production, hypertrophic impact and favorable effect on fall risk and physical function and mobility. Resistance training and endurance training are especially beneficial for pain and balance in osteoarthritis of large joints such as the knee (Bielecki & Tadi, 2021).

Many recent available studies have concluded that backward walking or retrowalking can improve the symptoms of KOA patients and represents one of the kinetic choices, but there is a lack of evidence-based medical research. As opposed to forward walking, retrowalking is a counter sequential exercise and has a helpful effect on improving lower limb proprioception, gait synergy and limb balance (Wu Y et al., 2020).

The Otago exercise program, formulated in 1997, is a home-based fall prevention program, to target the modifiable fall risk factors of lower limb weakness and impaired balance of old people, by guiding the elderly to carry out individual and step-by-step muscle strength and balance function exercise. Otago exercise consists of 2 parts of training, with clear indications for the time, intensity and frequency of the exercise. The first part includes flexibility training, lower limb muscle strength training, and balance function training. The second part is walking training (Punlomo et al., 2020). A single recent review reports the evidence of higher methodological quality for the effects of Otago exercise on falls and balance in patients suffering from OA (Xie C et al., 2020).

Tai Chi is a form of mind-body therapy and low impact

and aerobic exercises. Previous biomechanical studies of Tai Chi only focus on pain, physical function, kinematics and kinetics of the knee joint for KOA. This type of kinetic program includes many fundamental postures that flow smoothly from one to another, and it is an effective management for individuals with KOA because it can reduce pain and promote muscle endurance, motor control and postural stability (Zhang et al., 2020). It can be an appropriate and safe therapy for old-aged people (Ren et al., 2020).

Baduanjin kinetic therapy is a Chinese form of low-intensity aerobic exercise, containing eight movements, with a real benefit on reducing pain and improving physical function in KOA patients (Li J et al., 2020). One review was performed based on a literature search conducted in 10 databases and included eligible trials in which Baduanjin was applied either alone or as an adjuvant treatment for baseline pharmacological measures in patients with KOA. The results proved that this Chinese type of kinetic program could improve physical function and pain in KOA (Zeng et al., 2020).

Also, proprioceptive neuromuscular facilitation and static stretching show excellent results as an adjunctive treatment in an exercise program for OA management; only a few studies included that therapy as a favorable technique in the rehabilitation program of osteoarthritic patients (Rocha et al., 2020).

Elastic taping has significant effects on pain, physical function, range of motion, and quadriceps muscle strength in KOA patients. The elastic bands used had 8 levels of resistance divided by colors, in which the more intense coloring indicated greater resistance. The sessions were held three times a week, over 8-10-12 weeks, on alternate days, lasting approximately 90 min each. The current evidence is insufficient to draw conclusions on the effects of elastic taping combined with other physiotherapy procedures for KOA. Further studies are needed to investigate the long-term effects of elastic taping combined with other forms of physiotherapy (Ye et al., 2020).

Of the exercise types available for physical therapy, the most effective appear to be strengthening and aerobic exercises, although proprioceptive exercises can also be beneficial. Backward walking, blood flow restriction, and hydrotherapy can increase tolerance to training. Physical exercise should be combined with educational and habit change measures. Today, self-efficacy and self-management kinetic programs are promoted. A novel finding is the conceptual link of self-determination to high adherence to strength-training exercises over 2 years among adults with KOA (Kamsan et al., 2020).

d) The rehabilitation exercise program

The SRs in 2020 performed for KOA rehabilitation are focused on three aspects: exercise-therapy, methods to deliver exercise-therapy remotely, and approaches to facilitate exercise-therapy behavior change (Whittaker et al., 2020).

In designing a rehabilitation program, consideration should be given to exercises that simulate the type of muscle activity that patients use in their daily routines.

The pathogenic knowledge of KOA allows the election and performance of an optimal rehabilitation program. Each method of rehabilitation justifies its choice by its effects on the physiology of the organism, especially on the components of the neuromyoarthrokinetic system (Hislop et al., 2020). Holden and colleagues mentioned in their narrative review that numerous types of therapeutic exercise may be utilized at varying doses and in different settings to improve pain and function for people with knee and hip osteoarthritis. Moreover, this review informs us how to implement best practice therapeutic exercise, at a sufficient and appropriate dose (Holden et al., 2020). Active exercise and sport are effective to improve pain and physical function in elderly people with osteoarthritis. However, the benefit seems to be short (< 6 months)

and most clinical trials assessing the impact of physical activity, especially land-based exercises, have a short-term follow-up ranging from 6 to 12 weeks (Zampogna et al., 2020).

Most SRs promote low-impact, moderate-intensity physical activity for adults with KOA, which includes aerobic, balance, and muscle strengthening components. Until now, no optimal dose of therapeutic exercise (intensity, frequency, duration) that produces improvements in clinically and person-relevant KOA outcomes has been identified (2). Exercise regimens (different protocols used, optimal combination) may be adapted according to the clinical and functional KOA patient status (Table I).

Table I

Types of physical therapy / exercises recommended in KOA in accordance with 2019 ACR Guidelines published in 2020.

Types of exercises	Description	References
Strengthening exercises (land-based) (for any type of KOA) Strongly recommended	Muscle strengthening in their daily schedule / resistance training (high-intensity / low-intensity) - improves symptoms (patient-reported pain) and physical function	Shamsi et al., 2020
	For resistance training, two sessions per week, with two sets of 8 to 12 repetitions at a load of 60% to 70% of one repetition maximum with a rest period of 48 h between resistance training sessions are indicated.	Smith, 2020
	Resistance training can produce favorable responses independently of the type of equipment (dynamometers, weights, bands) utilized, the type of exercise (e.g., isokinetic, isotonic), and the muscle action (i.e., isometric, eccentric, concentric) performed.	Hislop et al., 2020
	Mixed program - strengthening and endurance training / aerobic exercise - reduces pain, relieves stiffness, and improves physical function; it should include low impact like walking or preferably cycling, daily, and a minimum of 150 min of moderate intensity or 75 min of vigorous intensity aerobic exercise per week in sessions of at least 10 min	Rocha et al., 2020
Functional neuromuscular exercises (land-based) Strongly recommended	Stepping, single-leg squat, step-downs. Effects on psychosocial characteristics such as kinesiophobia or self-efficacy. Adding resistance hip exercises to quadriceps exercises is beneficial for patient-reported outcomes and physical function in the short-term. Functional neuromuscular hip exercises combined with quadriceps exercises improved physical function (walking)	Hislop et al., 2020
Aquatic cycling (for any type of KOA) Strongly recommended	Improves knee stiffness and pain, and physical functioning. An intensive aquatic resistance training program had a small short-term impact on knee stiffness.	Zampogna et al., 2020
Home exercise program (especially for severe KOA) Strongly recommended	Exercise is highly recommended (walking, stretching, home cycling and muscle strengthening, gymnastics), alongside: <ul style="list-style-type: none"> proper nutrition virtual education on self-management strategies range of motion activities in their daily schedule use of corrective and assistive orthotics In accordance with various exercise protocols, each training session comprised a 10-min warm-up, a 40 min period of elastic resistance exercises and a 10-min cooldown period. The following exercises have to incorporate into the training design: seated chest press, seated now, seated shoulder press, hip circumduction, leg press, leg curl.	Karasavvidis et al., 2020
Tai-chi Strongly recommended	These non-traditional exercises have been shown to be effective in the management of KOA, because they can reduce pain and promote muscle endurance, motor control and postural stability.	Li Ret al., 2020
Cognitive behavioral therapy Conditionally recommended	It is important to control the emotional, cognitive and behavioral outcomes that contribute to KOA pain. The cognitive behavioral sessions ended with exercises, diaphragmatic breathing, knee muscle relaxation and walking.	Pitsillides et al., 2021
Kinesiotaping Conditionally recommended	Theraband products, whose colors denote the degree of elasticity and indicate the corresponding resistance level (yellow, red, green, blue, black or gray) Kinesiotaping combined with physical therapy provided better therapeutic effects regarding pain reduction and functional improvement in KOA patients	Banerjee et al., 2020
Balance training Conditionally recommended	Otago exercise has effects on falls and balance in patients suffering from OA.	Xie et al, 2020
Telecare (for any type of KOA) Significance uncertain	Telephone delivered physiotherapist-led exercises advice and support modestly improved physical function but not the co-primary outcome of knee pain at 6 months. Functional benefits were not sustained at 12 months.	Chen T et al., 2021

Balneotherapy

Balneotherapy, involving immersion in mineral and/or thermal waters from natural springs, interventions with natural gases, peloids / mud, and other traditional remedies (spa-therapy), has been frequently used in rehabilitation of KOA patients as a complementary and/or alternative therapy. The complete effects (mechanical, thermal, and chemical) of mineral water (sulfur and sodium chloride mineral baths) and mud on changes in pain, stiffness and the functional state (walking speed, flexion and extension range, flexor and extensor strength) of patients with KOA are mentioned in the medical literature (Varzaityte et al., 2020; Raza et al., 2020).

These mineral baths, peat mud applications alongside physiotherapy were more effective than physiotherapeutic treatment alone (Karagulle & Karagulle, 2015). Future studies will be able to determine the role of mineral water ingestion on human microbiome dynamics, with a subsequent impact on the general status of the human body.

In their review, Kamioka and colleagues set themselves the goal to summarize systematic reviews with meta-analyses of balneotherapy and spa therapy based on randomized controlled trials, and to provide a perspective for future research. They concluded that both balneotherapy and spa therapy, especially exercises under mineral water, provided significant pain relief and improved physical fitness and quality of life in chronic diseases of the musculoskeletal system and connective tissues (Kamioka et al., 2020).

Psychosocial interventions

Cognitive behavioral therapy (CBT) is important to control the emotional, cognitive and behavioral outcomes that contribute to KOA pain. Its goal is to change the patterns of thinking, behavior and attitude underlying the disorder and pathologies. It helps in relief of knee pain, improvement in functional ability when performing activities of daily living and improved ability to cope with depression and anxiety as well as to better respond to pain catastrophizing. In the last years, it has been mentioned that chronic KOA pain can result in brain structural and organizational changes, with a negative impact on patients' perception of their condition (Pitsillides et al., 2021). So, based on a small number of studies, combining exercise with CBT may enhance the therapy for patient's pain level and emotional status.

External devices

Walking aids, knee braces and modified shoes, with lateral and medial wedged insoles for patients with KOA, have a sufficiently large impact on ambulation, joint stability and/or pain to warrant use of an assistive device, and are able to tolerate the associated inconvenience. Knee bracing and foot orthoses are effective by either correcting the knee position or providing shock absorption, and may contribute to countering the pain coming from excessive knee adduction moment during walking (Zafar et al., 2020).

Various walking aids (cane, crutch, walking frame / walker) and assistive technology play a crucial role in the management of knee OA, since 90% of adult people suffering from severe knee pain report the use of canes. Reduction of pain can be achieved by using walking aids, and patients should be taught the optimal use of a cane or crutch in the contralateral hand, while wheeled walkers

are ideal for those suffering from bilateral pathologies and require maximum assistance, particularly for the elderly (Karasavvidis et al., 2020).

The monitoring of patients with KOA in the rehabilitation program is done especially for two parameters - pain and function, with the help of evaluation scales (Table II). Different generic scales are also used for quality of life. Through the variation of the score, results are obtained which allow the suited studies to be carried on, in conformity with evidence-based medicine, a long-debated feature for physical and rehabilitation medicine.

Table II
Tools/Questionnaires for Outcome Measures in KOA rehabilitation program.

Parameter	Scales
Pain	AIMS (pain subscale)
	Global knee pain (VAS)
	HAQ (pain subscale)
	Knee-Specific Pain Scale (KSPS)
	Lequesne algofunctional index (pain subscale)
	McGill Pain Questionnaire (pain intensity)
	Number of painful days (days)
	Pain during activity (VAS or NRS)
	Pain during walking (VAS or NRS)
	Pain at night (VAS)
	Pain at rest (VAS)
Stiffness	SF-36 (bodily pain (BP) subscale)
	WOMAC pain subscale (Likert/100mm) or KOOS or HOOS
Function	WOMAC stiffness scale
	ASES (disability subscale)
	HAQ (disability subscale)
	PDI (pain disability index)
	Self Reported Physical composite score (PCS) based on SF-36, SF-12
	SF-36 (subscales physical function (PF))
	WOMAC subscale Function (Likert/100mm) or KOOS or HOOS
	Performance Based Aerobic capacity/walking long distances (6-min walk test)
	Ambulatory transitions (timed up and go)
	Sit-to-stand (30-sec chair stand test)
Walking short distances (4x10m fast paced walk)	
Quality of life	SF-36 / SF-12
	KOOS QOL

Legend: KOA = knee osteoarthritis; AIMS = Arthritis Impact Measurement Scale; ASES = Arthritis Self Efficacy Scale; HAQ = Health Assessment Questionnaire; HOOS = Hip Disability and Osteoarthritis Outcome Score; KOOS = Knee Injury and Osteoarthritis Outcome Score; NRS = Numerical Rating Scale; SF-36 / SF-12 = 36-Item Short Form Health Survey / 12-Item Short Form Health Survey; VAS = Visual Analog Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Discussions

Our review does not detail all the remarkable work that has been published over the last year, but we intended to highlight common research topics that were studied by multidisciplinary medical teams and significant breakthroughs in the field of KOA rehabilitation international research.

A review of the reviews since at least the late 1980s, proposed by the National Institute on Disability, Independent Living and Rehabilitation Research, has proven that Clinical Practice Guidelines (CPGs) in principle are an ideal means to move the knowledge obtained from clinical research to practice, but all CPGs commonly have deficits, especially in terms of applicability (Dijkers et al., 2020).

Despite some guideline recommendations for physical therapy and lifestyle changes as primary treatments, the use of physical therapy for KOA declined between 2007 and 2015. In practice, non-pharmacological treatments are under-utilized (Khoja et al., 2020).

After 2015, the worldwide attitude towards KOA rehabilitation in complete management was reconsidered. We took into consideration only SRs focusing on RCTs with critical information for the formulation of a recommendation, because SRs of observational studies unrelated to adverse effects and the subsequent updates of their guidelines did not evidence critical information about how to best use and implement the recommendations in physical or kinetic therapy clinical practice for KOA patients. There was minimal overlap of the primary studies that were included in the systematic reviews. Thus, the estimates pooled separately from these systematic reviews contain some of the same data.

All included SRs reported substantial heterogeneity in their included studies due to variations in patient characteristics, disease severity, co-morbidity status, types of interventions used and choice of controls, and methodological characteristics. The heterogeneity potential of the results of studied SRs limits the generalization of results. It was unclear whether the observed outcomes were entirely due to the interventions and controls of interest, or the results were influenced by other factors. Also, none of the included SRs provided enough information about the type, intensity, duration, or frequency of physical activity to achieve optimal clinical effectiveness for KOA patients.

Furthermore, information about adherence to exercise programs and adverse events associated with exercise in patients with KOA was limited.

Based on the studied SRs, it could be concluded that there is high-quality evidence that exercise and weight loss reduce pain and improve physical function in patients with KOA. There is moderate-quality evidence that acupuncture, TENS stimulation and low-level laser therapy reduce pain and that psychoeducational interventions improve psychological outcomes. For other interventions and outcomes, the quality of evidence is low or there is no evidence from SRs (Kolasinski et al., 2020).

Physical therapy confers various term-related results (short-term <6 months, intermediate-term ≥6 to <12 months and long-term ≥12 months) for relief of symptoms, a decreased need for pain medications, functional improvements (possible articular malalignments, range of motion, aerobic capacity, quadriceps muscle strength, flexibility and lower extremity stability and performance, gait pattern), physiological well-being (Rat et al, 2020).

There is no consensus on what represents an optimal rehabilitation exercise program for KOA patients with one exception - regularly performed physical exercise should become a lifetime commitment and should be done in sufficient volume to relieve pain and improve function.

Methods to determine and promote ideal exercise-therapy prescription are needed in the future (Whittaker et al., 2020).

After all SRs, we consider the two following fundamental aspects correlated with the kinetic program in KOA patient rehabilitation:

- a variety of choices for exercise programs with positive recommendations for strengthening, without standard protocols, probably due to co-morbidities;
- the necessity to develop combined exercise protocols, both in supervised and home-based exercise programs, to preserve patient compliance and sustain long-term outcomes for pain, function and quality of life.

To increase the value of rehabilitation scoping reviews, rehabilitation stakeholders need to use existing methodological standards for the conduct, reporting, and appraisal of scoping reviews. Much work needs to be done by guideline developers to make it easier for the average rehabilitation organization and clinician to implement CPGs in daily practice. Optimal evidence-based models may use the PICO (Population, Intervention, Comparison, and Outcome) process for the management of KOA (Colquhoun et al., 2020). In the future, all rehabilitation medical professionals focused on KOA patients have to solve the debate regarding the optimal electric, thermal and kinetic modalities and their real effect on symptoms, joint function and quality of life, as well as their feasibility in the long term in accordance with KOA phenotypes (Fig. 2).

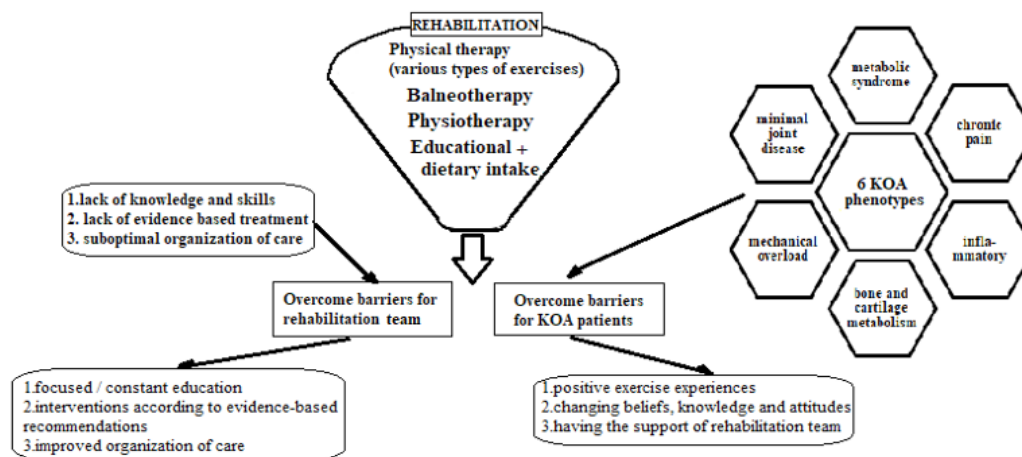


Fig. 2 – Rehabilitation in patients with KOA.

Conclusions

Our narrative review allows all members of the KOA rehabilitation team to improve and upgrade the synoptic knowledge about KOA patients.

We consider that an optimal rehabilitation program for KOA patients is possible only with the involvement of the entire team.

The role of the physiotherapist is well established in non-pharmacological management and to evaluate its effectiveness in treating pain, functional disability and the psychological outcomes of KOA patients. Also, the physiotherapist may overcome the problem of the lack of clinical psychologists to advise patients in self-managing their own conditions.

Conflict of interests

There are no conflicts of interests.

References

Abdallat R, Sharouf F, Button K, Al-Amri M. Dual-Task Effects on Performance of Gait and Balance in People with Knee Pain: A Systematic Scoping Review. *J.Clin. Med.* 2020;9(5):1554. doi:10.3390/jcm9051554.

Aguiar GC, Rocha SG, Rezende GAS, do Nascimento MR, Scalzo PL. Effects of resistance training in individuals with knee osteoarthritis. *Fisioter Mov* 2016;29(3):589-596. <http://dx.doi.org/10.1590/1980-5918.029.003.AO17>.

Arden NK, Perry TA, Bannuru RR, Bruyère O, Cooper C, Haugen IK, Hochberg MC, McAlindon TE, Mobasheri A, Reginster JY. Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. *Nat Rev Rheumatol.* 2021;17(1):59-66. doi: 10.1038/s41584-020-00523-9.

Arribas-Romano A, Fernández-Carnero J, Molina-Rueda F, Angulo-Díaz-Parreño S, Navarro-Santana MJ. Efficacy of Physical Therapy on Nociceptive Pain Processing Alterations in Patients with Chronic Musculoskeletal Pain: A Systematic Review and Meta-analysis. *Pain Med.* 2020; 21(10): 2502-2517. doi: 10.1093/pm/pnz366.

Avendano-Coy J, Comino-Suarez N, Grande-Munoz J, Avendano-Lopez C, Gomez-Soriano J. Extracorporeal shockwave therapy improves pain and function in subjects with knee osteoarthritis: A systematic review and meta-analysis of randomized clinical trials. *Int J Surg.* 2020;82:64-75. doi: 10.1016/j.ijssu.2020.07.055.

Banerjee G, Johnson MI. Should kinesiology taping be used to manage pain in musculoskeletal disorders? An evidence synthesis from systematic reviews. *Physiother - J Indian Ass Physiother.* 2020;14(1):17-21. DOI: 10.4103/PJIAP.PJIAP_31_19.

Bielecki JE, Tadi P. Therapeutic Exercise. [Updated 2021 Jan 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK555914>.

Bierma-Zeinstra S, van Middelkoop M, Runhaar J, Schiphof D. Nonpharmacological and nonsurgical approaches in OA. *Best Pract Res Clin Rheumatol.* 2020;34(2):101564. doi: 10.1016/j.berh.2020.101564.

Billesberger LM, Fisher KM, Qadri YJ, Boortz-Marx RL. Procedural Treatments for Knee Osteoarthritis: A Review of Current Injectable Therapies. *Pain Research and Management.* 2020; 2020:3873098. doi:10.1155/2020/3873098.

van den Bosch MHJ. Osteoarthritis year in review 2020: biology. *Osteoarthritis Cartilage.* 2021;29 (2):143-150. doi: 10.1016/j.

joca.2020.10.006.

Bricca A, Harris LK, Jäger M, Smith SM, Juhl CB, Skou ST. Benefits and harms of exercise therapy in people with multimorbidity: A systematic review and meta-analysis of randomised controlled trials. *Ageing Res Rev.* 2020;63:101166. doi: 10.1016/j.arr.2020.101166.

Byra J, Czernicki K. The Effectiveness of Virtual Reality Rehabilitation in Patients with Knee and Hip Osteoarthritis. *J Clin Med.* 2020;9(8):2639. doi: 10.3390/jcm9082639.

Cant JV, Dawe-Coz A, Aoun E, Esculier JF. Quadriceps strengthening with blood flow restriction for the rehabilitation of patients with knee conditions: A systematic review with meta-analysis. *J Back Musculoskelet Rehabil.* 2020;33(4):529-544. doi: 10.3233/BMR-191684.

Chen AT, Shrestha S, Collins JE, Sullivan JK, Losina E, Katz JN. Estimating contextual effect in nonpharmacological therapies for pain in knee osteoarthritis: a systematic analytic review. *Osteoarthritis Cartilage.* 2020;28(9):1154-1169. doi: 10.1016/j.joca.2020.05.007.

Chen L, Zheng JY, Li G, Yuan J, Ebert JR, Li H, Papadimitriou J, Wang Q, Wood D, Jones CW, Zheng M. Pathogenesis and clinical management of obesity-related knee osteoarthritis: Impact of mechanical loading. *J Orthop Translat.* 2020;24:66-75. doi:10.1016/j.jot.2020.05.001.

Chen T, Or CK, Chen J. Effects of technology-supported exercise programs on the knee pain, physical function, and quality of life of individuals with knee osteoarthritis and/or chronic knee pain: A systematic review and meta-analysis of randomized controlled trials. *J Am Med Inform Assoc.* 2021;28(2):414-423. doi: 10.1093/jamia/ocaa282.

Colquhoun HL, Jesus TS, O'Brien KK, Tricco AC, Chui A, Zarin W, Lillie E, Hitzig SL, Seaton S, Engel L, Rotenberg S, Straus SE. Scoping Review on Rehabilitation Scoping Reviews. *Arch Phys Med Rehabil.* 2020;101(8):1462-1469. doi: 10.1016/j.apmr.2020.03.015.

Dalle S, Koppo K. Is inflammatory signaling involved in disease-related muscle wasting? Evidence from osteoarthritis, chronic obstructive pulmonary disease and type II diabetes. *Exp Gerontol.* 2020; 137:110964. doi: 10.1016/j.exger.2020.110964.

Dijkers MP, Ward I, Annaswamy T, Dedrick D, Feldpausch J, Moul A, Hoffecker L. Quality of Rehabilitation Clinical Practice Guidelines: An Overview Study of AGREE II Appraisals. *Arch Phys Med Rehabil.* 2020;101(9):1643-1655. doi: 10.1016/j.apmr.2020.03.022.

Ferreira RM, Duarte JA, Goncalves RS. Non-pharmacological and non-surgical interventions to manage patients with knee osteoarthritis: an umbrella review. *Acta Reumatol Port.* 2018;43(3):182-200.

Ganjeh S, Rezaeian ZS, Mostamand J. Low Level Laser Therapy in Knee Osteoarthritis: A Narrative Review. *Adv Ther.* 2020;37(8):3433-3449. doi: 10.1007/s12325-020-01415-w.

Gregory CM, Bickel CS. Recruitment patterns in human skeletal muscle during electrical stimulation. *Phys Ther.* 2005;85(4):358-364.

Haj-Mirzaian A, Guermazi A, Pishgar F, Roemer FW, Sereni C, Hakky M, Zikria B, Demehri S. Patellofemoral morphology measurements and their associations with tibiofemoral osteoarthritis-related structural damage: exploratory analysis on the osteoarthritis initiative. *Eur Radiol.* 2020; 30(1):128-140. doi: 10.1007/s00330-019-06324-3.

Hall M, Dobson F, Plinsinga M, Mailloux C, Starkey S, Smits E, Hodges P, Vicenzino B, M Schabrun S, Masse-Alarie H. Effect of exercise on pain processing and motor output in people with knee osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage.* 2020;28 (12):1501-1513. doi: 10.1016/j.joca.2020.07.009.

- Hislop AC, Collins NJ, Tucker K, Deasy M, Semciw AI. Does adding hip exercises to quadriceps exercises result in superior outcomes in pain, function and quality of life for people with knee osteoarthritis? A systematic review and meta-analysis. *Br J Sports Med.* 2020;54:263-271. doi:10.1136/bjsports-2018-099683.
- Holden MA, Button K, Collins NJ, Henrotin Y, Hinman RS, Larsen JB, Metcalf B, Master H, Skou ST, Thoma LM, Wellsandt E, White DK, Bennell K. Guidance for implementing best practice therapeutic exercise for people with knee and hip osteoarthritis: what does the current evidence base tell us? *Arthritis Care Res (Hoboken).* 2020. Online ahead of print. doi: 10.1002/acr.24434.
- Kamioka H, Nobuoka S, Iiyama J. Overview of Systematic Reviews with Meta-Analysis Based on Randomized Controlled Trials of Balneotherapy and Spa Therapy from 2000 to 2019. *Internat J Gen Med.* 2020;2020:429-442. doi.org/10.2147/IJGM.S261820.
- Kamsan SS, Singh DKA, Tan MP, Kumar S. Systematic review on the contents and parameters of self-management education programs in older adults with knee osteoarthritis. *Australas J Ageing.* 2020;40(1):e1-e12. doi: 10.1111/ajag.12844.
- Kanamoto T, Mae T, Yokoyama T, Tanaka H, Ebina K, Nakata K. Significance and definition of early knee osteoarthritis. *Ann Joint.* 2020;(5):4. doi: 10.21037/aoj.2019.09.02.
- Karagulle M, Karagulle MZ. Effectiveness of balneotherapy and spa therapy for the treatment of chronic low back pain: a review on latest evidence. *Clin Rheumatol.* 2015;34(2):207-214. doi: 10.1007/s10067-014-2845-2.
- Karasavvidis T, Hirschmann MT, Kort NP, Terzidis I, Totlis T. Home-based management of knee osteoarthritis during COVID-19 pandemic: literature review and evidence-based recommendations. *J Exp Orthop.* 2020;7(1):52. doi: 10.1186/s40634-020-00271-5.
- Kawabata S, Murata K, Nakao K, Sonoo M, Morishita Y, Oka Y, Kubota K, Kuroo-Nakajima A, Kita S, Nakagaki S, Arakawa K, Kokubun T, Kanemura N. Effects of exercise therapy on joint instability in patients with osteoarthritis of the knee: A systematic review. *Osteoarthritis and Cartilage Open.* 2020; 2(4):100114. DOI:10.1016/j.ocarto.2020.100114.
- Khoja SS, Almeida GJ, Freburger JK. Recommendation rates for physical therapy, lifestyle counseling and pain medications for managing knee osteoarthritis in ambulatory care setting: cross-sectional analysis of the National Ambulatory Care Survey (2007-2015). *Arthritis Care Res (Hoboken).* 2020;72(2):184-192. doi: 10.1002/acr.24064.
- Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzig E, Kwok CK, Nelson AE, Samuels J, Scanzello C, White D, Wise B, Altman RD, DiRenzo D, Fontanarosa J, Girardi G, Ishimori M, Misra D, Shah AA, Shmigel AK, Thoma LM, Turgunbaev M, Turner AS, Reston J. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care Res (Hoboken).* 2020; 72(2):149-162. doi: 10.1002/acr.24131.
- Kundu S, Ashinsky BG, Bouhrara M, Dam EB, Demehri S, Shifate-Rabbi M, Spencer RG, Urish KL, Rohde GK. Enabling early detection of osteoarthritis from presymptomatic cartilage texture maps via transport-based learning. *Proc Natl Acad Sci USA.* 2020;117(40):24709-24719. doi: 10.1073/pnas.1917405117.
- Lau LCM, Fan JCH, Chung K-Y, Cheung K-W, Man GCW, Hung Y-W, Kwok CKB, Ho KKW, Chiu K-H, Yung PSH. Satisfactory long-term survival, functional and radiological outcomes of open-wedge high tibial osteotomy for managing knee osteoarthritis: Minimum 10-year follow-up study. *J Orthop Transl.* 2021;26:60-66. doi.org/10.1016/j.jot.2020.03.003.
- Lee H, Clark A, Draper DO. Effects of Transcutaneous Electrical Nerve Stimulation on Pain Control in Patients with Knee Osteoarthritis a Systematic Review. *Anesth Pain Res.* 2020;4(3):1-4.
- Lee SS, Kim HJ, Ye D, Lee DH. Comparison of proprioception between osteoarthritic and age-matched unaffected knees: a systematic review and meta-analysis. *Arch Orthop Trauma Surg.* 2021; 141(3):355-365. doi: 10.1007/s00402-020-03418-2.
- Li J, Yin S, Li R, Ge B, Su K, Song X, Zhang Z, Chang Y, Feng X, Wu N. Baduanjin exercise for patients with knee osteoarthritis. A protocol for systematic review and meta-analysis. *Medicine.* 2020;99: 44(e22963). doi: 10.1097/MD.0000000000022963.
- Li R, Chen H, Feng J, Xiao Y, Zhang H, Lam CW, Xiao H. Effectiveness of Traditional Chinese Exercise for Symptoms of Knee Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Int J Environ Res Public Health.* 2020;17(21):7873. doi:10.3390/ijerph17217873.
- Liao CD, Wu YT, Tsauo JY, Chen PR, Tu YK, Chen HC, Liou TH. Effects of Protein Supplementation Combined with Exercise Training on Muscle Mass and Function in Older Adults with Lower-Extremity Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Trials. *Nutrients.* 2020;12(8):2422; doi:10.3390/nu12082422.
- Lin CH, Lee M, Lu KY, Chang CH, Huang SS, Chen CM. Comparative effects of combined physical therapy with Kinesio taping and physical therapy in patients with knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil.* 2020;34(8):1014-1027. doi: 10.1177/0269215520928398.
- Lo JH, Uk P, Yiu T, Ong MT, Lee WY. Sarcopenia: Current treatments and new regenerative therapeutic approaches. *J Orthop Translat.* 2020;23:38-52. doi: 10.1016/j.jot.2020.04.002.
- Luan L, Bousie J, Pranata A, Adams R, Han J. Stationary cycling exercise for knee osteoarthritis: A systematic review and meta-analysis. *Clin Rehabil.* 2021;35(4):522-533. doi: 10.1177/0269215520971795.
- Ma H, Zhang W, Shi J, Zhou D, Wang J. The efficacy and safety of extracorporeal shockwave therapy in knee osteoarthritis: A systematic review and meta-analysis. *Int J Surg.* 2020;75:24-34. doi: 10.1016/j.ijsu.2020.01.017.
- Ma W, Wang S, Xu H, Xie W, Bi R. The effect of curcuminoids for treating knee osteoarthritis: a protocol for systematic review and meta-analysis. *Medicine* 2020;99:25(e20556). doi: 10.17605/OSF.IO/FZ29B.
- Mazzei DR, Ademola A, Abbott JH, Sajobi T, Hildebrand K, Marshall DA. Are education, exercise and diet intervention a cost-effective treatment to manage hip or knee osteoarthritis? A systematic review. *Osteoarthritis and Cartilage.* 2021;29(4):456-470. doi: 10.1016/j.joca.2020.10.002.
- Mobasheri A, Costello KE. Podcasting: An innovative tool for enhanced osteoarthritis education and research dissemination. *Osteoarthr Cartil Open.* 2021; 3(1):100130 <https://doi.org/10.1016/j.ocarto.2020.100130>.
- Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: the chronic osteoarthritis management initiative of the US bone and joint initiative. *Semin Arthritis Rheum.* 2014;43(6):701-712. doi: 10.1016/j.semarthrit.2013.11.012.
- Niemeijer A, Lund H, Stafne SN, Ipsen T, Goldschmidt CL, Jørgensen CT, Juhl CB. Adverse events of exercise therapy in randomised controlled trials: a systematic review and meta-analysis. *Br J Sports Med.* 2020;54(18):1073-1080. doi:

- 10.1136/bjsports-2018-100461.
- Novak S, Guerron G, Zou Z, Cheung G, Berteau JP. New Guidelines for Electrical Stimulation Parameters in Adult Patients with Knee Osteoarthritis Based on a Systematic Review of the Current Literature. *Am J Phys Med Rehabil.* 2020;99(8):682-688. doi: 10.1097/PHM.0000000000001409.
- Peprah K, Argáez C. Physical activity for chronic osteoarthritic knee pain: a review of clinical effectiveness. CADTH rapid response report: summary with critical appraisal. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2020 Jan 29.
- Peters M, Godfrey C, McInerney P, Munn Z, Tricco A, Khalil H. Chapter 11: Scoping Reviews. In Aromataris E & Munn Z (Eds.). *Manual for Evidence Synthesis.* JBI, 2020. Available from: <https://synthesismanual.jbi.global>. <https://doi.org/10.46658/IBIMES-20-12>.
- Pitsillides A, Stasinopoulos D, Giannakou K. The effects of cognitive behavioral therapy delivered by physical therapists in knee osteoarthritis pain: A systematic review and meta-analysis of randomized controlled trials. *J Bodyw Mov Ther.* 2021;25:157-164. doi: 10.1016/j.jbmt.2020.11.002.
- Primorac D, Molnar V, Rod E, Jelec Ž, Cukelj F, Matišić V, Vrdoljak T, Hudetz D, Hajsok H, Boric I, Review. Knee Osteoarthritis: A Review of Pathogenesis and State-Of-The-Art Non-Operative Therapeutic Considerations. *Genes (Basel).* 2020;11(8): 854. doi:10.3390/genes110808.
- Punlomso S, Srimuang P, Tudpor K. Fall Prevention by Otago Exercise Program based on Health Belief Model in Community-Dwelling Older Persons. *Ind J Physiother Occup Ther.* 2020;14(1):245-252. DOI: 10.5958/0973-5674.2020.00044.1.
- Quicke JG, Runhaar J, van der Windt DA, Healey EL, Foster NE, Holden MA. Moderators of the effects of therapeutic exercise for people with knee and hip osteoarthritis: A systematic review of sub-group analyses from randomised controlled trials. *Osteoarthr Cartil Open.* 2020;2(4): 100113. doi: <https://doi.org/10.1016/j.ocarto.2020.100113>.
- Rat AC, Locuille D, Vallata A, Bernard L, Spitz E, Desvignes A, Boulange M, Paysant J, Guillemin F, Chary-Valckenaere I. Spa therapy with physical rehabilitation is an alternative to usual spa therapy protocol in symptomatic knee osteoarthritis. *Sci Rep.* 2020;10(1):11004. <https://doi.org/10.1038/s41598-020-67436-1>.
- Raza HMA, Krutulyte G, Rimdeikiene I, Savickas R. Efficacy of balneotherapy and mud therapy in patients with knee osteoarthritis: a systematic literature review. *Aktuelle Rheumatol.* 2020 Oct. (Online). DOI: 10.1055/a-1157-8570.
- Ren R, Tang G, Tang C, Zhang J, Xiao X, Zhang Q. The Tai Chi training for middle-aged and elderly patients with knee osteoarthritis. A protocol for systematic review and meta-analysis. *Medicine.* 2020;99(20):e20242. doi: 10.1097/MD.00000000000020242.
- Rocha TC, Ramos PDS, Dias AG, Martins EA. The Effects of Physical Exercise on Pain Management in Patients with Knee Osteoarthritis: A Systematic Review with Metanalysis. *Rev Bras Ortop (Sao Paulo).* 2020;55(5):509-517. doi: 10.1055/s-0039-1696681.
- Saltzman BM, Frank RM, Davey A, Cotter EJ, Redondo ML, Naveen N, Kevin C Wang, Cole BJ. Lack of standardization among clinical trials of injection therapies for knee osteoarthritis: a systematic review. *Phys Sportsmed.* 2020;48(3):266-289. doi: 10.1080/00913847.2020.1726716.
- Sandhar S, Smith TO, Toor K, Howe F, Sofat N. Risk factors for pain and functional impairment in people with knee and hip osteoarthritis: a systematic review and meta-analysis. *BMJ Open.* 2020; 10:e038720. doi: 10.1136/bmjopen-2020-038720.
- Schulz JM, Birmingham TB, Atkinson HF, Woehrl E, Primeau CA, Lukacs MJ, Al-Khazraji BK, Khan MCM, Zomar BO, Petrella RJ, Beier F, Appleton CT, Shoemaker JK, Bryant DM. Are we missing the target? Are we aiming too low? What are the aerobic exercise prescriptions and their effects on markers of cardiovascular health and systemic inflammation in patients with knee osteoarthritis? A systematic review and meta-analysis. *Br J Sports Med.* 2020;54(13):771-775. doi: 10.1136/bjsports-2018-100231.
- Shamsi S, Al-Sheri A, Al Amoudi KO, Khan S. Effectiveness of physiotherapy management in knee osteoarthritis: A systematic review. *Indian J Med Spec.* 2020;11(4):185-191. doi: 10.4103/INJMS.INJMS_96_20.
- Smith JK. Review - Exercise as an Adjuvant to Cartilage Regeneration Therapy. *Int. J. Mol. Sci.* 2020;21(24):9471. doi: 10.3390/ijms21249471.
- Smith TO, Hawker GA, Hunter DJ, March LM, Boers M, Shea BJ, Christensen R, Guillemin F, Terwee CB, Williamson PR, Dodd S, Roos EM, Loeser RF, Schnitzer TJ, Kloppenburg M, Neogi T, Ladel CH, Kalsi G, Kaiser U, Buttel TW, Ashford AE, Mobasheri A, Arden NiK, Tennant A, Hochberg MC, de Wit M, Tugwell P, Conaghan PG. The OMERACT-OARSI Core domain set form measurement in clinical trials of hip and/or knee osteoarthritis. *J Rheumatol.* 2019; 46 (8):981-989. doi: 10.3899/jrheum.181194.
- Sprouse RA, Harris GD, Sprouse GDE. A practical approach to knee OA. *The Journal of Family Practice.* 2020;69(7):327-334.
- Tang JZ, Nie MJ, Zhao JZ, Zhang GC, Zhang Q, Wang B. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. *J Orthop Surg Res.* 2020;15(1):403. doi: 10.1186/s13018-020-01919-9.
- Tayfur B, Charupongsas C, Morrissey D, Miller SC. Neuromuscular Function of the Knee Joint Following Knee Injuries: Does It Ever Get Back to Normal? A Systematic Review with Meta-analysis. *Sports Med.* 2021;51(2):321-338. doi: 10.1007/s40279-020-01386-6.
- Teo PL, Bennell KL, Lawford BJ, Egerton T, Dziedzic KS, Hinman RS. Physiotherapists may improve management of knee osteoarthritis through greater psychosocial focus, being proactive with advice, and offering longer-term reviews: a qualitative study. *J Physiother.* 2020;66(4):256-265. doi: 10.1016/j.jphys.2020.09.005.
- Turner MN, Hernandez DO, Cade W, Emerson CP, Reynolds JM, Best TM. The Role of Resistance Training Dosing on Pain and Physical Function in Individuals with Knee Osteoarthritis: A Systematic Review. *Sports Health.* 2020;12(2):200-206. doi: 10.1177/1941738119887183.
- Varzaityte L, Kubilius R, Rapoliene L, Bartuseviciute R, Balcius A, Ramanauskas K, Nedzelskiene I. The effect of balneotherapy and peloid therapy on changes in the functional state of patients with knee joint osteoarthritis: a randomized, controlled, single-blind pilot study. *Int J Biometeorol.* 2020;64(6):955-964. doi: 10.1007/s00484-019-01785-z.
- Vongsirinavarat M, Nilmart P, Somprasong S, Apinonkul B. Identification of knee osteoarthritis disability phenotypes regarding activity limitation: a cluster analysis. *BMC Musculoskelet Dis.* 2020;21(1):237. doi: 10.1186/s12891-020-03260-y.
- Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, et al., Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012;380 (9859):2163-2196. doi: 10.1016/S0140-6736(12)61729-2.
- Wei HM, Shi ZJ, Zhou D, Wang J. The efficacy and safety of extracorporeal shockwave therapy in knee osteoarthritis: A systematic review and meta-analysis. *Int J Surg.* 2020;75:24-34. doi: 10.1016/j.ijssu.2020.01.017.

- Whittaker JL, Truong LK, Dhiman K, Beck C. Osteoarthritis year in review 2020: rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2021;29(2):190-207. doi: 10.1016/j.joca.2020.10.005.
- Wu SY, Lin CH, Chang NJ, Hu WL, Hung YC, Tsao Y, Kuo CE. Combined effect of laser acupuncture and electroacupuncture in knee osteoarthritis patients: A protocol for a randomized controlled trial. *Medicine (Baltimore)*. 2020;99(12):e19541. doi: 10.1097/MD.00000000000019541.
- Wu Y, Lei C, Huangfu Z, Sunzi K, Yang C. Effect of backward walking training on knee osteoarthritis: protocol of a systematic review and meta-analysis. *BMJ Open*. 2020;(10)10:e040726. doi:10.1136/bmjopen-2020-040726.
- Xie C, Wang W, Pei J, Wang H, Lv H. Effect of Otago exercise on falls in patients with osteoarthritis: a protocol for systematic review and meta-analysis. *Medicine*. 2020;99:50(e23559). doi.org/10.1097/MD.00000000000023559.
- Xie SH, Wang Q, Wang LQ, Wang L, Song KP, He CQ. Effect of Internet-Based Rehabilitation Programs on Improvement of Pain and Physical Function in Patients with Knee Osteoarthritis: Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Med Internet Res*. 2021;23(1):e21542. doi: 10.2196/21542.
- Yang X, He H, Ye W, Perry TA, He C. Effects of Pulsed Electromagnetic Field Therapy on Pain, Stiffness, Physical Function, and Quality of Life in Patients With Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Placebo-Controlled Trials. *Phys Ther*. 2020;100 (7):1118-1131. doi: 10.1093/ptj/pzaa054.
- Ye W, Jia C, Jiang J, Liang Q, He C. Effectiveness of Elastic Taping in Patients With Knee Osteoarthritis A Systematic Review and Meta-Analysis. *Am J Phys Med Rehabil*. 2020;99(6):495-503. doi: 10.1097/PHM.0000000000001361.
- Zafar AQ, Zamani R, Akrami M. The effectiveness of foot orthoses in the treatment of medial knee osteoarthritis: A systematic review. *Gait and Posture*. 2020;76:238-251. doi: 10.1016/j.gaitpost.2019.12.016.
- Zampogna B, Papalia R, Papalia GF, Campi S, Vasta S, Vorini F, Fossati C, Torre G, Denaro V. The Role of Physical Activity as Conservative Treatment for Hip and Knee Osteoarthritis in Older People: A Systematic Review and Meta-Analysis. *J. Clin. Med.*2020;9(4):1167. doi:10.3390/jcm9041167.
- Zeng ZP, Liu YB, Fang J, Liu Y, Luo J, Yang M. Effects of Baduanjin exercise for knee osteoarthritis: A systematic review and meta-analysis. *Complement Ther Med*. 2020;48:102279 doi: 10.1016/j.ctim.2019.102279.
- Zhang Z, Huang L, Liu Y, Wang L. Effect of Tai Chi training on plantar loads during walking in individuals with knee osteoarthritis. *Biomed Res Int*. 2020;2020:3096237. doi. org/10.1155/2020/3096237.
- Zhou X, Xiang K, Yuan X, Wang Z, Li K. A comparison of the effects of acupoint injection combined with hyaluronic acid versus isolated hyaluronic acid for knee osteoarthritis: A protocol for systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2020; 99(47): e23262. doi: 10.1097/MD.00000000000023262.

Websites

1. <https://www.icfresearchbranch.org/images/ICF%20Core%20Sets%20Download/>. *Comprehensive_and_Brief_ICF_Core_Sets_Osteoarthritis.pdf*. Accessed on 02.03.2021.
2. <https://www.cdc.gov/arthritis/docs/oaagenda2020.pdf>. A national public health agenda for osteoarthritis: 2020 update. Accessed on 23.02.2021.
3. <http://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice>. ACR/AF 2019. Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee; Guidelines. Accessed on 22.03.2021.