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Effectiveness of Exercise Therapy in Treatment of Patients With Patellofemoral Pain Syndrome: Systematic Review and Meta-Analysis

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Background and Purpose. This systematic review and meta-analysis was accomplished to determine whether exercise therapy is an effective intervention to reduce pain and patient-reported measures of activity limitations and participation restrictions (PRMALP) in patients with patellofemoral pain.

Data Sources and Study Selection. Randomized controlled trials in English and German languages published in the MEDLINE, Physiotherapy Evidence Database (PEDro), International Clinical Trials Registry Platform, and Cochrane databases were searched. Eligibility was assessed in 2 stages. The methodological quality of the studies was rated using the PEDro scale. Data were pooled using random-effects meta-analysis, allowing for variability among studies. For clinical use, overall estimates were re-expressed in the original visual analog scale scores. Significance was set at 5%.

Data Extraction and Data Synthesis. Fifteen studies, with a total of 748 participants, were included and pooled for the meta-analysis. Six studies compared the effect of exercise therapy with a control group receiving neither exercise therapy nor another intervention. Four studies compared the effect of exercise therapy versus additive therapy, and 5 studies compared different exercise interventions. In both comparisons, exercise therapy resulted in strong pain reduction and improvement of PRMALP effects. Significant short-term effects (≤12 weeks) of exercise therapy were found for pain and PRMALP, whereas long-term effects (≥26 weeks) were observed for PRMALP only.

Limitations and Conclusion. The 15 studies included in this analysis were of variable quality. Large-scale, high-quality randomized controlled trials are needed to further the evaluation of the possible effects of different exercise therapy modalities on patellofemoral pain. This meta-analysis presents evidence that exercise therapy has a strong pain-reducing effect and decreases PRMALP in patients with patellofemoral pain. However, the question of which exercise modality yields the strongest reducing effect on pain and PRMALP remains unanswered.

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Patellofemoral pain syndrome (PFPS) is a common musculoskeletal disorder in physically active individuals aged 15 to 30 years.[1,2] The prevalence ranges from 21% to 45% in active adolescents and from 15% to 33% in adults[3] and is higher in females than in males.[2,4] However, there are limited epidemiological incidence data.[2,5,6] The most reported complaint is retropatellar pain or diffuse peripatellar pain during activities such as running, ascending and descending stairs, squatting, and sitting with flexed knees for prolonged periods of time.[7,8] Other common symptoms are crepitation and the giving-way phenomenon.[9–11]

The etiology of PFPS appears to be multifactorial. Several causative factors relating to the malalignment of the lower extremity kinematics are described in the literature. Altered or excessive foot pronation may result in a compensatory internal rotation of the tibia and increased valgus stress.[12–15] The quadriceps muscle stabilizes the gliding of the patella through the femoral groove. An imbalance between the force of the vastus medialis obliquus muscle and other quadriceps muscle groups can lead to a lateral displacement of the patella, resulting in patellofemoral joint stress on the lateral facet.

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- eFigure 1: Flowchart Describing the Systematic Review Procedure
- eFigure 2: Forest Plot of the 6 Studies Evaluating the Short-Term Effect of Exercise Therapy Versus No Exercise on Pain
- eFigure 3. Forest Plot of 2 Studies Evaluating the Long-Term Effect of Exercise on Pain Compared With No Exercise Therapy

Biomechanical studies have demonstrated that patients with patellofemoral pain exhibit greater frontal-plane[16] and transverse-plane[17,18] hip motion during activities of daily living. It has been hypothesized that increased frontal- and transverse-plane hip motion may affect the lateral forces acting on the patella.[13] Furthermore, internal rotation of the femur during the stance phase is related to lateral patellar displacement and thus may be a contributor to altered patellofemoral joint kinematics.[13] Hamstring muscle tightness, iliotibial band tightness, patellar retinaculum tightness, and overactivity also may increase patellofemoral joint stress.[19–21] Although different hypotheses of the biomechanical and neurophysiological mechanisms of the beneficial effects of exercise therapy exist, there is considerable individual variation. For example, malalignment of the patellofemoral joint does not necessarily correlate with pain,[22] indicating that no particular exercise program is effective for all patients with PFPS.[1,7,11,19,23]

Currently, the most accepted theory behind PFPS relates the symptoms to excessive patellofemoral joint stress[13,22,24] modifying the soft tissue homeostasis.[15,22,25] The hyperinnervation and vascularization resulting from the ischemic tissue can cause the pain sensation.

Because no consensus exists on the definition of a clinical diagnosis or classification,[26] no validation of clinical tests is possible. Therefore, PFPS is often a diagnosis based on the exclusion of other pathologies.[24]

A conservative approach has been recommended as a first-line treatment for patients with PFPS.[9,19,27] The most successful rehabilitation should progress without increasing symptoms.[28,29] Currently, consensus regarding the most appropriate conservative treatment for PFPS is still lacking. A widely accepted intervention to treat PFPS is exercise therapy.[19,23,30–32] Good clinical results have been achieved with different variations of quadriceps muscle strengthening.[11] Exercise therapy is often combined with static quadriceps muscle stretching exercises (Tab. 1).

The aim of this systematic review was to establish an overview of the currently available evidence for the effectiveness of exercise therapy on pain and functional improvement, which was defined as "patient-reported measures of activity limitations and participation restrictions" (PRMALP), in patients with PFPS.[33] Furthermore, this study aimed to reach more conclusive results by summarizing the available studies in a meta-analysis.

Method

Data Sources and Search Strategy

The systematic literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[34] An electronic search was conducted during the period of January to August 2011 and updated at the end of December 2013 on the following databases: MEDLINE (PubMed), Cochrane Database of Systematic Reviews, Physiotherapy Evidence Database (PEDro),[35] and the International Clinical Trials Registry Platform. A manual search of the reference lists of retrieved publications was completed to screen for topic-related studies.

The sensitive search strategy was established combining the following MeSH-listed key words in the search algorithm: ("patellofemoral pain syndrome" OR "anterior knee pain" OR "chondromalacia patellae") AND ("exercise therapy" OR "therapy").

Table 1.
RCTs Comparing Exercise Therapy and No Exercise[a]

Study	PEDro Score	Participants (Age: $\bar{X}$±SD in Years)	Intervention Group	Control Group (or Intervention 2)	Outcome Variables	Main Results
Clark et al,[23] 2000	7	17 f, 25 m EX group age: 29.5±6.2 CON group age: 27.1±7.2	Duration: 12 wk EX: 6 sessions; warm-up, squatting on the wall, sit-to-stand, proprioceptive balance work, EX for gluteus medius and maximus muscles, progressive step-down Home program: daily exercises	Duration: 6 sessions Advice and (1) explanation about anterior knee pain, (2) footwear and sporting activities, (3) pain-controlling drugs, (4) stress relaxation, (5) diet and weight advice, and (6) prognosis and self-help	VAS and WOMAC scores after 12 wk and 52 wk	After 12 wk, pain reduction and PRMALP improvement in both groups (*P*<.0001), no significant difference in pain and PRMALP improvement between groups After 52 wk, pain reduction (*P*=.005) and PRMALP improvement (*P*=.007) in both groups, no difference in pain and PRMALP improvement between groups (*P*>.05)
Herrington and Al-Sherhi,[48] 2007	6	45 m Age: 26.9±5.6	Duration: 6 wk EX: 3 sessions per week for 6 wk; warm-up, OKC in a seated position, CKC on leg press	No intervention	VAS and functional performance (modified Kujala scale) after 6 wk during different activities	Pain reduction in EX groups (*P*=.015), difference between groups in pain (*P*=.01), PRMALP improvement in EX groups (*P*<.05), no difference between EX groups (*P*>.05)
van Linschoten et al,[43] 2009	6	84 f, 47 m EX group age: 24.7±8.6 CON group age: 23.3±7.8	Duration: 12 wk EX: 9 sessions in 6 wk under supervision; daily EX for 25 min over 12 wk; warm-up on ergometer; different muscular EX for quadriceps, adductor, and gluteal muscles; flexibility EX for thigh muscles	Duration: 12 wk Advice: rest during periods of time, refraining from pain-provoking activities and usual care	VAS during rest and activity and functional disability (Kujala scale) after 12 and 52 wk	Pain reduction in EX group after 12 wk (*P*=.02) and 52 wk (*P*<.02), difference between groups in pain (*P*<.01) after 12 wk and 52 wk, higher function score in EX group after 12 wk (*P*=.04), no difference in PRMALP between EX and CON groups (*P*=.09) after 52 wk
Song et al,[49] 2009	8	69 f, 20 m EX group age: 39.4±10.3 CON group age: 43.9±9.8	Duration: 8 wk EX: 3 sessions per week for 8 wk; leg press or leg press combined with isometric hip adduction	Duration: 8 wk Advice: health educational material regarding PFPS	VAS-U and VAS-W and functional ability (Lysholm scale) after 8 wk	Pain reduction in EX group (*P*<.005), difference in pain between EX and CON groups (*P*<.008), PRMALP improvement in EX group versus CON group (*P*<.005)
Fukuda et al,[47] 2010	8	70 f EX group age: 25.0±6.5 CON group age: 24.0±7.0	Duration: 4 wk EX: 12 sessions in 4 wk; strengthening and stretching, strengthening of the hip abductor and lateral rotator muscles	No intervention	NPRS and functional improvement (LEFS) after 4 wk during different activities	Pain reduction in EX group (*P*<.008), difference in pain between EX and CON groups (*P*<.01), PRMALP improvement (LEFS) in EX group (*P*<.05)
Khayambashi et al,[38] 2012	5	28 f EX group age: 28.9±5.8 CON group age: 30.5±4.8	Duration: 8 wk EX: 3 sessions per week for 8 wk; 5-min warm-up, 20-min hip strengthening, 5-min cool-down	No intervention	VAS and WOMAC after 8 wk and 26 wk	Pain reduction in EX group (*P*<.001); after 26 wk, pain reduction in EX group compared with baseline level (*P*<.001), PRMALP improvement in EX group compared with CON group (*P*<.001)

[a] RCT=randomized controlled trial, f=female, m=male, EX=exercise, CON=control, OKC=open kinetic chain, CKC=closed kinetic chain, VAS=visual analog scale, PRMALP=patient-reported measures of activity limitations and participation restrictions, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, PFPS=patellofemoral pain syndrome, LEFS=Lower Extremity Functional Scale, NPRS=numerical pain rating scale, VAS-U=VAS usual score, VAS-W=VAS worse score.

Table 2.
RCTs Comparing Exercise and Exercise With Additive Therapy (EMS or Splints)[a]

Study	PEDro Score	Participants (Age: $\bar{X}$±SD in Years)	Intervention Group	Control Group (or Intervention 2)	Outcome Variables	Main Results
Dursun et al,[46] 2001	5	48 f, 12 m EX group age: 36.6±10.6 CON group age: 36.9±9.2	Duration: 12 wk EX: 5 days per week for the first 4 wk and 3 days per week thereafter; strengthening of the quadriceps and vastus medialis obliquus muscles, flexibility training, proprioception training, endurance training	Duration: 12 wk EMG + EX program: 3 days per week for 4 wk	VAS and FIQ after 4, 8, and 12 wk	Significant ($P<.0001$) improvements (VAS and FIQ) in both groups, no difference between groups ($P>.05$)
Schneider et al,[50] 2001	4	28 f, 12 m EX group age: 23 CON group age: 21	Duration: 8 wk EX: 2 sessions per week of 1 h duration for 8 wk; exercise based on proprioceptive neuromuscular facilitation	Duration: 8 wk Knee splint: 15 min 3×/d combined with exercise therapy to strengthen the ischiocrural muscles	VAS after exposure and Bessette and Hunter scale at rest after 4 and 8 wk	Pain reduction in both EX group ($P=.003$) and EX + splint group ($P=.0005$), differences between groups in VAS ($P=.0065$) and Bessette and Hunter ($P=.0047$) scores in favor of EX + splint group
Yip and Ng,[42] 2006	6	16 f, 10 m Age: 32.5±8.8	Duration: 8 wk EX: home program for 15 min daily; quadriceps muscle strengthening, balance and proprioception training, plyometric and agility training, flexibility training	Duration: 8 wk EX: home program like intervention 1, additionally EMG biofeedback system	Patellofemoral Pain Syndrome Severity Scale after 4 and 8 wk	Pain reduction ($P=.088$), no difference in pain between groups ($P>.05$)
Bily et al,[41] 2008	5	14 m, 24 f EX group age: 23.7±5.5 CON group age: 27.0±7.7	Duration: 12 wk EX: 7 sessions per week for 2 wk, 3 sessions per week thereafter under supervision; isometric, concentric, and eccentric leg raises and pulls, stepping, squatting, balance exercises, static stretching	Duration: 12 wk EX program (like intervention group) + daily EMS of the quadriceps muscles, 2 sessions for 20 min/d	VAS (maximum) and Kujala patellofemoral score after 12 and 52 wk	Pain reduction ($P=.003$) and PRMALP improvement ($P<.001$) in both groups without significant difference between groups

[a] RCT=randomized controlled trial, f=female, m=male, EX=exercise, CON=control, EMS=electrical muscle stimulation, EMG=electromyography, VAS=visual analog scale.

Research Question and Study Selection

To establish the research question, the recommendations from the PICO model (Population: patients with patellofemoral pain syndrome; Intervention: exercise therapy; Comparator: no exercise or exercise with additive intervention [electrical muscle stimulation (EMS) or splints]; Outcome: pain and PRMALP) were used.

Randomized controlled trials (RCTs) regarding the effect of exercise therapy in patients with PFPS were sourced. Studies comparing participants with pathological conditions and those with nonpathological conditions and studies with comparisons based on taping, chiropractic interventions, foot orthoses, and surgical treatments were excluded. Studies including participants with other knee pathologies were not included. Full texts of articles written in German or English were included. No restrictions were imposed on the year of publication.

Identification of Literature and Quality Assessment

Eligibility, based on the a priori set inclusion and exclusion criteria, was assessed in 2 stages. First, studies were screened on titles and abstracts. In a second step, full texts of the eligible publications were analyzed. Additional information was requested from the corresponding authors in case of missing data.

The methodological quality of the studies was assessed using the PEDro rating scale. For studies retrieved from PEDro, the mentioned PEDro scores were accepted. If the score was not available, the quality was evaluated by 2 reviewers (M.K. and F.J.) independently using the PEDro rating scale. Disagreements were resolved in a consensus meeting.

Data Synthesis and Meta-Analysis

The primary outcome measure for this meta-analysis was pain, assessed with a visual analog scale. From the retrieved studies, PRMALP data evaluated with standardized scoring scales (Kujala patellofemoral score, Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC], Lysholm scale, Functional Index Questionnaire [FIQ], Lower Extremity Functional Scale [LEFS]) were extracted as a secondary outcome. Most studies presented VAS and PRMALP data as means and standard deviations, making pooling of the data possible.

A meta-analysis with a random-effects model (specified a priori), accounting for possible between-studies heterogeneity, was used to calculate the overall effect size of exercise therapy on patellofemoral pain and PRMALP. Effect sizes of the RCTs included in the present meta-analysis were expressed as Hedges' g to correct for small-scale studies' effect of overestimating the true effect size. Ninety-five percent confidence intervals (95% CIs) were calculated for the individual studies and the overall estimates of the different meta-analyses. The Q statistic and its *P* value were calculated to assess between-studies heterogeneity, and I^2 was used to express the degree of heterogeneity. For the purpose of better clinical understanding of the results for pain, the overall estimates were re-expressed as the original VAS scores.[36] Publication bias was assessed by visually analyzing the funnel plot and by formal testing for funnel plot asymmetry[37] using the "trim and fill" and the "fail 'n safe" algorithms scores. All meta-analytic calculations and plots were conducted using CMA-2 software (Comprehensive Meta-Analysis, version 2, Biostat, Englewood, New Jersey).

Results

Flow of the Search Procedure

The initial literature search resulted in a total of 285 studies. Two hundred two publications were excluded after screening the title and abstract. Out of the remaining 83 studies, 27 had to be excluded because of insufficient information, 4 were excluded for justifiable reasons (healthy versus unhealthy participants, no isolated effect elucidated), and 39 duplicates were removed, resulting in 13 studies meeting the inclusion criteria. The final update search (December 2013) yielded 2 more publications.[38,39] Thus, 15 studies were included in the present meta-analysis (eFig. 1, available at ptjournal.apta.org).

Study Design and Characteristics of Population

Tables 1, 2, and 3 depict the general characteristics of the 15 included studies by different comparisons (ie, therapy versus no therapy, exercise versus exercise with additive therapy, and knee extension exercises versus other forms of exercises, respectively).

Exercise characteristics. Exercise modalities, regimens, and settings varied widely across the trials. In 4 studies, patients were instructed to exercise daily.[40–43] In 9 studies, the therapy program consisted of 3 to 5 weekly exercise sessions.[20,38,39,44–49] Two studies reported 2 sessions or less per week.[23,50] Four studies used home-based exercise therapy interventions.[20,23,43,44] From the 15 included studies, only 6 provided sufficient information regarding the exercise therapy load.[20,38,39,42,43,50]

Exercise therapy versus no exercise. Exercise therapy was based on quadriceps muscle strength training in open or closed kinetic chain,[23,43,47–49] hip strength training,[23,38,43,47] adductor training,[43,49] and proprioceptive and flexibility training.[23,43] Control group participants received advice on pain origin[23,43,49] or no information at all[38,47,48] (Tab. 1).

Meta-Analyses

Short-term and long-term effects of exercise therapy versus no exercise on pain. A total of 6 studies providing data on 349 participants (exercise group: n=189; control group: n=160) were included in the meta-analysis.[23,38,43,47–49] Negative overall estimates represent pain reduction and thus favor exercise therapy. The mean overall effect size (Hedges' g) for postintervention values was −1.18 (95% CI=−1.86, −0.51), favoring exercise therapy. Between-studies heterogeneity for postintervention values was significant ($Q=39.57$, $P<.0001$) and high ($I^2=87.4\%$). A subgroup analysis showed that part of this heterogeneity could be explained by sex and the type of intervention (hip training, knee training, or combined). For the purpose of a better clinical understanding, these values were re-expressed as the original pain scale scores.[36] An overall estimate (Hedges' g) of −1.18 represents a

Table 3.
RCTs Comparing Knee Extension Exercises and Other Forms of Exercises[a]

Study	PEDro Score	Participants (Age: $\bar{X}$±SD in Years)	Intervention 1	Intervention 2	Outcome Variables	Main Results
Witvrouw et al,[20] 2000	6	40 f, 20 m Age: 20.3	Duration: 5 wk EX: 3 sessions per week for 5 wk of 30–45 min duration; OKC maximum, static quadriceps muscle contraction, SLR, short-arc movements, leg adduction, stretching Home EX: participants advised to maintain their muscle strength	Duration: 5 wk EX: 3 sessions per week for 5 wk of 30–45 min duration; CKC leg presses, knee bends, bicycling, rowing machine exercises, step-up and step-down, jumping exercises, stretching Home EX: participants advised to maintain their muscle strength	VAS and functional performance (Kujala scale) after 5 and 12 wk	Pain reduction in the CKC group (P<.05), no pain reduction in the OKC group (P>.05); PRMALP improvement in both groups; after 5 wk, CKC group (P=.002) and OKC group (P=.001); after 12 wk, CKC group (P=.001) and OKC group (P=.0004); difference between groups for pain (P=.024); no difference between groups for PRMALP (P>.05)
Bakhtiary and Fatemi,[40] 2008	6	32 f Group 1 age: 22.3±1.7 Group 2 age: 21.8±0.6	Duration: 3 wk EX: 42 sessions in 3 wk (2 sessions per day); SLR exercises (OKC) in supine position until 45° hip flexion and hold it for 3–4 s	Duration: 3 wk EX: 42 sessions in 3 wk (2 sessions per day); semi-squat exercises (CKC) until 15°−20° of knee flexion, hold for 3–4 s	VAS and MIVCF after 3 wk	Pain reduction in both groups, with no difference between groups (P=.13); increased muscle force in the semi-squat group (P=.01)
Nakagawa et al,[45] 2008	7	10 f, 4 m Age: 23.6±5.9	Duration: 6 wk EX: 5 sessions per week for 6 wk; quadriceps muscle strengthening and stretching	Duration: 6 wk EX: 5 sessions per week for 6 wk; quadriceps muscle strengthening and stretching supplemented by strengthening and functional training focused on the transversus abdominis, hip abductor, and lateral rotator muscles	VAS-U and VAS-W after 6 wk	Pain reduction in group 2 (P<.05), no decrease in pain in group 1; increased eccentric isokinetic knee extensor peak torque for both intervention groups (P=.04) and control group (P=.02)
Balci et al,[44] 2009	5	40 f Group 1 age: 39.1±8.0 Group 2 age: 36.1±8.7	Duration: 4 wk EX: 20 sessions in 4 wk under supervision; functional squat exercises with hip internal rotation and 0°−45° flexion interval of the knee Home EX program: 6 wk; SLR in supine position, strengthening hip adductor muscles in side-lying position, isometric	Duration: 4 wk EX: 20 sessions in 4 wk under supervision; functional squat exercise with hip external rotation and 0°−45° flexion interval of the knee Home EX program: 6 wk; SLR in supine position, strengthening hip adductor muscles in side-lying position, isometric	VAS in rest and activity after 4 wk and 10 wk Functional capacity after 4 wk and 10 wk	Pain reduction in both groups (P=.01), no difference between groups; PRMALP improvement in both groups (P=.001) and control group (P=.001), no difference between groups
Dolak et al,[39] 2011	6	33 f Group 1 age: 26±6 Group 2 age: 25±5	Duration: 8 wk EX (weeks 2–4): 3 sessions per week consisting of short-arc squats, SLR, and terminal knee extensions with progression of the resistance EX (weeks 5–8): single-leg balance with either front or diagonal pull, wall slides, step-downs, calf raises, lunges, squats, flexibility and balance training	Duration: 8 wk EX (weeks 2–4): standing hip abduction, side-lying hip abduction, seated hip external rotation, combined hip abduction and external rotation with progression of the resistance EX (weeks 5–8): the same intervention as the other group	VAS, functional improvement (LEFS) and isometric strength of HABD, HER, and KE after 4 wk, 8 wk, and 12 wk	Pain reduction in group 1 after 8 wk (P=.028), in group 2 after 4 and 8 wk (P=.001, P=.003); improvement in LEFS scores in both groups after 4 wk (P=.006) and 8 wk (P=.006); increased HABD strength after 8 wk (P=.001); increased HER strength after 8 wk in both groups (P=.004); in both groups, no increase in KE strength (P=.39)

[a] RCT=randomized controlled trial, f=female, m=male, EX=exercise, OKC=open kinetic chain, CKC=closed kinetic chain, VAS=visual analog scale, VAS-U=VAS usual score, VAS-W=VAS worse score, SLR=straight leg raise, LEFS=Lower Extremity Functional Scale, PRMALP=patient-reported measures of activity limitations and participation restrictions, MIVCF=maximal isometric voluntary contraction force, HABD=hip abductors, HER=hip extensors, KE=knee extensor.

Study	Subgroup Within Study	Time Point	Hedges' g	Standard Error	Variance	Lower Limit	Upper Limit	z Value	P Value
Clark et al,[23] 2000	FM	12	−0.082	0.325	0.106	−0.719	0.555	−0.253	.801
Herrington and Al-Sherhi,[48] 2007	M	6	−3.438	0.477	0.228	−4.374	−2.503	−7.202	.000
van Linschoten et al,[43] 2009	FM	12	−0.342	0.175	0.031	−0.685	0.001	−1.956	.050
Song et al,[49] 2009	FM	8	−0.922	0.251	0.063	−1.413	−0.431	−3.681	.000
Fukuda et al,[47] 2010	F	4	−0.721	0.265	0.070	−1.240	−0.201	−2.719	.007
Khayambashi et al,[38] 2012	F	8	−2.896	0.533	0.284	−3.941	−1.851	−5.430	.000
			−1.301	0.410	0.168	−2.105	−0.497	−3.172	.002

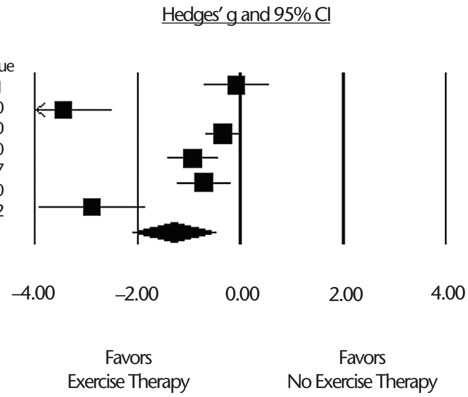

Figure 1.
Forest plot of 6 trials evaluating the short-term patient-reported measures of activity limitations and participation restrictions (PRMALP) improvement of exercise therapy versus no therapy in the treatment of patellofemoral pain syndrome. 95% CI=95% confidence interval, F=female, M=male.

Study	Subgroup Within Study	Time Point	Hedges' g	Standard Error	Variance	Lower Limit	Upper Limit	z Value	P Value
Clark et al,[23] 2000	FM	52	−0.078	0.376	0.141	−0.815	0.658	−0.209	.835
van Linschoten et al,[43] 2009	FM	52	−0.315	0.180	0.033	−0.668	0.039	−1.744	.081
Khayambashi et al,[38] 2012	F	26	−2.820	0.526	0.277	−3.851	−1.789	−5.362	.000
			−0.993	0.658	0.433	−2.282	0.297	−1.509	.131

Figure 2.
Forest plot of 3 studies evaluating the short-term patient-reported measures of activity limitations and participation restrictions (PRMALP) improvement of exercise therapy versus no therapy in the treatment of patellofemoral pain syndrome. 95% CI=95% confidence interval, F=female, M=male.

pain reduction of ≈40 mm on the 100-mm VAS pain scale after re-expression (eFig. 2, available at ptjournal.apta.org).

To evaluate the long-term (≥26 weeks) effect of exercise therapy on pain, 2 studies providing data on 197 patients comparing exercise therapy with no exercise therapy[23,43] could be analyzed. The mean overall effect size (Hedges' g) for postintervention values was −0.48 (95% CI=−0.80, −0.16), yielding a statistically nonsignificant pain reduction after re-expression on the VAS pain scale of ≈10 mm (eFig. 3, available at ptjournal.apta.org).

Short-term PRMALP improvement exercise therapy versus no therapy. The meta-analysis on the effectiveness of exercise therapy versus no therapy on the short-term (≤12 weeks) PRMALP improvement revealed a negative overall estimate (Hedges' g) of −1.30 (95% CI=−2.11, −0.50), indicating PRMALP improvement favoring exercise therapy. Between-studies heterogeneity for postintervention values was significant (Q=57.99, $P<.0001$) and high (I^2=91.4%). Again, subgroup analysis showed that part of this heterogeneity could be explained by sex and the type of intervention (Fig. 1).

Three studies were selected for a subgroup analysis, comparing the outcome of exercise therapy on long-term (≥26 weeks) PRMALP improvement.[23,38,43] The overall summary estimate (Hedges' g) of the pooled standard deviation for post-treatment values on PRMALP was −0.99 (95% CI=−2.28, −1.51), favoring exercise therapy (P=.131) (Fig. 2).

Exercise therapy versus additive therapy. Two included studies examined the efficacy of biofeedback supplementation in addition to exercise therapy in PFPS treatment.[42,46] The study by Bily et al[41] evaluated the efficacy of a training program including electrical muscle stimulation in which the electrodes were positioned on the vastus medialis and lateralis muscles. The application was performed daily[41,42] or 3 times per week.[46] Schneider et al[50] evaluated the use of a knee splint. The comparative exercise therapy consisted of strengthening, flexibility, proprioceptive, and endurance training[41,42,46] and proprioceptive neuromuscular facilitation[50] (Tab. 2).

Four studies providing data after 4, 8, and 12 weeks of intervention in 81 patients receiving an exercise intervention and 81 patients receiving exercise plus an additive therapy (EMS or splints) were included to evaluate the short-term (≤12 weeks) pain effect on PFPS.[41,42,46,50] To avoid erroneous deflating of the variance, the number of participants was divided by the number of measurement sessions for meta-analysis. The overall summary estimate (Hedges' g) for posttreatment values was 0.12 (95% CI=−0.29, 0.53, P=.57). The observed moderate heterogeneity was not significant (Q=11.92, P=.103, I^2=41.3%).

Of the above-mentioned studies, only 2 reported on PRMALP in 48 patients receiving an exercise intervention and 45 patients receiving exercise plus an additive therapy.[41,46] The overall summary estimate for posttreatment values was −0.60 (95% CI=−1.00, −0.19, P=.004), favoring exercise therapy only. No heterogeneity was observed (Q=0.07, P=.79, I^2=0%).

Effect of different exercise interventions on pain. Two studies compared the effect of closed and open kinetic chain exercises.[20,40] Open chain exercises relative to the hip are based on straight leg raises, whereas closed chain exercises relate to leg press or squat exercises. The additional effect of hip strength training to quadriceps muscle strength training was evaluated in 2 studies.[39,45] The focus was set on the hip joint abductors and lateral rotators (Tab. 3).

Two subgroup analyses were performed to compare different exercise interventions. The first comparison was between closed and open kinetic chain exercises.[20,40] Ninety-two participants were included. The mean overall effect size (Hedges' g) for the postintervention values was 0.08, although this value was not statistically significant (95% CI=−0.32, 0.48, P=.695). No heterogeneity was observed (Q=0.23, P=.634), I^2=0%).

The second comparison was between patients with exercise therapy focused on quadriceps muscle strength training and exercise therapy focused on hip muscle strength training. The mean overall effect size (Hedges' g) for postintervention values was 0.32 (95% CI=−0.33, 0.98, P=.337). The results of these 2 subgroup analyses do not provide convincing evidence to make conclusive decisions on favoring a specific intervention over another. No significant heterogeneity was observed (Q=1.32, P=.250, I^2=24.33%).

Methodological quality. The quality of the included studies varied widely according to the PEDro rating scale, with scores ranging from 4 positive items (out of 10 items)[50] to 8 positive items (out of 10 items).[49] Twelve studies described the procedure of the randomization: 6 used shuffled sealed envelopes,[20,41,47–49] 4 made use of a computer-generated randomization list,[23,39,40,43] 1 used a drawing lot,[42] 1 did the randomization manually,[38] and 3 did not explain the randomization procedure in detail.[44,46,50] Unfortunately, the corresponding authors did not react on the request to describe the randomization procedure. Six studies[23,42,45,47–49] reported that a blinded assessor was involved for all outcome measurements.

Funnel plots are a way of detecting whether selective publication of small-scale studies with positive results and nonpublication of small-scale studies with negative results influence the outcome of a meta-analysis (Fig. 3). If all points are evenly distributed on both sides of the solid vertical line, it indicates no publication bias. One outlier on the left side could be detected.[48] This finding was considered throughout the statistical analysis. The exclusion decreased the heterogeneity, although the significance of exercise therapy was still confirmed.

Not only visual inspection of the funnel plot can help to interpret the results but also mathematical measures. The "fail-safe N" statistic can be calculated to define the number of new unpublished or unretrieved nonsignificant or "null result" studies that would be required to change the overall estimate value toward a nonsignificant value.[37] Calculations have indicated that it would take 89 unpublished null result studies to decrease the overall estimate toward 0.

Discussion

This systematic review and meta-analysis of 15 studies totaling 748 participants (females: n=539; males: n=209) assessed the available evidence for the use of exercise therapy in the treatment of PFPS. Based on the results of the present study, exercise therapy appears to be an important strategy to achieve pain and PRMALP relief in patients with PFPS.

A few reasons could explain the convincing results observed by Khayambashi et al[38] and Herrington and Al-Sherhi.[48] As a result of the intervention of Khayambashi et al,[38] participants improved in hip abduction and external rotation strength. Excessive hip adduction and internal rotation have been postulated to influence patellofemoral joint kinematics.[13] Therefore, alterations in muscular hip strength might have resulted in a decrease in patellofemoral joint loading and in pain. In addition, the homogeneity of the study sample, with inclusion of female participants only, could have led to the strong pain-relieving and PRMALP-reducing effects, as females are more likely to have stronger internal rotator muscles and weaker external rotator muscles compared with males, in whom this relationship is inverse. Nevertheless, the study supports the importance of hip strengthening as a viable intervention to treat PFPS and, therefore, can be an important factor in the rehabilitation program. Possible reasons for the strong results achieved by Herrington and Al-Sherhi[48] may be the short follow-up time and the inclusion of male participants. Furthermore, it has to be noted that pain for at least 1 month was one of the inclusion criteria in this study, whereas in many of the other studies, participants fulfilled the inclusion criteria if the symptoms of anterior knee pain occurred for at least 2 months.[23,38,41–44,47,50,51]

Closed kinetic chain exercises are more associated with activities of daily living than open kinetic chain exercises. Two studies[20,40] demonstrated a significant decrease in pain in patients treated with closed kinetic chain exercises (as defined by the authors) as well as open kinetic chain exercises, with a tendency toward few significantly better functional results in the group treated with closed kinetic chain exercises. The overall estimate (Hedges' g=0.08) was not significant and, therefore, did not support the evidence of either closed kinetic chain or open kinetic chain exercises. Furthermore, the analysis included 2 studies with a sample size of 92 participants.[20,40] No valid conclusion can be drawn from the results and the study limitations.

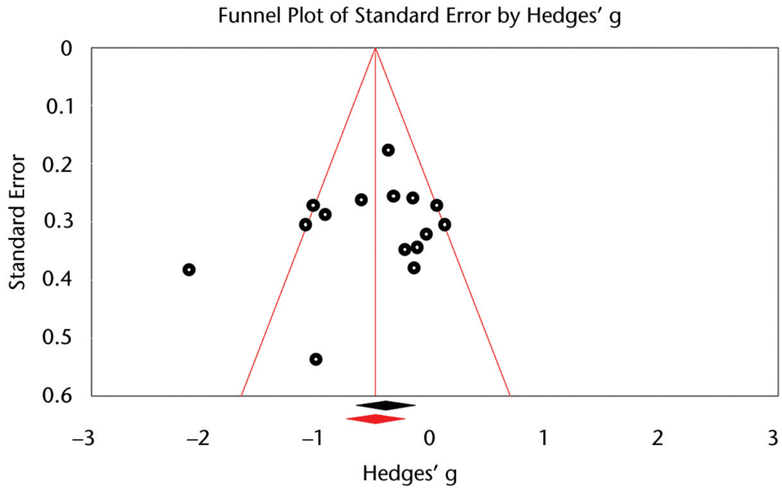

Figure 3.
Funnel plot of included studies.

Balci et al[44] confirmed the pain-reducing effects of closed kinetic chain exercises in patients with PFPS independent of internal or external hip rotation. Dolak et al[39] and Nakagawa et al[45] confirmed the importance of functional training in studies comparing knee exercise and other forms of exercise. Pain reduction was achieved in both exercise groups. However, the groups treated with supplemented hip and trunk strength training achieved stronger pain-reducing results. A possible reason may be improved lower extremity joint alignment leading to decreased patellofemoral joint pressure.

For better clinical understanding the Hedges' g, effect sizes were re-expressed in terms of VAS pain score reduction (ranging from −10 to −40 mm). Several studies have been published on VAS score reduction posttreatment and the clinical effectiveness of a treatment intervention. Grilo et al[52] stated that the minimum clinically significant difference in pain intensity is achieved by a 20-mm decrease in VAS pain score in patients with acute rheumatic conditions. Todd et al[53] found that a VAS score reduction of 13 mm was perceived as clinically significant in patients with acute pain from a trauma. A clinically relevant 10-mm VAS score reduction was found for the long-term follow-up studies in the present meta-analysis. The absence of statistical significance could be a result of the low number of studies and study participants. Therefore, the observed effects justify the conclusion that exercise therapy can have a short-term and long-term pain- and PRMALP-relieving effect in patients with PFPS.

Reduction in pain can be observed in control groups, too. There are different arguments that could explain this phenomenon. The observed improvement in the studies by Clark et al[23] and van Linschoten et al[43] could have been due to the natural course of the disease because the follow-up was done after 52 weeks. Another possible explanation could relate to the Hawthorne effect. The Hawthorne effect refers to a phenomenon in which human behavior or performance is altered as a result of being part of an experiment or study.[54]

The results of the studies by Biley et al,[41] Yip and Ng,[42] and Schneider et al[50] demonstrate that exercise therapy with an additive therapy (EMS or EMG biofeedback) provides no additional benefit for patients with PFPS, which is important in the context of allocation of resources.

Although patellofemoral pain syndrome is one of the most prevalent musculoskeletal injuries encountered in an active population, a unique definition of the syndrome is still not available. The exact pathomechanism is an unsolved issue as well. However, various theories concerning the etiology have been proposed.

Because of the complex etiology of PFPS in humans, the "universal PFPS patient" does not exist. Therefore, it is difficult to find consensus concerning the most appropriate conservative treatment. Although exercise therapy as a PFPS treatment is widely accepted, a comprehensive treatment program should adapt to the individual needs of each patient.

Quality Assessment

The PEDro summed item score was chosen to assess the quality of the RCTs included in this meta-analysis because of its documented reliability[55] and its widespread use in physical therapy. To analyze a possible effect of study quality on the overall estimate, a meta-regression was performed. Individual studies' effect sizes (Hedges' g) were regressed over their study quality (PEDro score), indicating an increasing effect size of exercise therapy and increasing study quality ($B=0.237$, $P=.0009$). Details of the randomization procedure were missing in 3 studies with a total of 140 participants.[44,46,50] The corresponding authors did not answer our requests for more information. Sensitivity analysis excluding the 3 studies did not influence the overall effect size. However, the PEDro scale does not include field-specific items. A more research-specific tool (eg, GRADE)[56] or a component approach to analyzing the risk of bias[36] could have influenced the overall effect estimate.[57]

Several authors discussed possible explanations for the effectiveness of exercise programs in relieving pain in patients with PFPS. Most studies associated the increase in functional muscle strength, altered sensorimotor behavior, and the restoration of patella alignment with a reduction of stress on the patellofemoral joint. The improvements of motor control motion and patellofemoral joint performance appear to be important factors in the management of patellofemoral pain syndrome. Although there is available evidence for the effectiveness of exercise programs in the treatment of patients with PFPS, there is general agreement that no single intervention is superior to others and no particular program is effective for all patients.

The main aim of this review was to assess the pain-reducing effect of exercise therapy in patients with patellofemoral pain. Among other reasons, we chose pain and PRMALP as outcome measures because they correlate with human well-being as well as with the adaptation in daily life.

Besides the strengths of this study, 2 major limitations should be discussed. First, a language bias may be present because of the restriction to publications in German and English languages. Second, publication bias and citation bias cannot be excluded.

In conclusion, this meta-analysis of 15 RCTs provides evidence that exercise therapy favors reduction of pain and PRMALP in patients with PFPS. Studies comparing exercise intervention with no intervention as well as studies comparing exercise intervention with exercise combined with an additive intervention (EMG or knee splint) resulted in clinically important effects. Furthermore, the results were independent of time. Short-term (≤12 weeks) as well as long-term (≥26 weeks) follow-up periods have confirmed the evidence in support of exercise therapy. However, there is not enough evidence to prefer one specific exercise intervention over another.

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Effectiveness of Exercise Therapy in Treatment of Patients With Patellofemoral Pain Syndrome: Systematic Review and Meta-Analysis

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