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SYSTEMATIC REVIEW

Strengthening the quadriceps femoris muscle versus other knee training programs for the treatment of knee osteoarthritis

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Abstract

People with knee osteoarthritis have atrophy of the muscles surrounding the knee joint. Therefore, exercise programs primarily have been focused on the strengthening of quadriceps femoris muscle (QFM). Primary aim of this systematic review was to determine which exercise increases strength of the QFM and describe the details of the training programs. Secondary aim was to determine effectiveness of strengthening of the QFM alone on pain and dysfunction in patient with knee osteoarthritis. PubMed, PEDro, and Cochrane were searched. PEDro for methodological quality of randomized controlled trials and Cochrane Collaborations' tool for risk of bias were used. A total of 1128 articles were identified from the database searches. Ten studies which were moderate-to-high level of evidence were included. In the comparison of different strengthening exercises of the QFM, significant difference was not found between training groups. However, strengthening of the QFM exercise training was superior to proprioceptive training. Additional hot packs plus shortwave diathermy or ultrasound or transcutaneous electrical nerve stimulation had superiority to isokinetic strengthening of the QFM alone. Only additional Russian electrical stimulation showed the significant difference compared with strengthening of the QFM exercise. Most of the included studies showed that strengthening of the QFM exercises has an effect on pain reduction and improvement of function. This review indicated that the strengthening of QFM training compared with other knee exercises provided muscle strengthening, pain reduction, and improved function while combination with other electrotherapy modalities or combination with Russian electrical stimulation had superiority to alone strengthening QFM training.

Keywords Electric stimulation therapy · Exercise · Pain · Rehabilitation · Resistance training

Introduction

Knee osteoarthritis (OA) is the most common disease which affects primarily the articular cartilage and the subchondral bone of synovial joints in adults [1]. The prevalence of symptomatic knee OA ranges between 10 and 30% among older individuals around worldwide [2].People older than 65 years have a radiologic evidence of joint degeneration in more than 50% and women prone to symptomatic OA [3, 4]. Typical symptoms of knee OA include joint stiffness, reduced strength of the quadriceps femoris muscle (QFM), pain, physical disability which limited joint function and reduced physical fitness [5].

Recently, a systematic review and meta-analysis reported the association between the weakness of knee extensor muscle and the risk of having knee OA [6]. People with knee OA have weakness of the muscles surrounding the joint [7], and this causes an increased joint stress [8, 9]. Also, it has been known that the weakness of the QFM is one of the major factors in functional disability [10–14]. In addition, it has been demonstrated that there was a correlation between the weakness of the QFM and knee pain or function [15, 16]. Therefore, most of the exercise programs primarily have been focused on the strengthening of the QFM which is an

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important rehabilitation target for individuals with knee OA [17–20]. Although strengthening of the QFM is emphasized in many exercise programs, it remained unclear whether these exercises increase the strength of the QFM. Furthermore, the details of the treatment programs (such as the type of exercise, type of electrical stimulation or combined treatment) are not precisely described [21, 22]. The other unknown question is whether strengthening of the QFM alone can provide decreased pain and functional improvement in knee OA. The primary aim of this systematic review was to determine which exercise increases the strength of the QFM and to describe the details of the training programs. The secondary aim was to determine the effectiveness of strengthening of the QFM alone on pain and dysfunction in the patient with knee OA.

Methods

Data sources

This systematic review was conducted according to the guidelines defined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) [21]. The search was performed in PubMed, PEDro, and Cochrane, using The Medical Subject Headings (MeSH) terms and keywords. The following search was used to search in PubMed: (((((((((Muscle Strength*[Title/Abstract]) OR Muscle Strength*[MeSH Terms]) OR resistance exercise*[Title/Abstract]) OR resistance training[Title/Abstract]) OR resistance training[MeSH Terms]) AND quadriceps muscle*[Title/Abstract]) OR quadriceps muscle*[MeSH Terms]) AND osteoarthritis knee[Title/Abstract]) OR osteoarthritis knee[MeSH Terms]) OR Osteoarthrosis*[Title/Abstract]) OR Osteoarthrosis*[MeSH Terms].

PEDro and Cochrane were searched with similar terms and key words which were used in PubMED. The searches were limited to the studies published in English. Clinical trials published from January 1st 2006 to July 18th 2017 were included. The search yield was imported into Endnote X6.0.1 (Thomson Reuters, USA) for evaluation. The studies were selected by two reviewers based on titles, abstracts, and full text. Disagreements between reviewers were resolved by consensus.

Inclusion and exclusion criteria

We included the randomized controlled trials (RCTs) which applied the strengthening of the QFM with exercise training or electrical stimulation or combination of them and measuring the strength of the QFM in individuals with knee OA. We excluded the protocols for RCTs, nonrandomized clinical trials, conference proceedings, cross-sectional analysis, thesis, randomized controlled pilot studies, and reviews. A total of 1128 studies were recruited to the study (Fig. 1). We included studies which scored at least five points on PEDro score. This score was considered high quality in the criteria given by Moseley et al. [23]. In case of any discrepancy, the reviewers discussed and resolved by consensus.

Assessment of methodological quality

Methodological quality of the included RCTs was evaluated by two reviewers working independently with PEDro scale (Table 1) [24]. PEDro scale is a reliable tool to assess the quality of trials (ranging from 0 to 10 with 10 showing higher quality). All included studies evaluated and studies were included scored at least five points on PEDro score. The risk of bias assessment was applied using the Cochrane Collaborations' tool [25] for studies which included after PEDro assessment. Two reviewers rated the included studies on items using three different categories (high risk of bias, low risk of bias or unclear risk of bias) (Table 2). The risk of bias assessment was applied on pairs of reviewers working independently. Disagreements between reviewers were resolved by consensus for assessment of methodological quality and risk of bias of the studies.

Results

Study characteristics

Ten studies were included in the review. A summary of the included studies is presented in Table 3. A total of 759 patients were included in the studies and the majority of them was women. The number of included subjects was ranged from 30 to 108. The mean of age ranged from 55.73 ± 8.23 to 69.4 ± 7.7 years. The mean of body mass index ranged from 27.40 ± 4.24 to 33.9 ± 8.3 kg/m^2 (Table 3).

Study interventions

The content and design of interventions were shown in Table 4. Two studies compared different types of strengthening of the QFM training [26, 27]. Three studies compared the strengthening of the QFM training with other knee exercise training or control group [28–30]. Five studies compared the strengthening of the QFM training alone or with combined electrotherapy [26, 31–34]. In one study, strengthening of the QFM training compared only Neuromuscular Electrical Stimulation (NMES) [31]. Other studies included additional Continuous Passive Motion-Electrical Stimulation (CPM–ES) [35], NMES

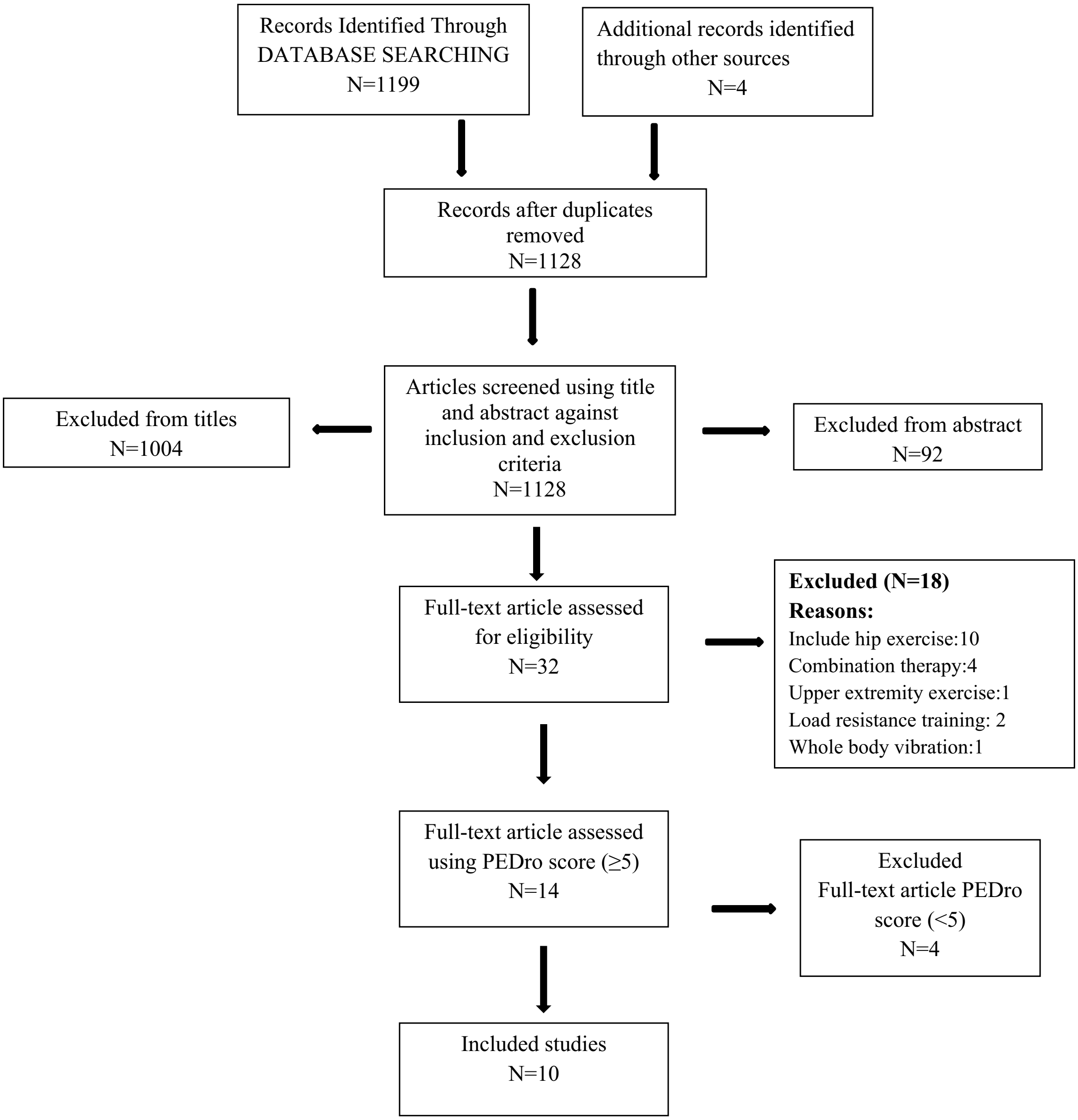

Fig. 1 Flow diagram for study selection

or Shortwave Diathermy (SWD), Hot packs (HP), Ultrasound (US), Transcutaneous Electrical Nerve Stimulation (TENS) [31, 32].

Treatment protocol

The shortest and longest follow-up durations were 3 and 12 weeks, respectively [29, 30, 35]. The minimum and maximum numbers of the sessions were 12 and 60 sessions, respectively [29–31]. The shortest and longest treatment time (duration of session x number of the session) were 360 and 1200 min, respectively [27, 31].

Outcome measurements

The summary of within- and between-groups results in terms of strength the QFM, pain, and function are shown in Table 5.

Primary outcome

The strength of the QFM

Nine studies used isokinetic dynamometry [26–30, 32–35] and one study used myometry system [31] to evaluate the strength of the QFM.

Table 1 The quality assessment of RCTs using the PEDro

Studies	Items											Total point
	1	2	3	4	5	6	7	8	9	10	11	
The comparison of different strengthening exercises of the QFM												
Jan et al. [27]	1	1	1	0	0	0	1	1	1	1	0	7
Salli et al. [26]	1	1	1	0	1	0	1	1	0	1	0	7
The comparison of strengthening of the QFM training versus other knee exercises training or control group												
Lim et al. [29]	1	1	1	1	0	0	1	1	1	1	1	8
Lin et al. [28]	1	1	1	0	0	0	1	1	1	1	1	8
Kean et al. [30]	1	1	1	1	0	0	1	1	0	1	1	8
The comparison of strengthening of the QFM training versus alone or combined electrotherapy												
Cetin et al. [32]	1	1	0	1	0	0	1	0	0	1	0	5
Tok et al. [35]	1	1	0	1	0	0	0	1	1	1	0	6
Bruce-Brand et al. [33]	1	1	0	1	0	0	1	0	0	1	0	5
Laufer et al. [31]	1	1	1	1	0	1	0	0	0	1	1	7
Park et al. [34]	1	1	0	1	0	0	0	1	0	1	1	6

QFM quadriceps femoris muscle

1—Eligibility criteria specified, 2—random allocation, 3—concealed allocation, 4—groups similar at baseline, 5—subject blinding, 6—therapist blinding, 7—assessor blinding, 8—less than 15% dropouts, 9—intention-to-treat analysis, 10—between-group statistical comparisons, 11—point measures and variability data

Table 2 The assessment of risk of bias

Studies	1	2	3	4	5	6	7	Total point
The comparison of different strengthening exercises of the QFM								
Jan et al. [27]	0	0	1	0	0	0	0	1
Salli et al. [26]	0	0	0	0	0	0	0	0
The comparison of strengthening of the QFM training versus other knee exercises training or control group								
Lim et al. [29]	0	1	1	0	0	0	0	2
Lin et al. [28]	0	0	1	0	0	0	0	1
Kean et al. [30]	0	1	1	0	0	0	0	2
The comparison of strengthening of the QFM training versus alone or combined electrotherapy								
Cetin et al. [32]	0	1	1	0	1	0	0	3
Tok et al. [35]	0	1	1	1	0	0	0	3
Bruce-Brand [33]	0	1	1	0	1	0	0	3
Laufer et al. [31]	0	0	0	1	1	?	0	2
Park et al. [34]	0	1	1	1	0	0	0	3

QFM quadriceps femoris muscle

1—random sequence generation, 2—allocation concealment, 3—blinding of participants and personnel, 4—blinding of outcome assessment, 5—incomplete outcome data, 6—selective reporting 7—other bias

(1) High risk, (0) Low risk, (?) Unclear

The comparison of different strengthening exercises of the QFM A study found significant improvement in both high-resistance training (HR) and low-resistance training (LR) groups, but there was no significant difference between groups [27]. Another study found significant improvement in both isometric and combined concentric-eccentric isokinetic types of exercise [26]. Similarly, there was no significant difference between groups.

The comparison of strengthening of the QFM training versus other knee exercises training or control group An included study which compared proprioceptive training

Table 3 The studies and subjects' characteristics

Studies	Subjects (*n*)	Groups (*n*)	Age (year) Mean ± SD	BMI (Kg/m^2) Mean ± SD	Female (%)
The comparison of different strengthening exercises of the QFM					
Jan et al. [27]	102	High-resistance exercise group (34)	63.3 ± 6.6	Not reported	79
		Low-resistance exercise group (34)	61.8 ± 7.1		79
		Control group (34)	62.8 ± 6.3		83
Salli et al. [26]	71	Concentric-eccentric group (23)	55.73 ± 8.23	31.5 ± 4.4	83
		Isometric group (24)	57.1 ± 6.75	32.65 ± 4.29	83
		Control group (24)	58.3 ± 6.67	32.82 ± 5.05	79
The comparison of strengthening of the QFM training versus other knee exercises training or control group					
Lim et al. [29]	107	Strengthening group (52)			
		More varus malaligned (26)	67.2 ± 6.7	28.2 ± 3.7	50
		More neutrally aligned (26)	64.1 ± 9.3	29.0 ± 5.2	63
		Control group (55)			
		More varus malaligned (27)	66.6 ± 8.9	30.3 ± 5.3	46
		More neutrally aligned (28)	60.8 ± 7.8	28.4 ± 5.0	61
Lin et al. [28]	108	Proprioceptive training (36)	63.± 8.2	Not reported	69
		Strength training (36)	61.6 ± 7.2		67
		Control group (36)	62.2 ± 6.7		72
Kean et al. [30]	97	Strength training group (49)	65.7 ± 8.2	28.6 ± 4.4	52
		Control group (48)	63.8 ± 8.2	28.5 ± 6.7	54
The comparison of strengthening of the QFM training versus alone or combined electrotherapy					
Cetin et al. [32]	100	Group 1 (SWD + HP + isokinetic exercises (20) Group 2 (TENS + HP + isokinetic exercises) (20) Group 3 (US + HP + isokinetic exercises) (20) Group 4 (HP + isokinetic exercises) (20) Group 5 (only isokinetic exercises) (20)	59.75 ± 11.63 61.85 ± 8.64 57.60 ± 7.33 61.05 ± 8.26 58.85 ± 9.08	27.94 ± 4.24 29.49 ± 4.60 29.80 ± 5.71 27.71 ± 4.17 27.40 ± 4.24	100
Tok et al. [35]	40	Group 1 (conventional physical therapy + CPM–ES combination) (20)	Not reported	Not reported	80
		Group 2 (conventional physical therapy and isometric exercise) (20)			30
Bruce-Brand et al. [33]	41	Resistance training group (14)	63.4 ± 5.9	33.9 ± 8.3	40
		NMES group(14)	63.9 ± 5.8	33.7 ± 5.6	40
		Control group(13)	65.2 ± 3.1	31.7 ± 4.1	50
Laufer et al. [31]	63	Exercise program (33)	69.4 ± 7.7	30.5 ± 5.3	84
		Exercise program + NMES (30)	68.3 ± 7.7	31.4 ± 6.7	84
Park et al. [34]	30	Control group (10)	68.4 ± 1.5	Not reported	30/0
		Progressive resistance training group (PRT)(10)	67.9 ± 2.0		
		PRT + Russian electrical stimulation group (10)	68.2 ± 2.1		

QFM quadriceps femoris muscle, *BMI* body mass index, *NMES* neuromuscular electrical stimulation, *SWD* shortwave diathermy, *HP* hot packs, *TENS* transcutaneous electrical nerve stimulation, *US* ultrasound, *CPM-ES* continuous passive motion-electrical stimulation

(PrT), strength training (ST) and control group found significant improvement in both exercise groups, but there was no change in the control group [28]. ST group showed significant improvement compared to other groups. Two studies found significant improvements in home-based strengthening exercise group [29, 30]. But only one of them found a significant difference in strengthening training group compared with the control group [30].

The comparison of strengthening of the QFM training versus alone or combined electrotherapy When resistance exercise of QFM was compared with NMES or control group, there was no difference within and between groups [33]. Another study compared strengthening exercise with CPM–ES combination and similarly found that there were no significant improvements in within and between groups [35]. Park et al. who compared progressive resistance training group with additional Russian electrical stimulation or control group, found significant improvement at the strength

Table 4 The content and design of interventions

Studies	Groups	Details of quadriceps femoris muscle training	Duration (week)	Sessions (number)	Duration of session	Frequency (days/week)	Supervised
The comparison of different strengthening exercises of the QFM							
Jan et al. [27]	High-resistance exercise Low-resistance exercise Control	High-resistance exercise (HRE) group Knee flexion and extension (60% of 1 RM, 8 repetitions, 3 sets) Low-resistance exercise (LRE) group Knee flexion and extension (10% of 1 RM, 15 repetitions, 10 sets) * Every 2 weeks, 1 RM was retested, and the training weight for both groups was progressively increased by 5% of the new 1 RM, as tolerated Control group No exercise	8	24	HRE group 30 min LRE group 50 min	3	Yes
Salli et al. [26]	Concentric-eccentric Isometric Control	Concentric-eccentric group Using the isokinetic dynamometer, knee extension/flexion (70% maximal voluntary contraction, 10 repetitions at each angular velocity: 60, 90, 120, 150, and 180/s) Isometric group Using the isokinetic dynamometer Control group Only given paracetamol	8	24	Not reported	3	Yes
The comparison of strengthening of the QFM training versus other knee exercises training or control group							
Lim et al. [29]	Home-based strengthening Control	Home-based strengthening group Long arc knee extension using ankle weight in sitting position from 90°–0° Inner range knee extension in supine lying or long sitting position 30°–0° Straight leg raise using ankle weight in supine lying or elbow-supported Isometric knee extension at 30° knee flexion using ankle weight in sitting position Isometric knee extension at 60° knee flexion using Thera-Band in sitting position Control group No intervention	12	60	Duration was changed following week	5	No

Table 4 (continued)

Studies	Groups	Details of quadriceps femoris muscle training	Duration (week)	Sessions (number)	Duration of session	Frequency (days/week)	Supervised
Lin et al. [28]	Proprioceptive training Strength training Control	Proprioceptive training (PrT) Computer game foot-stepping exercise Strength training (ST) −90°–0 concentric, 0–90° eccentric quadriceps action The baseline resistance 50% of 1-RM, progressive increment of 5% of the original 1-RM every 2 weeks Control group No intervention	8	24	PrT 20 min ST Not reported	3	Yes
Kean et al. [30]	Strengthening training Control	Strength training group Home-based program (5 non-weight bearing exercises targeting the quadriceps) Control group No intervention	12	60	Not reported	5	No
The comparison of strengthening of the QFM training versus alone or combined electrotherapy							
Cetin et al. [32]	Group 1 (SWD + HP + isokinetic exercises) Group 2 (TENS + HP + isokinetic exercises) Group 3 (US + HP + isokinetic exercises) Group 4 (HP + isokinetic exercises) Group 5 (Only isokinetic exercises)	Group 1 SWD (27.12 MHz, 15 min) Isokinetic strength training of the knee flexor and extensor muscle groups No information about HP Group 2 TENS (60–100 Hz, the pulse duration 60 ms. 20 min) Isokinetic strength training is the same as above Group 3 US (1-MHz head, intensity of 1.5 W/cm^2, with full contact, 10 min) Isokinetic strength training is the same above protocol Group 4 Isokinetic strength training is the same as above Group 5 Isokinetic strength training is the same as above	8	24	Not reported	3	Yes

Table 4 (continued)

Studies	Groups	Details of quadriceps femoris muscle training	Duration (week)	Sessions (number)	Duration of session	Frequency (days/week)	Supervised
Tok et al. [35]	Group 1 (Conventional physical therapy + CPM–ES combination) Group 2 (Conventional physical therapy + isometric exercise)	Group 1 Infrared (10 min), Interferential current (0–100 Hz frequency, 10 min) Therapeutic ultrasonography (1.5 W/cm^2 dosage, 5 min) CPM–ES therapy (20 min to both knees) *Asymmetric biphasic wave (intensity 70–120 mA, 50 Hz frequency 200 ms to rectus femoris, vastus lateralis, biceps femoris and semitendinosus) with CPM *CPM (0-90^{0}in 15 s and 90°-0 in 15 s. ES (10-s contraction and 10-s rest) simultaneously to CPM Group 2 Conventional physical therapy is the same as Group 1 Isometric exercises for 20 min as 10-s contraction and 20-s rest	3	15	45 min	5	Yes
Bruce-Brand et al. [33]	Resistance training NMES Control	Resistance training group The bottle knee press The bottle provided Resistance to knee extension The leg extension exercise Wall squat exercise The hamstring curl NMES group Each stimulation cycle comprised a 10 s contraction period and a 50 s relaxation period, excluding the 1 s ramp-up and 0.5 s ramp-down Control group Standard care (OA education, weight loss, pharmacologic, and physical therapy)	6	18	Resistance training (30 min) NMES (20 min)	3	No
Laufer [31]	Exercise Exercise + NMES	Exercise Not reported NMES – 10 contractions per session, at maximal tolerated intensity	6	12	Not reported	2	Yes

Table 4 (continued)

Studies	Groups	Details of quadriceps femoris muscle training	Duration (week)	Sessions (number)	Duration of session	Frequency (days/week)	Supervised
Park et al. [34]	Control group General physical therapy treatment Progressive resistance training group Russian electrical stimulation group Electrical stimulation and the same treatment as the PRT group	Control group General physical therapy treatment Hot packs, ultrasound application, and isometric knee extension exercise Progressive resistance training group Hot packs, ultrasound application and progressive resistance training (PRT) knee extension exercise. PRT knee extension exercises applied were set at 50%, 75%, and 100% of the 10 RM for each set Russian electrical stimulation group Hot packs, ultrasound application, progressive resistance training knee extension exercise and electrical stimulation	8	24	45 min	3	Yes

* To define training programs of the groups

QFM quadriceps femoris muscle, *SWD* shortwave diathermy, *HP* hot packs, *TENS* transcutaneous electrical nerve stimulation, *US* ultrasound, *CPM–ES* continuous passive motion-electrical stimulation, *NMES* neuromuscular electrical stimulation, *min* minute, *s* second

of the QFM in all groups [34]. In terms of the difference between the groups, additional Russian electrical stimulation group was found superior over other groups. Besides, the study which compared exercise training with additional NMES found significant improvement at only maximum voluntary isometric contraction in additional NMES group, but there was no difference between groups [31]. Another study compared isokinetic exercises with additional SWD + HP, TENS + HP, US + HP, and HP found significant improvement in within-groups. Although there was no difference among groups, a significant difference was found in additional SWD + HP, TENS + HP, and US + HP compared with isokinetic exercises [32].

Secondary outcomes

The effect of strengthening the QFM on pain

Four studies used The Western Ontario and McMaster Universities Arthritis Index (WOMAC)–pain [27–29, 33] one study used Visual Analog Scale (VAS) [32] and three studies used both WOMAC-pain and VAS [26, 31, 35] to assess pain. Two studies did not use any pain outcome measurement [28, 34]. The results of strengthening of the QFM exercises on pain for each trial are summarized in Table 5.

The comparison of different strengthening exercises of the QFM The study performed by Jan et al. compared different loaded strengthening training (HR, LR or control group) and found significant improvement in training groups, but there was no significant difference between training groups [27]. The other study which compared different types of exercise (isometric, combined concentric-eccentric or control group) found significant improvement on VAS score, but no significant improvement on WOMAC-pain score in within-training groups [26]. There were no significant differences in both VAS and WOMAC-pain scores between groups.

The comparison of strengthening of the QFM training versus other knee exercises training or control group The study performed by Lin et al. which compared proprioceptive training, strength training or control group found significant improvement in training groups and, no significant difference between training groups [28]. The other study which compared home-based strengthening exercise with the control group found significant improvement within and between groups in favor of strengthening group [29].

The comparison of strengthening of the QFM training versus alone or combined electrotherapy In the study performed by Bruce-Brand et al. which compared resistance exercise training with NMES or control group, significant

Table 5 The summary of the results of the studies

Studies	Assessment times	Outcome measures	Results
The comparison of different strengthening exercises of the QFM			
Jan et al. [27]	At baseline 8th week	Strength of the QFM Isokinetic dynamometer Pain WOMAC-pain Function WOMAC-PF, Walking times on four different grounds	HR Group *WOMAC-pain and function, walking times on four different terrains LR Group *WOMAC-pain and function, walking times on four different terrains HR Group versus Control Group **WOMAC-pain and function, walking times on four different terrains in HR Group LR Group versus Control Group **WOMAC-pain and function, walking times on four different terrains in LR Group
Salli et al. [26]	At baseline 8th week 20th week	Strength of the QFM Isokinetic dynamometry Pain VAS, WOMAC-pain Function WOMAC-PF	C-E/G *VAS-rest and motion, WOMAC-PF, strength of the QFM between baseline and 8 weeks or 20 weeks I/G *VAS-rest and motion and WOMAC-PF, strength of the QFM at week 8 and 20 compared to baseline values I/G versus control group **VAS-rest and motion in I/G at 8 and 20 weeks, strength of the QFM in I/G C-E/G versus control group **VAS-rest and motion in C-E/G at 8 and 20 weeks, WOMAC-PF scores in C-E/G at 8 and 20 weeks, strength of the QFM in C-E/G C-E/G versus I/G **WOMAC-PF in C-E/G Among groups ***WOMAC-PF in C-E/G
The comparison of strengthening of the QFM training versus other knee exercises training or control group			
Lim et al. [29]	At baseline 12th week	Strength of the QFM Isokinetic dynamometry Pain WOMAC-pain Function WOMAC-PF, Step test, Stair climb test	Strengthening group *Strength of the QFM, WOMAC-pain in more neutrally aligned Between groups **WOMAC-pain in strengthening group
Lin et al. [28]	At baseline 8th week	Strength of the QFM Isokinetic dynamometer Pain WOMAC-pain Function WOMAC-PF, Walking time on 3 different terrains	PrT *WOMAC-pain and PF, strength of the QFM and walking time on three different terrains ST *WOMAC-pain and PF, strength of the QFM and walking time on three different terrains PrT versus Control Group **WOMAC-pain and PF, strength of the QFM at 60/s, walking time on three different terrains in PrT ST versus Control Group **WOMAC-pain and PF, strength of the QFM and walking time on three different terrains in ST PrT versus ST **Walking time on spongy surface in PrT **WOMAC-PF, strength of the QFM and walking time on stair in ST Among Groups ***Strength of the QFM in ST

Table 5 (continued)

Studies	Assessment times	Outcome measures	Results
Kean et al. [30]	At baseline 13th week	Strength of the QFM Isokinetic dynamometer Function Three-dimensional gait assessment	Strength training group *Strength of the QFM Between groups **Strength of the QFM in strength training group
The comparison of strengthening of the QFM training versus alone or combined electrotherapy			
Cetin et al. [32]	At baseline 8th week	Strength of the QFM Isokinetic dynamometer Pain VAS Function 50-m walk test	Group 1 (SWD + HP + isokinetic exercises) *Strength of the QFM, VAS, 50-m walk test Group 2 (TENS + HP + isokinetic exercises) *Strength of the QFM, VAS, 50-m walk test Group 3 (US + HP + isokinetic exercises) *Strength of the QFM, VAS, 50-m walk test Group 4 (HP + isokinetic exercises) *Strength of the QFM, VAS, 50-m walk test Group 5 (only isokinetic exercises) *Strength of the QFM, VAS, 50-m walk test Between groups **Isokinetic dynamometer in groups 1, 2, and 3 compared with group 5 at all angular velocities **VAS in groups 1 through 4 compared to group 5
Tok et al. [35]	At baseline 3rd week	Strength of the QFM Isokinetic dynamometer Pain VAS (at rest and activity), WOMAC-pain Function WOMAC-PF	Group 1 (conventional physical therapy + CPM–ES combination) *VAS-activity, stiffness and social function dimensions of WOMAC Group 2 (conventional physical therapy and isometric exercise) *VAS-activity, stiffness dimension of WOMAC, bodily pain
Bruce-Brand et al. [33]	1th week 8th week 14th week	Strength of the QFM Isokinetic dynamometer Pain WOMAC-pain Function WOMAC-PF, 25 m walk test, Stair climb test, Chair rise test	RT group *25 m walk test, stair climb test, chair rise test at week 8 or 14 compared to week 1 NMES group *25 m walk test, stair climb test, chair rise test at week 8 or 14 compared to week 1, WOMAC-pain at week 8 compared to week 1, WOMAC physical function at week 14 compared to week 1 Between groups **25 m walk test, stair climb test, chair rise test in training groups compared control group
Laufer et al. [31]	At baseline 6th week 12th week	Strength of the QFM Myometry system (MVIC and VA) Pain VAS, WOMAC-pain Function WOMAC-PF, 10-m walk test, TUG, Stair test	Exercises group *VAS, WOMAC, 10-m walk test, TUG, MVIC, stair Exercises group + NMES *VAS, WOMAC, 10-m walk test, TUG, MVIC, stair Between groups **Pain in exercise group + NMES

Table 5 (continued)

Studies	Assessment times	Outcome measures	Results
Park et al. [34]	At baseline 4 week 8 week	Strength of the QFM Isokinetic dynamometer	Control group (general physical therapy) *Strength of the QFM baseline-4 week; baseline – 8 week Progressive resistance training (PRT) group *Strength of the QFM baseline-4 week; baseline – 8 week PRT + Russian electrical stimulation group (RES) *Strength of the QFM baseline-4 week; baseline – 8 week between groups Between groups **Strength RES than other groups

QFM quadriceps femoris muscle, *WOMAC* The Western Ontario and McMaster Universities Arthritis, *PF* physical function, *PrT* proprioceptive training, *ST* strength training, *HR Group* high-resistance exercise, *LR Group* low-resistance exercise, *VAS* visual analogue scale, *C-E/G* concentric-eccentric group, *I/G* isometric group, *SWD* shortwave diathermy, *HP* hot packs, *TENS* transcutaneous electrical nerve stimulation, *US* ultrasound, *CPM–ES* continuous passive motion-electrical stimulation, *RT* resistance training, *NMES* neuromuscular electrical stimulation, *MVIC* maximal voluntary isometric contraction, *VA* voluntary activation

*$P<0.05$ Intergroup; **$P<0.05$ Between group; ***$P<0.05$ Among group

improvement was shown in NMES group [33]. But there was no significant difference between intervention groups. Besides, when strengthening exercise compared with CPM–ES combination, there was a significant improvement in training groups, but no significant difference between groups [35]. Significant improvement was found in both groups when exercise training was compared with additional NMES. There was a significant difference in favor of additional NMES [31]. Isokinetic exercise, additional SWD + HP or TENS + HP or US + HP or HP groups showed significant improvements. When groups were compared, there was a significant difference in additional SWD + HP, TENS + HP, US + HP and HP groups compared with isokinetic exercises. But there was no significant difference among groups [32].

The effect of strengthening the QFM on function

For functional assessment, two studies used objective methods [30, 32] two studies used subjective outcomes (WOMAC-physical function (PF) [26, 35] and five studies used combined them (WOMAC-PF + timed performance test) [27–29, 31, 33]. Only one study did not use any function outcome measurement [34]. The results of the strengthening of the QFM training programs on physical function for each trial are summarized in Table 5.

The comparison of different strengthening exercises of the QFM HR and LR exercise groups showed significant improvements, but there was no significant difference between these groups [29]. In another study, significant improvements were found in training groups (Concentric-eccentric and isometric Group). There was a significant difference in favor of Concentric-eccentric group in between group [26].

The comparison of strengthening of the QFM training versus other knee exercises training or control group In two studies which compared home-based strengthening program versus the control group, the authors did not find any significant improvement in within- and between-groups [29, 30]. When strengthening exercise was compared with PrT exercise or control group, significant improvements were found in both training groups, but there was no significant difference between them [28].

The comparison of strengthening of the QFM training versus alone or combined electrotherapy There were significant improvements in both resistance training and NMES group, but there was no significant difference between these two groups [33]. Similarly, when isometric exercise was compared with CPM–ES combination, there were significant improvements in both groups, but no significant difference between groups [35]. Çetin et al. compared isokinetic exercises with additional various electrotherapy modalities, and they found significant improvement in all groups. Additional SWD + HP or TENS + HP were superior to isokinetic exercise [32]. There was no significant difference among groups. In the study which compared strengthening of the QFM training with additional NMES, there were significant improvements in both groups, but there was no significant difference between groups [31].

The methodological quality of the studies and risk of bias assessment

Quality Studies included in this review had moderate-to-high level of evidence. The methodological quality scores of the studies ranged from 5 to 8. Table 1 provides an overview of the methodological quality of the included studies.

Risk of bias Each risk of bias item is presented as percentages in Table 2. Overall, a few of studies performed allocation concealment, blinding of participants and therapist and blinding of assessors. The risk of bias was moderate in four studies [32–35] and low in others [26–31].

Discussion

The studies included in this review widely varied in terms of population and intervention durations. In addition, the studies showed conflicting results in terms of strength the QFM. Among the available studies, it was shown that strengthening of the QFM training was superior to PrT. Additional electrotherapy modalities had superiority to strengthening of the QFM alone-training. In terms of additional electrotherapy stimulation, the difference was found in only additional Russian electrical stimulation. Most of the included studies showed that strengthening of the QFM programs had an effect to reduce pain and improve function.

Knee OA is a common disease and numerous studies including exercise training have been investigated in the literature. However, we included only 10 studies in our review, because we included only randomized controlled trials which investigate strengthening of the QFM training, assess the strength of the QFM and have at least 5 points on PEDro scale. The overall methodological quality of the included studies was considered moderate to high with an average score of 6.7 (range 5–8) on the PEDro scale [23]. In addition, when the biases were evaluated, the studies had moderate to low risk. The methodological failure and risk of bias of the studies comprised the lack of concealed allocation, therapist blinding, assessor blinding and intention to treat. For these reasons, the findings of studies might have some risk of bias, especially the evaluation of the outcome measures.

Patients with knee OA often show a gradually decreased strength in the QFM [36]. In literature, there was no review study showed whether strengthening of the QFM alone-training is effective on strength of the QFM in knee OA. The comparison of different strengthening of the QFM exercise demonstrated that there was no significant difference in strength of the QFM and pain, but concentric-eccentric training was superior to isometric training on function [26, 27]. These studies were high methodological quality and low risk of bias. Another two studies compared home-based strengthening exercise training with the control group [29, 30]. While one of the studies found a significant difference in strength of the QFM, other study found a significant difference in pain score. Different results may derive from lack of subject or therapist blinding and intention-to-treat analysis which found a significant difference on strength of the QFM between groups. One study found a significant difference in the strengthening of the QFM group when compared with the PrT group on strength of the QFM, but improvement on pain and function was nonsignificant [28]. In the strengthening of the QFM exercise program, patients were asked to perform concentric and eccentric quadriceps femoris strengthening exercise while they sat on a chair with knees at 90° of flexion and they were supervised three times a week for 8 weeks. The baseline resistance was set at 50% of 1-RM, with a progressive increment of 5% of the original 1-RM every 2 weeks. All of these studies had high methodological quality and low risk of bias.

A study which had moderate methodological quality and risk of bias reported that there was no significant difference between the strengthening of the QFM training and NMES on strength of the QFM and pain. The only significant difference between groups was an improvement on timed performance test in favor of strengthening of the QFM training [33]. It may be caused from inclusion of home-based exercise training, limited sample size, and the short duration periods of training. Although additional NMES improved pain, there was no significant difference between the strengthening of the QFM exercise and additional NMES on strength of the QFM and function [26, 31]. Also, both of them had a short duration of training and lack of assessor blinding. These studies were moderate to high methodological quality and low to moderate risk of bias. Between-groups difference, additional Russian current stimulation has superiority on strengthening the QFM when compared to progressive resistance training or control group in elderly women with knee osteoarthritis [34]. Russian current, a pulse frequency of 50hz, burst duration of 10 ms, symmetric pulses of sinusoidal form, with a duty cycle of %25 (5 s/20 s) and a pulse duration of 400 qs. Groups were treated 45 min each session, 3 times weekly for 8 weeks in this study. However, only elderly women were included, in terms of methodological quality was moderate and risk of bias was low in this study. Additional SWD + HP or TENS + HP or US + HP had superiority on strength of the QFM over quadriceps-alone strengthening exercise, but there was no significant difference among groups [32]. In addition, pain improved in all additional physical modalities including HP or HP plus SWD, TENS or US compared with alone-exercise training. All groups have a significant improvement in function, but there was no difference between groups. This study had moderate methodological quality and risk of bias including lack of concealed allocation, subject and therapist blinding, intention-to-treat analysis. It could be said that additional physical modalities aiming pain reduction are more effective than NMES or CPM-ES on strength of the QFM.

In a recent review investigating weakness of the QFM and the risk of developing knee osteoarthritis, it was concluded that greater strength of the QFM seemed to be related to lower risk of incident symptomatic, but not radiographic knee osteoarthritis [37]. The treatments of knee OA mainly focus on pain reduction and functional disability of patients. The strength of the QFM was an important predictor of walking speed and functional performance in patients with knee OA [15]. Harrison et al. have reported that weakness of the QFM correlates with knee pain and functional disability [38]. Similarly, most of the included studies in this review showed that strengthening of the QFM exercises had an impact on pain reduction and improvement of function.

The studies included in this review showed differences in terms of duration and content of exercise programs. Considering the findings, the results of the strengthening of the QFM training depend on the delivery of exercise training, frequency, and duration of the intervention. To obtain an increased strengthening of the QFM in the least duration, while supervised exercise training showed beneficial effects 3 times weekly for 8 weeks, home-based exercise training revealed similar effects 5 times weekly for 12 weeks. However, it is required to carefully comment on the results of these studies because of their limited number.

A major strength of this review is that most of the included studies have a high level of evidence methodological quality and low risk of bias. However, the limitations of this review were heterogeneity of study designs (in methodological outcome measures and timing of assessments), the small number of available studies, and limited to studies published in English. These limitations need to be considered when interpreting the results of this review.

This review showed that strong evidence is limited about the effectiveness of strengthening of the QFM training in patients with knee OA. The implications of this review revealed that strengthening of the QFM training is superior to PrT and additional electrotherapy modalities have superiority to the strengthening of the QFM training. Additional hot pack plus shortwave diathermy or ultrasound or transcutaneous electrical nerve stimulation had superiority to isokinetic strengthening alone of the QFM exercise. Only additional Russian electrical stimulation showed the significant difference compared with the strengthening of the QFM exercise. Most of the included studies showed that strengthening of the QFM exercises have an effect on pain reduction and improvement of function.

Conclusions

The results of this systematic review provided moderate-to-high evidence to support that (1) there was no significant difference between strengthening types of the QFM exercise training, (2) strengthening of the QFM exercise training was superior to PrT, (3) in terms of strengthening the QFM, additional Russian current stimulation had superiority to progressive resistance training or control group, (4) there was no significant difference in comparison of strengthening of the QFM with combination of NMES or CPM-ES, and (5) additional SWD plus HP, TENS plus HP or US plus HP had superiority over strengthening of the QFM alone-exercise training. It was demonstrated that strengthening of the QFM exercises has an effect on pain reduction and improvement of function. In light of the current findings, it is considered that the strengthening of the QFM exercise program is effective for patients with knee OA. Further high-quality trials with long-term follow-up are needed to investigate the effect of the strengthening of the QFM on weak muscle, pain, and dysfunction for the treatment of knee OA.

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