## **Review Article**

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## Non-Aggressive Treatment in Knee Osteoarthritis Patients: A Literature Review

Vahid Mazloum¹ 💿, Hadi Akbari²\* 💿

1. Clinical Care and Health Promotion Research Center, Karaj Branch, Islamic Azad University, Karaj, Iran.

2. Department of Sport Sciences, Faculty of Literature and Humanities, University of Zabol, Zabol, Iran.



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### ABSTRACT

**Introduction:** High prevalence of knee osteoarthritis (OA) in Iran and the subsequent disability have resulted in representing multifarious non-aggressive interventions with distinct influences on the disease. The aim of this study was to review previous domestic studies about the effects of conservative therapeutic options on patients with knee OA.

**Materials and Methods:** Using search engines involving IranMedex, MedLib, ISC, Google Scholar, Magiran, SID, rehabilitation, and medical journals based on defined keywords, 98 Persian language articles were found, and 37 studies were finally included in our study after applying the exclusion criteria. The type of study, the pattern of choosing subjects, patient information, the measurements, interventions, and the results were exploited from each article, and the physiotherapy evidence database (PEDro) scale was administrated to evaluate the studies.

**Results:** Based on analysis of PEDro scale results (Mean±SD for articles score: 5.89±1.29), the quality of most articles was as fair and good. The focus of conservative treatments was on exercise therapy methods, assistive devices, and physical therapy management. From a clinical perspective, the evidence indicates the appropriate effects of such treatment choices on alleviating pain, enhancing function, and improving quality of life in individuals with knee OA.

**Conclusion:** Most conservative methods can reduce pain, and improve quality of life and physical performance in patients with knee OA. However, further high-quality studies with larger sample sizes and long-term follow-ups are required to determine whether knee OA can be managed by conservative methods.

#### Keywords:

Knee osteoarthritis; Conservative treatments; Exercise therapy; Physical therapy; Pain; Function

## \* Corresponding Author:

Hadi Akbari, Assistant Professor.

Address: Department of Sport Sciences, Faculty of Literature and Humanities, University of Zabol, Sistan and Baluchestan, Iran. Tel: +98 (912) 6801872

E-mail: h.akbari@uoz.ac.ir



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#### 1. Introduction

he knee articulation, as an important joint, is exposed to multiple forces in daily activities, which makes it prone to chronic disorders, such as rheumatoid arthritis, patellar chondromalacia syndrome, arthropathies caused by certain diseases, including hemophilia or osteoarthritis (OA) [1, 2]. Among these, OA is a multifactorial disease characterized by inflammation and joint degeneration that results in progressive cartilage loss, usually accompanied by subchondral sclerosis, and in many cases, the formation of bone cysts and marginal bone growths occur [1]. In addition to these internal joint disorders, there are other symptoms, such as decreased range of motion, joint pain and effusion, cryptosis, deformity, and decreased level of function [3, 4].

OA is one of the most common diseases in the world and often occurs in the knee joint [5]. Its complications cause physical limitations and reduced quality of life [4]. OA involves more than 60% of people over the age of 40 [6]. The exact cause of this disease is still unknown; however, endocrinological disorders, heredity, obesity, overload on the joint, and recurrent microtrauma have been suggested as some possible causes [7-9]. In Iran, various studies have pointed to the high prevalence of this complication, especially in the elderly. It has been stated that factors, such as deformity of the joint in a standing position, knee range of motion, and menisci rupture, have a significant effect on this disease. These studies indicate that variables, such as height, weight, knee injury, history of knee infection, and lifestyle are among the factors affecting this complication [10, 11].

The high prevalence of knee OA, along with the progressive disability in performing daily activities, has caused special attention of researchers and therapists to provide optimal treatment methods to eliminate this complication or maximize the patient's ability [9]. Treatment for knee OA consists of two main parts: Aggressive treatments (such as total knee arthroplasty) and conservative treatments [12, 13]. Knee OA should first be managed using conservative or nonsurgical treatment options (such as exercise, heat, cold, ultrasonic therapy, electromagnetic therapy, transcutaneous electrical nerve stimulation, orthoses, patellar taping, acupuncture, patients' training, and low-level laser therapy) [14]; however, if this approach fails, the surgical option can be performed. In Iran, in recent years, various treatment methods with different goals for these patients have been considered in previous studies; however, the effectiveness of these treatments is not well-known, and no studies are available to compare these treatments. Therefore, this study was conducted to review Persian language studies on conservative methods in the treatment of patients with knee OA and introduce the most appropriate treatment option for these patients.

#### 2. Materials and Methods

#### Type and design of the study

This review study was conducted to review Persian language studies between April 7, 2001, to March 18, 2021, on the effect of conservative treatment methods on knee OA.

#### Search strategy

Selected databases for the search included IranMedex, MedLib, ISC, Google Scholar, Magiran, SID, and all journals related to rehabilitation, physical medicine, physiotherapy, and sports medicine. Keywords used in this search included knee osteoarthritis, osteoarthritis of the internal compartment of the knee, degenerative knee joint disease, exercise therapy, hydrotherapy, electrotherapy, physiotherapy, manual therapy, taping, orthoses, brace, strengthening exercises, stretching exercises, conservative therapies, and non-aggressive treatment [15, 16]. The search strategy is listed in Appendix 1.

#### Selection criteria and study appraisal

The inclusion criteria were as follows: Persian language articles in the form of quasi-experimental studies or clinical trials about the effects of conservative therapies on pain intensity, balance, proprioception, muscle strength, performance level, physical ability, quality of life, and muscle activity in patients with knee OA, full-text articles, and studies, in which subjects were humans [16-19]. Exclusion criteria were as follows: Studies, in which subjects with knee OA were compared with healthy individuals, articles presented at student or national or international conferences and seminars, student dissertations of all degrees in different fields, review studies, and case studies. Also, studies, in which subjects had other knee joint problems (such as ligament rupture or meniscus lesions) in addition to knee OA, studies, in which conservative treatment was used combined with an aggressive therapeutic intervention (such as surgery or acupuncture), were removed from the review [15, 18, 19].

After searching in the mentioned databases, 98 articles were found and following reviewing and applying the inclusion and exclusion criteria, 37 articles were finally included in the study (Figure 1). The following items

were extracted from each article: Type of study, sampling method, characteristics of the subjects participating in the study, therapeutic intervention used and the duration of its application, outcome measures examined, and research results.

In the present study, the physiotherapy evidence database (PEDro) scale, one of the practical and valid methods for evaluating studies in review studies, was used to evaluate the validity of selected studies (Table 1) [20]. This method, which was last reviewed and modified in 1999 and has previously been used in review studies of various treatments for knee OA [21-23], consists of 11 items, and the answer to each item is marked with two signs: Positive (correct execution of the item in the study) or negative (incorrect execution of the item or not mentioning it in the study). Scoring on this scale is such that each positive answer has a score, and a negative answer has no score. A positive answer to the first question is not considered as a positive score. The total score was calculated from the sum of scores obtained, which varies from zero to ten, and a higher total score indicates a higher quality of study. The final evaluation of this scale is as follows: (1-3=poor; 4-5=fair; 6-8=good; and 9-10=excellent).

The information on the reviewed articles is shown in Table 2. After peer-reviewing the selected articles, the quality of the evidence was evaluated using the PEDro index (Table 3). Qualitative evaluation of evidence (Table 3) showed that the Mean±SD of the total score of articles is 5.89±1.2, respectively. Among these studies, only one article had an excellent quality [24], and one had a poor quality [25]. Among them, 22 articles (59.46%) had good quality [26-47] and 13 articles (35/14%) were also of fair quality [23, 48-59]. As can be seen in Table 2, the reviewed articles in terms of study type, sampling methods, subjects used, interventions used, and outcome measures evaluated, and the results were also analyzed so that in each of these cases, there were differences. Among the evaluated studies, 14 articles were designed as clinical trials [24, 27, 31-33, 35, 37, 39, 44, 45, 47, 48, 51, 52] and 20 articles were experimental and quasi-experimental [23, 26, 28-30, 34, 36, 38, 40-43, 46, 49, 50, 55-59].

Among the reviewed studies, in two articles, the sampling method was random [23, 54]. In nine studies, the sampling method was not mentioned [29-31, 33, 44, 49, 51-53], while in other studies, other sampling methods, such as non-random sampling method or purposive/targeted and convenience/accidental sampling were used [24-26, 28, 32, 34-43, 45-48, 50, 55-59]. In terms of gender, 14 articles used male and female subjects [23-25, 27, 31-34, 48, 51, 53, 54, 56, 58], 18 articles used only female subjects [29, 30, 35, 37, 39-47, 49, 50, 52, 55, 57], and five articles also used only male subjects [26, 28, 36, 38, 59].

The column for the interventions used in studies in Table 2 shows the various methods used to treat knee OA, of which 15 studies used exercise approach (such as exercise therapy, core stability exercises, pilates, and hydrotherapy) as their intervention [25, 26, 28, 29, 36, 40, 41, 43, 46, 49, 50, 54, 55, 57, 59], while in six studies, assistive devices were used [30, 31, 34, 53, 54, 58]. Manual therapy approaches (such as taping, massage, and mobilization) were used as therapeutic interventions in three studies [27, 35, 48]. Physiotherapy intervention in the various forms of electrotherapy [39] and joint traction [32, 33, 37, 51, 52] were used in six articles to treat knee OA. In 12 articles, combination therapies (including both exercise therapy and electrotherapy or manual therapies and exercise therapy) were utilized [23, 24, 27, 33, 35, 37, 38, 42, 44, 45, 47, 56].

Among the evaluated studies, 22 articles examined the performance and physical ability of patients with knee OA [24, 26-29, 31-34, 36-40, 43, 45, 48-50, 52, 53, 56], of which, only seven articles used field tests [24, 26, 36-38, 40, 53] to evaluate this variable and the rest of the research often used standard the Western Ontario and McMaster universities osteoarthritis index (WOMAC) and knee injury and osteoarthritis outcome score (KOOS) questionnaires to evaluate performance. Among the evaluated outcome measures, pain intensity was considered in 19 articles [24, 25, 29, 32, 33, 35-37, 39, 40, 42, 43, 45, 46, 51, 53-55, 57], and most used the visual analogue scale (VAS) or WOMAC questionnaire to assess pain intensity. Balance variables (static and dynamic) were also studied in 11 studies [25, 26, 30, 40-42, 44, 46, 47, 55, 59]. Other variables, such as muscle strength and function, proprioception, and knee joint range of motion were also considered by researchers in eight articles [23, 24, 33, 36, 37, 52, 57, 58].

Among the treatments used, 14 studies used an intervention lasting six weeks or more, and other studies identified a shorter duration to determine the effectiveness of treatment [26, 28, 29, 31, 32, 36, 40, 42, 43, 46, 49, 50, 55, 56, 59]. Among them, only five studies [27, 37, 39, 41, 51] examined the long-term effects of the interventions used in a one-month or one-week follow-up period.

#### 3. Results

Based on analysis of PEDro scale results (Mean±SD for articles score: 5.89±1.29), the quality of most articles was as fair and good. The focus of conservative treatments was on exercise therapy methods, assistive devices, and physical therapy management. From a clinical perspective, the evidence indicates the appropriate effects of such treatment choices on alleviating pain, enhancing function, and improving quality of life in individuals with knee OA.

#### 4. Discussion

This study aimed to review Persian articles related to the effects of non-aggressive and conservative treatments on patients with knee OA. For this purpose, 37 articles were carefully examined and analyzed, which showed that researchers in Iran consider different methods of conservative treatment for this disease, and each of them will discuss in detail.

#### **Exercise therapy intervention**

Studies have shown that the therapeutic exercise approach has been considered more than other conservative methods in the rehabilitation of patients with knee OA. Methods used in therapeutic exercises for knee OA patients included neuromuscular control exercises, Pilates, hydrotherapy, Tai Chi, and core stabilization exercises.

The intervention used in five studies was hydrotherapy [26, 43, 49, 50, 57]. The duration of treatment in four studies [43, 49, 50, 57] was eight weeks, and in one study [26] was six. The results of those five articles showed that the use of hydrotherapy could reduce pain and improve quality of life and function in patients with knee OA. However, in the study by Yalfani et al. (2012), the dynamic balance variable was also evaluated, and the results indicated the favorable effects of exercise therapy in water on this variable [26]. In this study, a group received hydrotherapy as their rehabilitation protocol and a group received routine physiotherapy treatment (ultrasound, TENS, infrared, and stretching exercises for the quadriceps and strengthening exercises for the vastus medialis muscle) and the results showed no significant difference between the effectiveness of these two methods on dynamic balance and physical performance of subjects with this disease. The findings of this study are not consistent with the results of a previous study by Silva et al. (2008), because these researchers showed that hydrotherapy is superior to land-based training (including stretching and strengthening of the major muscle groups of the lower extremities, along with gait training) [60]. Yalfani et al. (2012) attribute this difference to the different water temperatures in this study because, in the research by Silva et al. (2008), a hydrotherapy pool with a higher temperature (30-37°C) was used that this higher water temperature can cause a relaxing effect on the muscles adjacent to the knee joint and reduce stiffness in them and in ultimately improve movement and increase physical ability. While in the study by Yalfani et al., according to the limitations mentioned by the authors, a swimming pool with a temperature of less than 27°C was used for exercise therapy in water. On the other hand, in the study by Yalfani et al. (2012) [26], the opposite group of hydrotherapy, in addition to land-based exercises, also received physiotherapy (ultrasound, TENS, and infrared), which could be another reason for the closer scores of the subjects in the two groups and the lack of significant differences. In this regard, it seems necessary to conduct further studies with longer therapeutic interventions to find out the other possible reasons for the differences found in these articles. In general, all studies have acknowledged that the effect mechanism of hydrotherapy exercises on knee OA is related to improved neuromuscular function related to movement (increased strength, endurance, and flexibility) due to the buoyancy of the water, which causes the load on the knee joint to be absorbed by the muscles around the joint, which in turn can lead to considerable pain relief and thus improve the function and quality of life of patients with this complication. Failure to absorb the loads applied to the knee joint by the muscles during daily activities or sports will cause minor fractures in the cartilage tissue and increase the severity of pain [61, 62]. Etesami et al. (2016) concluded that if the exercise program was discontinued, the beneficial effects of the hydrotherapy program will cause a decline in performance indices of patients with knee OA and suggested that the exercises continued to take advantage of the benefits [43].

Other exercise training interventions used in the studies are related to special exercises of Pilates, Tai Chi, core stability exercises, or neuromuscular control exercises. In ten studies, this type of exercise training was used as an intervention [25, 28, 29, 36, 40, 41, 44, 46, 55, 59]; in three of them, Pilates exercises were used [28, 36, 46]. In a study by Erfani et al. (2012), it was found that Pilates exercises can improve performance and quality of life in people with knee OA [28]. While a study by Mazlum and Rahnama (2014) showed that Pilates could improve proprioception and function in patients with knee OA; however, there was no significant difference compared to regular exercises [36]. The messages sent from the spindle are related to the sense of position and move-



Figure 1. Search results during the review process

ment of the limbs. These spindles may be activated during a Pilates program following an eccentric contraction or a stretching exercise. Pilates can increase the sensitivity of mechanical receptors, which enhances the mechanism of neuromuscular protective reflex [63, 64]. Jamali Masoumi et al. (2019) in their study on 26 women with knee OA, showed that 24 sessions of Pilates exercises have a positive effect on reducing pain and improving patients' balance [46]. Balance and proprioception in patients with OA are of considerable importance because many of them are elderly and have a high probability of falling; however, a review of studies showed that only two studies had examined the effect of conservative interventions on the proprioception of these patients [36, 38]. Therefore, it is necessary to investigate the effects of different types of conservative treatment methods on the knee proprioception in these patients. Among the reviewed studies, Barati et al. (2012), for the first time in Iran, examined the effect of core stabilization training programs on patients with knee OA [29]. Most research on the relationship between core stability and the occurrence of lower limb injuries suggests that strength and endurance of core muscle are associated with lower limb

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injuries in such a way that the weakness of these muscles in the closed kinetic chain can cause faulty arthrokinematic movements in the knee joint and on the other hand, strengthening of these muscles can also prevent injury [65]. Therefore, in order to investigate the effect of this type of exercise on the prevention of knee OA, a prospective study is suggested.

#### Assistive devices

A review of studies showed that six studies utilized assistive devices as a conservative intervention in the treatment of patients with knee OA. Among these studies, four articles used lateral wedge with or without subtalar joint support as their intervention [30, 31, 34, 58] and two articles used neoprene orthoses for this purpose [53, 54]. In most of these studies, it has been shown that the lateral wedge orthosis with subtalar joint support significantly improved the symptoms of knee OA. Only in research by Ahmadi and Forghani (2014), it was stated that there is no significant difference between lateral wedge and simple insole in improving the static stability of patients with knee OA [30]. In this Table 1. PEDro scale items

No.	Criteria
1	Eligibility criteria were specified
2	Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated and treatments were received)
3	Allocation was concealed
4	The groups were similar at baseline regarding the most important prognostic indicators
5	Blinding of all subjects was done
6	Blinding of all therapists who administered the therapy was done
7	Blinding of all assessors who measured at least one key outcome was done
8	Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
9	All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"
10	The results of between-group statistical comparisons are reported for at least one key outcome
11	The study provides both point measures and measures of variability for at least one key outcome

study, four types of lateral wedges were used. Among the four methods of using lateral wedges in this study, a lateral wedge outside the shoe compared to the orthosis of the lateral heel wedge inside the shoe led to a significant improvement in some variables related to balance indicating the more significant effect of using a lateral wedge outside the shoe on the static balance of people with OA in the medial side of the knee. Previous studies have not recommended the use of a lateral heel wedge inside the shoe compared to a full-length lateral wedge due to its weak effects on knee pain, function (maximum distance walked), and biomechanics [66]. However, in the study by Kamali et al. (2016), walking with an arched insole with a lateral wedge was compared with walking barefoot in terms of temporal variables of walking (stride length, rhythm, and walking speed), kinematic variables (flexion angle, extension, abduction, adduction, and rotation of the knee), and the kinetic variables (ground reaction force, anterior-posterior forces, internal-external forces, and vertical joint reaction forces of the knee) and they concluded that the lateral wedge reduces the knee adduction moment [58]. Decreased knee adduction moment is associated with a reduction in forces applied to the medial side of the knee joint. Therefore, it was suggested that the use of arched insoles will reduce pain and will make walking easier in patients with OA due to the reduction of knee adduction moment [58]. One of the models of lateral wedges is the lateral wedge with subtalar supporting [66]. In this model, the goal is to limit the movements

of the subtalar joints and, to some extent, the ankle, and as a result, the main effects of the lateral wedge applied in the knee joint [66, 67]. It seems that further studies in this field are required to make appropriate decisions.

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The use of orthoses in patients with knee OA has received much attention. Among these, two neoprene orthoses, which are usually available to everyone, and a three-pressure point corrective orthosis made by technical and orthopedic centers, are more acceptable [68]. There is little information on how and to what extent these orthoses work in improving the symptoms of these patients. Considering that the most critical symptoms of patients with knee OA are pain and decreased functional capacity of the knee in daily activities [3], assessing the effect of these orthoses on these variables is of particular importance. However, three-pressure point correction orthosis is recommended for patients to reduce or prevent the progression of articular degeneration associated with a progressive increase in the varus of the knee. However, patients' tendency to longterm usage of these orthoses occurs if their immediate effects on reducing pain and improving joint function are significant for the patients. In previous research, the duration of using orthoses, as an intervention, was short, suggesting that this issue should be considered in future studies.

Table 2. Information and details of the reviewed articles

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Yalfani et al. 2012 [26]	Quasi-exper- imental with pre-test and post-test	Targeted	36 men with knee OA (hydrotherapy group: 40.9±16.06; physiotherapy group: 40.75±5.83)	Hydrotherapy vs. physiotherapy (6 weeks)	Physical perfor- mance (up & go test) dynamic bal- ance (step test)	Physical performance and dynamic balance were improved in both groups (P<0.05), no significant difference between the effectiveness of these two methods
Tavakoli and Bahrpeyma 2011 [27]	Clinical trial	Conve- nience	30 patients (male and female) with grades 2-3 knee OA (demographic characteristics not mentioned)	Therapeutic exercises vs. mobilization vs. therapeutic exercises with mobilization (10 sessions)	Physical perfor- mance (WOMAC)	Therapeutic exercises with mobilization significantly improved physical perfor- mance
Erfani et al. 2012 [28]	Quasi-exper- imental	Targeted	15 men with knee OA (57.47±6)	Pilates (8 weeks)	Performance and quality of life (KOOS)	Pilates significantly im- proved performance and quality of life (P<0.01)
Kamali Sarvestani et al. 2012 [48]	Clinical trial	Conve- nience	36 patients with knee OA (50.6±31.65)	Manual thera- pies (10 ses- sions) vs. taping (6 sessions)	Physical perfor- mance (WOMAC)	Manual therapy and taping could improve physical performance, but manual therapies were more effec- tive (P<0.05)
Barati et al. 2012 [29]	Quasi-exper- imental	Not men- tioned	22 non-athlete women with knee OA (60.9±12.38)	Core stabiliza- tion training (8 weeks)	Pain (VAS) physi- cal performance (WOMAC)	Core stabilization training significantly reduced pain and improved performance (P<0.05)
Mehrabian et al. 2012 [49]	Quasi-exper- imental	Not men- tioned	12 elderly women with knee OA (52.70±4)	Hydrotherapy (8 weeks)	Performance (KOOS)	Performance improved significantly after perform- ing selected water exercises (P<0.05)
Ahmadi and Forghany 2014 [30]	Quasi-exper- imental	Not men- tioned	18 women with me- dial compartment knee OA (59.5±6.8)	External wedge vs. simple insole	Static stability (force plate)	There was no significant difference between an external wedge and simple insole in improving the static stability (P<0.05)
Malekzadeh et al. 2014 [50]	Quasi-exper- imental	Volun- tary and Targeted	24 women with knee OA (inter- vention group: 45.00±6.43; control group: 48.00±5.34)	Aquatic exercises (8 weeks)	Performance and the quality of life (KOOS)	Aquatic exercises can significantly improve per- formance and the quality of life (P<0.05)
Forough et al. 2007 [31]	Clinical trial	Not men- tioned	20 patients (male and female) with knee OA (lateral- wedge insole with subtalar support- ing group: Mean age=49; in-shoe lateral- wedge group: Mean age=50)	Lateral–wedge insole with sub- talar supporting vs. in–shoe lateral–wedge (8 weeks)	Performance and the quality of life (KOOS)	Lateral–wedge insole with subtalar supporting can significantly improve performance and the quality of life than in–shoe lateral–wedge in patients with varus deformity knee OA (P<0.05)
Ahadi et al. 2011 <mark>[32]</mark>	Clinical trial- randomized	Conve- nience	40 patients (male and female) with knee OA (Physical modality group: 52.30±8.48; isometric training group: 50.8±35.25)	Physical modality vs. knee isometric exercise training (4 weeks)	Pain (VAS) perfor- mance (KOOS)	Both physical modality and knee isometric exercise training can significantly reduce pain and improve performance (P<0.05)
Rahimi et al. 2012 [51]	Clinical trial	Not men- tioned	46 patients (male and female) with knee OA (demo- graphic characteris- tics not mentioned)	APS therapy vs. routine physiotherapy treatment (10 sessions)	Pain (VAS)	APS therapy can significant- ly reduce pain (P<0.05)

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Roustaei et al. 2012 [52]	Clinical trial	Not men- tioned	42 women with knee OA (aged 49-79 y)	Electrotherapy (phonophoresis) vs. iontophoresis of piroxicam gel (6 sessions)	Performance (KOOS) knee muscle function (dyna- mometer)	lontophoresis of piroxi- cam gel can significantly improve performance and enhance knee muscle func- tion (P<0.05)
Bagheri et al. 2011 [33]	Clinical trial	Not men- tioned	36 patients (male and female) with knee OA (pla- cebo laser group: 56.14±7.32; laser group: 58.32±6.45)	Low-level laser vs. placebo laser (10 sessions; 2 weeks)	Pain (VAS), knee flexion range of motion (goniom- eter), perfor- mance: quality of life (WOMAC)	All three variables im- proved significantly after the low-level laser was applied (P<0.05), no sig- nificant difference between the effectiveness of these two methods
Khademi Kalantari et al. 2009 [53]	Not men- tioned	Not men- tioned	20 patients (male and female) with medial compart- ment knee OA (53±12)	"Three pressure points" vs. "Neopran" knee orthosis	Pain (VAS) performance (6- min walk test)	Both knee orthosis can significantly reduce pain and improve the perfor- mance of patients with medial compartment knee osteoarthritis (P<0.01)
Esfandiari et al. 2012 [34]	Quasi-experi- mental	Non- random and Conve- nience	27 patients (male and female) with knee OA (47.4±3.96)	Lateral wedge insole with and without a sub-talar strap (4 weeks)	Pain, function, and quality of life (KOOS)	Using a lateral wedge insole with a sub-talar strap can significantly improve symptoms in medial knee osteoarthritis (P<0.05)
Fatemy et al. 2010 [35]	Clinical trial	Volun- tary	46 women with knee OA (demo- graphic characteris- tics not mentioned)	Swedish massage with routine physio- therapy treat- ment vs. routine physiotherapy treatment (10 sessions; 2 weeks)	Pain (VAS), per- formance: Quality of life (WOMAC)	Swedish massage with routine physiotherapy treatment can significantly reduce pain and improve performance (P<0.05)
Mazloum and Rahnama, 2014 [ <mark>36]</mark>	Quasi-exper- imental with pre-test and post-test	Targeted and con- venience	41 males with knee OA (52.8±1.9 aged)	Therapeutic exercise vs. pilates training (8 weeks)	Proprioception (Biodex system) function (aggre- gate time of four activities of daily living)	There was no significant difference between the effectiveness of these two methods on function and proprioception (P>0.05)
Mahmoodi Aghdam et al. 2013 [37]	Clinical trial	Conve- nience	40 women with knee OA (inter- vention group: 61.25±6.8 aged; control group: Aged 61.20±8.6 y)	Sustained trac- tion with routine physiotherapy treatment vs. routine physiotherapy treatment (10 sessions)	Pain (VAS) per- formance (6-min walk test) Range of motion (Goniometer)	Sustained traction with routine physiotherapy compared to routine physiotherapy treatment can significantly reduce pain (P<0.01) and improve performance (P<0.05)
Shah Hos- seini et al. 2004 [25]	Not men- tioned	Non- random and Conve- nience	30 patients (male and female) with knee OA (aged 50-65 y)	Traditional vs. new therapeu- tic methods (4 weeks)	Pain (VAS) balance (biodex system) daily ac- tivities (question- naire)	Both treatment methods were significantly effective on therapeutic parameters (P<0.05), but the neuro- muscular control treatment program was significantly more effective than the tra- ditional treatment program (P<0.05)
Majdolesl- ami et al. 2004 [54]	Quasi-experi- mental	Random, two- stage	30 patients (male and female) with knee OA (aged 33-75 y)	"Neopran" knee orthosis vs. elas- tic bandage	Pain (VAS)	"Neopran" knee orthosis is significantly more effective compared to the traditional treatment program for pain (P<0.05)

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Mazloum et al. 2016 [38]	Quasi-exper- imental with pre-test and post-test	Targeted and con- venience	26 men with unilateral knee OA (48.5±4.6)	Physiotherapy with kinesio taping® vs. phys- iotherapy with laser therapy (10 sessions)	Pain (VAS) perfor- mance (up & go test) knee joint position sense (reproduction of target angle)	Both treatment methods were significantly effective on the variables (P<0.001), but the kinesio taping <sup>®</sup> was significantly more effective on improving knee joint position sense
Taghizade Delkhosh et al. 2018 [39]	Randomized controlled clinical trial with 6 weeks follow-up	Targeted and con- venience	45 women with unilateral knee OA (demographic characteristics not mentioned)	Low vs. high power vs. place- bo laser (number of sessions not mentioned)	Pain (VAS), per- formance and dis- ability (WOMAC)	Low- and high-power lasers had Immediate and long-term effects in reducing pain and disability (P<0.001). There was no significant difference be- tween the two methods
Bagheri et al. 2016 [40]	Quasi-exper- imental with pre-test and post-test	Targeted	34 women with knee OA <45 γ)	Hip abductor- quadriceps strengthening vs. quadriceps strengthening alone (24 ses- sions; 8 weeks)	Pain (NRS), dis- ability (WOMAC) balance (single leg standing) performance (up & go test)	Both therapeutic methods on pain, disability and balance; and hip abductor- quadriceps strengthening group on performance were significantly effective (P<0.05). The mean scores of pain, balance and perfor- mance of the Hip abductor- quadriceps strengthening group were significantly better than the quadriceps strengthening alone group (P<0.05).
Zarei & Rahnama, 2018 [55]	Quasi-exper- imental with pre-test and post-test	Targeted and con- venience	25 women with knee OA (54.7±7.5)	Strengthening and Balanced vs. Strengthening, Balanced, and core-stability ex- ercise protocols (24 sessions; 8 weeks)	Static balance (single leg stand- ing) dynamic balance (Y) fear of falling (FES-I)	All variables were signifi- cantly improved in post-test of both exercise protocols (P<0.001). There was no significant difference be- tween the two groups
Kazemi et al. 2015 <mark>[56</mark> ]	Quasi-exper- imental with pre-test and post-test	Volun- tary	24 elderly patients (12 men and women) with knee OA (<40 y)	Physiotherapy- reflexology of foot vs physiotherapy (24 sessions; 6 weeks)	Knee OA symp- toms (KOOS)	The knee OA symptoms improved more in the physiotherapy-reflexology group than in the physio- therapy group (P<0.05) but no significant difference was observed between the two methods.
Ezadpanah et al. 2016 [41]	Quasi- experimental with pre-test, post-test and 1-month follow-up	Targeted and con- venience	24 inactive women with knee OA (53.58±4.94)	Therapeutic exercise (20 ses- sions; 4 weeks)	Balance (biodex balance system)	Therapeutic exercise had a significant effect on static and dynamic balance as well as overall stability (P<0.05). This change will be stable after one month of detraining.
Hassani Haghighi et al. 2016 [57]	Quasi-exper- imental with pre-test and post-test	Targeted and con- venience	30 women with knee OA (aged 50-65 γ)	Aquatic exercise therapy (20 ses- sions; 4 weeks)	Pain (VAS), electrical activ- ity of quadriceps muscle (electro- myography)	Aquatic exercise therapy did not significantly increase the electrical activ- ity of the vastus medialis, vastus lateralis, and rectus femoris, but did increase the mean of electrical activ- ity of these muscles. these exercises reduced the pain (p<0.001)

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Pouradeli et al. 2021 [42]	Quasi-exper- imental with pre-test and post-test	Targeted	31 elderly women with knee OA (aged 60-80 y)	External focus vs. the internal focus; electro- therapy and strength training of the quadri- ceps vs. hip ab- ductors muscles (24 sessions; 8 weeks)	Pain (VAS), static balance (rumberg) dynamic balance (time to get up and go) overall balance (total balance test)	A decrease showed in pain in both exercise protocols and in both types of focus of attention. Significant improvement was seen in dynamic and overall bal- ance (P<0.05). There was no significant difference in pain between two exercise protocols. There was a sig- nificant difference between internal and external at- tention in dynamic balance (P<0.05).
Etesami et al. 2016 [43]	Quasi-exper- imental with counterbal- anced mea- sures design (pre-test, post-test and mid-test)	Targeted and con- venience	30 women with knee ОА (aged 40-74 у)	Aquatic exercise therapy; during the 1 <sup>st</sup> 8-week (between pre- test and midtest), the 1 <sup>st</sup> group had no training, whilst the second group carried out their own exercise pro- gram. During the second 8-week (between midtest and post-test), the training program of groups got reversed.	Pain, disease signs and symp- toms, daily living activities, sports and functional activities, and quality of life (KOOS) in 3 time points of pre-test, post-test and midtest	<ul> <li>The results of both groups were the same;</li> <li>1) 8 weeks of no training led to no variation in any of 5 dimensions of KOOS.</li> <li>2) Training led to improve- ment of all dimensions of KOOS.</li> <li>3) Disruption of training led to lose of achievements.</li> <li>These findings were similar to those</li> <li>obtained by functional tests (P&lt;0.001).</li> </ul>
Attari et al. 2018 [44]	Clinical trial	Volun- tary and Targeted	75 women with knee OA (<60 y)	Tai Chi exercise vs. glucosamine supplementa- tion vs. control (36 sessions; 12 weeks)	Static balance (stabilometer [in both open and closed eye]) dynamic balance (TUG)	Tai Chi exercise had a significant effect on static [open and closed eye] and dynamic balance (P<0.001); the supplementation variable had a significant effect only on dynamic balance (P=0.040). A sig- nificant difference showed between the exercise and control group in static [open (P<0.001) and closed (P<0.001) eye] and dynamic balance (P=0.040).
Rafsanjani Dehghazi et al. 2016 [23]	Quasi-experi- mental	Random	15 patients with knee OA (9 men and 6 women, with the mean age of 53.50±12.31)	Proneal nerve electrical stimu- lation vs. quad- riceps electrical stimulation	Peak quadriceps- extensor moment	Peak quadriceps-extensor moment with common peroneal nerve electrical stimulation was significant- ly higher than peak quad- riceps-extensor moment with quadriceps electrical stimulation (P=0.023)

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Kamali et al. 2016 [58]	Quasi-experi- mental	Volun- tary and conve- nience	10 patients (male and female) with medial compart- ment knee OA (aged 30-60 y)	Medical insole with arch sup- port and lateral wedge vs bare- foot	Kinetics and kine- matics variables of the knee joint during gait (force plate and seven cameras)	There was no significant difference regarding the mean velocity of gait with or without wearing the medical insole (P=0.42). The 1 <sup>st</sup> peak of the applied ground reaction force on the knee joint was sig- nificantly increased while wearing the medical insole (P=0.031). The applied adductor moment on the knee joint during gait while wearing the medical insole was 0.45±0.05 N/m which was significantly lower than that of the barefoot (P<0.01).
Safari Bak et al. 2017 [59]	Quasi-experi- mental	Targeted and con- venience	24 elderly males with knee OA (aged 55-65 y)	Selected exer- cises include a variety of balance and Strengthening exercises aimed at improving strength and neuromuscu- lar control vs. control group (24 sessions; 8 weeks)	The balance indexes (biodex system; postural stability test)	A significant difference showed in the experimen- tal group between pre- and post-tests in AP (P=0.003), ML (P=0.006), and overall (P=0.001) indexes. There were significant differences between two groups in AP (P=0.03), ML (P=0.04), and overall (P=0.01) indices.
Abdollahi et al. 2019 [45]	Randomized clinical trial	Conve- nience	30 women with knee OA (aged 45-65 y)	Physiotherapy with isokinetic training (18 sessions) vs. Physiotherapy	Pain (McGill questionnaire), performance (WOMAC)	All parameters in both groups improved after treatment (P<0.05). Physiotherapy with isokinetic training was significantly more effective on improving performance (P<0.001) and reducing pain (P=0.008) compared to physiotherapy.
Jamali Masoomi et al. 2019 [46]	Quasi-experi- mental	Targeted and con- venience	26 women with knee OA (aged 50-65 y)	Pilates trainings (24 sessions; 8 weeks)	Postural stability (biodex system), pain (VAS)	Pilates training significantly reduced pain (P=0.019) and increased balance index (P=0.002). Pilates Training was significantly more effective in improving bal- ance index (P<0.001) and reducing pain (P<0.001) compared to the control group.
Moezy et al. 2018 [24]	Randomized clinical trial- double blind	Targeted and con- venience	60 patients (male and female) with knee OA (aged 50-75 y)	High Inten- sity Laser vs. conventional physiotherapy (10 sessions)	Pain, knee flexion range of mo- tion, functional tests (TUG and Six-minute walk), and WOMAC questionnaire	There were significant differences in all variables between pre and post- intervention in each group (P<0.001). There were also significant differences between groups in the pain (P<0.001), and function subscale (P=0.006), and total score (P=0.030) of WOMAC

Author(s)	Type of Study	Sam- pling Pattern	Patient Character- istics (Mean±SD of Age (y))	Intervention	The Outcome Measures (Test Used)	Results
Mohseni- pour et al. 2018 [47]	Randomized clinical trial- single blind	Targeted and con- venience	11 healthy women and 27 women with bilateral knee OA (aged 40- 72 γ)	Sham ultrasound with exercise (lower limb strengthen- ing exercises), ultrasound without exercise (10 sessions), and ultrasound with exercise	Postural sway were examined in comfort double leg standing (CDLS), Romberg standing (RS), and near tandem standing (NTS) positions on a force plate	COP displacements in the mediolateral direction were more affected than other sway directions. After the treatment, in the ultrasound without exercise group, the mediolateral (ML) range (P<0.001) and standard deviation of the ML range of COP (P<0.001) in CDLS position sig- nificantly increased. In the ultrasound with exercise group, anteroposterior (AP) range (P=0.010), the standard deviation of ML velocity (P=0.010), and ML mean velocity (P=0.010) significantly decreased in Romberg standing position.

#### Manual therapy intervention

Four studies examined the effect of different types of manual therapy interventions on patients with knee OA. In the study conducted by Tavakoli and Bahrpima (2011), three types of interventions, including therapeutic exercises, mobilization, and therapeutic exercises with mobilization were administrated to patients with knee OA [27]. This study showed that the use of therapeutic exercises combined with mobilization has more beneficial effects on physical performance. The authors also reported that these findings could persist for up to one week. Evidence suggests that mobilization improves motor activity by producing pain-reducing and sympathetic stimulus responses [69]. Suraj and Kumar (2006) stated that routine treatment of patients with OA (including TENS, ultrasound, and therapeutic exercises) could increase the knee range of motion; however, the addition of a knee mobilization technique increases the effectiveness of the treatments [70]. A review of the findings of these two researchers and other studies about the effects of mobilization technique on other joints and body segments show that the improvement in physical functioning because of using this method may be due to the reversal of reflex inhibition caused by either pain or a centrally directed response [69, 70].

In another study conducted by Kamali Sarvestani et al. (2012), the effect of manual therapy versus taping was investigated [48]. The researchers indicated that manual therapy and taping could improve physical performance in people with knee OA, but manual therapies were more effective. The authors of this article stated that the reason for the superiority of manual therapies over taping was that the taping applied only to the patellofemoral joint. In contrast,

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manual therapies were performed on both the patellofemoral and tibiofemoral joints, which in turn stimulated sensitivity and increased tensile strength of all structures around both joints. On the other hand, manual therapies cause synovial fluid to move and flow to the articular cartilage, which lacks blood vessels, due to joint movements, while taping does not have such an effect. Despite the logical documentation provided by these researchers to justify the greater effectiveness of manual therapy, it seems that another possible reason is related to the longer duration of its application compared to taping because they were applied in manual treatments for ten sessions and taping for six sessions.

Today, taping is an effective and safe intervention for many musculoskeletal disorders, and various mechanisms have been mentioned for its effectiveness. Patellofemoral joint degeneration due to abnormal patellar orientation and increased pressure on the lateral facet can be seen in most patients with knee OA. Therefore, it seems that taping can reduce pain by modifying the direction of the patella, improving patella movement, enhancing the functional mechanism of the quadriceps muscle, and reducing stress and strain on the soft tissues around the knee joint [22]. Another problem for the patient with knee disorders is the inflammation of the infrapatellar fat pad, being considered one of the causes of pain in patients with knee OA. It seems that applying taping leads to a reduction in the volume of this pad and, as a result, a significant pain reduction [71]. Despite the favorable effects of taping and being inexpensive and safe in the treatment of patients with knee OA, only two studies [38, 48] assessed the effect of this intervention on patients with knee OA, and the duration of the intervention was very short in one of them.

Author (c)		Eleven Items Based on Table 1						Total Casua	Quality of				
Author (s)	1	2	3	4	5	6	7	8	9	10	11	- Iotal Score	Evidence
Majdoleslami et al. 2004 [54]	+	+	-	-	-	-	-	+	+	+	+	5	Fair
Shah Hosseini et al. 2004 [25]	+	-	-	-	-	-	-	+	+	+	-	3	Poor
Forough et al. 2007 [31]	+	+	-	+	-	-	-	+	+	+	-	5	Good
Khademi Kalantari et al. 2009 [53]	+	-	-	-	-	-	-	+	+	+	+	4	Fair
Fatemy et al. 2010 [35]	+	+	+	+	-	-	-	+	+	+	+	7	
Ahadi et al. 2011 [32]	+	+	-	+	-	-	-	+	+	+	+	6	Cood
Bagheri et al. 2011 [33]	+	+	+	+	+	-	-	+	+	+	+	8	9000
Tavakoli and Bahrpeyma, 2011 [27]	+	+	+	-	-	-	-	+	+	+	+	6	
Kamali Sarvestani et al. 2012 [48]	+	+	-	-	-	-	-	+	+	+	+	5	Fair
Erfani et al. 2012 [28]	+	-	+	+	-	-	-	+	+	+	+	6	Cood
Barati et al. 2012 [29]	+	+	+	-	-	-	-	+	+	+	+	6	Good
Mehrabian et al. 2012 [49]	+	-	-	+	-	-	-	+	+	+	+	5	Fair
Yalfani et al. 2012 [26]	+	+	+	-	-	-	-	+	+	+	+	6	Good
Rahimi et al. 2012 [51]	-	+	+	-	-	-	-	+	+	+	+	5	<b>F</b> = in
Roustaei et al. 2012 [52]	+	+	-	-	-	-	-	+	+	+	-	4	Fair
Esfandiari et al. 2012 [34]	+	+	-	+	-	-	-	+	+	+	-	5	
Mahmoodi Aghdam et al. 2013 [37]	+	+	-	+	-	-	-	+	+	+	+	6	Good
Ahmadi et al. 2014 [30]	+	+	+	-	-	-	-	+	+	+	+	6	
Malekzadeh et al. 2014 [50]	+	+	-	-	-	-	-	+	+	+	+	5	Fair
Mazloum and Rahnama, 2014 [36]	+	+	-	+	-	+	+	+	+	+	+	8	Good
Kazemi et al. 2015 [56]	+	+	+	-	-	-	-	+	+	+	-	5	Fair
Mazloum et al. 2016 [38]	+	+	+	+	+	-	-	+	+	+	+	8	Good
Rafsanjani Dehghazi et al. 2016 [23]	+	+	+	-	-	-	-	+	+	-	+	5	Fair
Bagheri et al. 2016 [40]	+	+	+	-	+	-	-	+	+	+	-	6	
Ezadpanah et al. 2016 [41]	+	+	+	-	-	-	-	+	+	+	+	6	Good
Hassani Haghighi et al. 2016 [57]	+	+	+	-	-	-	-	+	+	+	-	5	<b>F</b> -i-
Kamali et al. 2016 [58]	+	+	+	-	-	-	-	-	+	+	+	5	Fair
Etesami et al. 2016 [43]	+	+	+	+	-	-	-	+	+	+	+	7	Good
Safari Bak et al. 2017 [59]	+	+	+	-	-	-	-	+	+	-	+	5	Fair
Taghizade Delkhosh et al. 2018 [39]	+	+	+	+	+	-	-	+	+	+	+	8	Good
Zarei and Rahnama, 2018 [55]	+	+	+	-	-	-	-	+	+	+	-	5	Fair
Mohsenipour et al. 2018 [47]	+	+	+	+	-	-	-	+	+	+	+	7	
Attari et al. 2018 [44]	+	+	+	+	-	-	-	+	+	+	+	7	Good
Moezy et al. 2018 [24]	+	+	+	+	+	-	+	+	+	+	+	9	Excellent
Abdollahi et al. 2019 [45]	+	+	+	+	-	-	-	+	+	+	+	7	
Jamali Masoomi et al. 2019 [46]	+	+	+	-	-	-	-	+	+	+	+	6	Good
Pouradeli et al. 2021 [42]	+	+	+	-	-	-	-	+	+	+	+	6	

Table 3. Evaluation of evidence based on the physiotherapy evidence database (PEDro] scale

The evaluation was as follows: 1-3=poor; 4-5=fair; 6-8=good; 9-10=excellent.

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In an investigation, Kazemi et al. (2015) compared the effects of physiotherapy on the treatment of knee OA with physiotherapy combined with reflexology [56]. They divided 24 patients with knee OA into two treatment groups, each lasting 24 sessions. The results of their study demonstrated that the symptoms of knee OA, including pain, joint stiffness, decreased daily activities and exercise, and recreation in the physiotherapy combined with the reflexology group improved more than the physiotherapy group. However, there was no significant difference between the two treatments. In another study. Fatemy et al. (2010) examined the effect of Swedish massage on pain intensity and quality of life in patients with knee OA [35]. Patients in this study were treated with two interventions for ten sessions: Routine physiotherapy treatments (ultrasound, infrared, and transcutaneous electrical nerve stimulation) and routine physiotherapy treatments combined with Swedish massage. The findings of this study indicated the positive effects of massage intervention on the variables. Similar studies have reported the positive effects of massage on complications with the knee joint and other parts of the body, such as the low back. For example, Mazloum and Mahdavi Nejad (2012) evaluated the effect of Swedish massage and exercise therapy on the symptoms of patellofemoral pain syndrome and concluded that Swedish massage was more effective in reducing pain compared to exercise therapy [72]. Various mechanisms have been proposed associated with the effect of this method, some of which are as follows: With gentle massage, low-threshold mechanical receptors that adapt slowly or quickly are activated in the peripheral system, leading to the stimulation of A-beta fibers. In the presence of pain, the stimulation reduces the transmission of nociceptors in the lamina of the spinal cord dorsal horn. If the massage is more intense, there is a possibility of activating high-threshold mechanical receptors that activate A-gamma fibers. Such stimulation transmitted from the spinothalamic tract to the lateral periaqueductal nucleus in the midbrain, activates inhibitory control, thereby reducing pain sensation and perception [73]. On the other hand, the sensation and perception of pain are primarily related to complex behavioral patterns, such as anxiety, stress reactions, and sleep disorders that are activated through higher centers. Evidence suggests that massage reduces the activity of the adrenal glands, thereby lowering adrenaline levels. In addition, decreased afferent sympathetic nerve activity can also be a reason for the anti-stress effects of massage [74]. Fatemy et al. (2010) conducted a study to evaluate the effect of Swedish massage in ten sessions over two weeks for patients with knee OA, which was associated with its favorable effects on pain intensity and quality of life [35]. It seems that the use of this method of manual therapy can be considered in a more extended period to achieve more potential positive effects.

#### Physiotherapy intervention

A variety of physiotherapy treatments were considered by researchers in 13 studies. In one study, joint traction, and in nine other studies, electrotherapy was used.

The effect of sustained traction on physical improvements of patients with severe knee OA was investigated by Mahmoodi Aghdam et al. (2013). The findings of this study indicate that the combination of knee joint traction technique with conventional treatment both reduces pain and increases the functional ability of these patients [37]. Considering the similarity of the mean scores of the variables between the two groups before interventions, it can be concluded that the only factor for further improvement in the group of knee joint traction techniques with conventional treatment is related to the application of traction. The researchers also found that the severity of pain in subjects who received knee traction was less during follow-up sessions than in the conventional treatment group. It seems that the mechanism of the positive effect of traction should be considered in the mechanics of the knee joint in patients with knee OA. Since applying an excessive compressive load to the joint is a main factor in the onset and progression of OA [4], joint traction reduces the symptoms by temporarily removing the mechanical pressure on the joint. Due to the high focus on articular cartilage in the treatment of knee OA, the primary source of the symptoms of this disease, which is biomechanical changes in the subchondral bone, has been ignored. Repeated and traumatic pressure on the joint causes sclerosis of the subchondral bone and the inability to absorb pressure, which in turn leads to the development of cartilage damage. The reason for the inconsistency of drug treatment to repair articular cartilage is the consistent application of excessive pressure on the knee. Increased hydrostatic pressure in the subchondral bone is one of the leading causes of pain in patients during daily activities and decreased functional ability [75]. The most significant effect of traction-decreased intra-articular pressure and possibly increased distance between joint surfaces- is at 30° flexion, as at this angle, the capsule and the ligaments around the joint are in their loosest position [76], and the pain reduction and the improvement in the patient's performance may be due to the reduction in the hydrostatic pressure imposed on the subchondral bone. Negative intra-articular pressure due to the application of traction, in addition to reducing the pressure on the subchondral bone, may improve the exchange of nutrients between the articular cartilage and the synovial fluid and possibly improve the trophic status of the articular cartilage. Better performance of articular cartilage, on the other hand, can reduce the pressure on the subchondral bone, thereby reducing pain and increasing patients' motor performance. Mahmoodi Aghdam et al. (2013) stated that the amount of joint traction applied in this study was about 10% of the patient's body weight [37]. Therefore, it is suggested to use joint traction with less or more load for a period longer than ten sessions in future studies to determine the effects of these methods.

In another study, Rahimi et al. (2012) in their study compared action potential stimulation (APS) therapy and routine physiotherapy in the treatment of patients with knee OA and concluded that APS therapy could reduce the pain caused by this complication [51]. APS therapy or reconstruction of the action potential is a new technique of electrotherapy that, unlike other electrotherapy methods, is not limited to rehabilitation techniques, and its scope is much broader. The basis of device is based on the theory that the existence of a balance between complex hemostatic systems of the body guarantees the survival of alive creatures, and its disruption leads to disease and, in more advanced stages, even leads to death [77]. In APS therapy, the treatment is based on the mimicking and induction of natural impulses of the nervous system on specific neural pathways and thus balancing the body's bioelectricity system. A bioelectricity system consists of cell membranes, ion maps, ion diffusion channels, and finally, polarities. Papendorp et al. (2002), in their study, considered the mechanism of the effect of pain relief by APS therapy on the gate control theory as well as the endorphins release [78].

Bagheri et al. (2011) investigated the effect of lowlevel laser therapy for two weeks on pain intensity, knee flexion range of motion, and quality of life in patients with knee OA [33]. The researchers concluded that all three variables improved significantly following the application of low-level laser therapy, but no significant difference was observed in the group receiving the placebo laser. There are various theories about the action mechanism of the laser. While some studies suggest anti-inflammatory and analgesic effects, others suggest inhibition of nerve activity as the therapeutic effect of the laser and state that laser waves selectively inhibit pain messages in peripheral nerves [79]. Bagheri et al. (2011) attributed the lack of significant difference between the effect of active laser and placebo on pain intensity in patients with knee OA to the type of laser, therapeutic dose, and the wavelength used [33]. Some sources state that due to the depth of knee OA, the laser cannot affect this complication as the laser penetration depth is only about a few millimeters; thus, this modality can only affect small joints.

The effect of another type of electrotherapy method, known as phonophoresis and iontophoresis of piroxicam gel, has also been investigated by Roustaei et al. (2012) on knee OA [52]. The researchers concluded that iontophoresis piroxicam gel could significantly improve physical performance and muscle function around the knee compared to other methods. The remarkable point in this study is that the effect on knee muscle function cannot be well documented due to using electrotherapy alone and the lack of a training program in the intervention designed by the researchers.

Some studies have compared exercise therapy and electrotherapy. In a randomized clinical trial, Ahadi et al. (2011) compared the effect of physical modality and knee isometric exercise training on the performance and pain intensity of subjects with knee OA and concluded that physical modality is more effective in reducing pain intensity and improving quality of life than isometric exercise [32]. However, the researchers did not report any reason for the superiority of physical modalities over isometric exercises. Mohsenipour et al. (2018) compared three protocols, including sham ultrasound with exercise (lower limb strengthening exercises), ultrasound without exercise (ten sessions), and ultrasound with exercise on postural sway in women with knee OA [47]. They concluded that center of pressure (COP) displacements in the mediolateral direction were more affected than other sway directions, and pulsed ultrasound could improve the postural sways in the mediolateral direction, and bring its parameters closer to the healthy group. Also, Abdollahi et al. (2019) compared physiotherapy (routine protocol of knee OA physiotherapy) versus isokinetic training (routine protocol with isokinetic training) [45]. They concluded that all parameters in both isokinetic exercises and physiotherapy groups improved following the treatment process, but isokinetic exercises along with physiotherapy treatment were more effective in improving function and reducing pain than physiotherapy treatment. On the other hand, Rafsanjani Dehghazi et al. (2016) showed that peroneal nerve electrical stimulation increases the extensor torque of quadriceps muscle compared to the electrical stimulation of quadriceps muscle [23]. They concluded that electrical stimulation of the common peroneal nerve with the maximum voluntary attempt of the individual to activate the quadriceps muscle, as used in the current study, is a useful way to strengthen

these groups of muscles. These studies indicated the positive effect of electrotherapy on pain, balance, and function in patients with OA. We suggest that conservative methods utilized in the studies can be used for longer periods of treatment, as many studies have evaluated the effectiveness of therapies over a 10-session period. Also, to determine the durability of the methods used, the use of studies with follow-up seems necessary. The use of combination therapies (such as various methods of electrotherapy and exercise therapy and manual therapies) to evaluate their effectiveness is another suggestion of researchers. On the other hand, due to the importance of knee muscles' weakness and changes in their utilization pattern in knee OA, the effect of non-aggressive treatment methods on the strength and coordination of knee muscles should be considered in future studies.

#### 5. Conclusion

A review of previous studies conducted in Iran on the effect of conservative interventions on knee OA showed that they have focused on therapeutic exercises, assistive devices, physiotherapy methods, and manual therapy, respectively. The main results of these interventions indicate the favorable effects of these methods on reducing pain intensity and improving physical performance and quality of life in patients with knee OA. However, it seems further high-quality studies are required.

#### **Ethical Considerations**

#### Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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#### Authors' contributions

All authors equally contributed to preparing this article.

#### Appendix 1. Search strategy

("استئوآرتریت زانو" OR "آرتروز زانو" OR "استئوآرتریت کمپارتمان داخلی زانو" OR " بیماری تخریب زانو" (AND ) "تمرین درمانی" OR " "حرکت درمانی" OR "آب درمانی" OR "هیدروتراپی" OR "الکتروتراپی" OR "فیزیوتراپی" OR "درمان دستی" OR "تیپینگ" OR " "نوارپیچی" OR "اورتز " OR "ارتز " OR "بریس" OR "تمرینات تقویتی" OR "تمرینات کششی" OR "درمان محافظه کارانه" OR "درمان نگهدارنده" OR "درمان غیرجراحی")

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