How effective is an evidence-based exercise intervention in individuals with patellofemoral pain?

ABSTRACT

Objectives

Guidelines for a comprehensive rehabilitation programme for patellofemoral pain (PFP) have been developed by international experts. The aim of this study was to analyse the effect of such a rehabilitative exercise programme on pain, function, kinesiophobia, running biomechanics, quadriceps strength and quadriceps muscle inhibition in individuals with PFP.

Design: Observational study

Setting: Clinical environment

Participants: Twenty-seven participants with PFP

Main outcome measures: Symptoms [numeric pain rating scale (NPRS)and the pain subscale of the Knee Injury and Osteoarthritis Outcome Score (KOOS)], function measured by using the KUJALA scale and KOOS, kinesiophobia measured by using the Tampa scale, three-dimensional biomechanical running data, quadriceps isometric, concentric and eccentric strength and arthrogenic muscle inhibition (AMI) were acquired before and after the six-week exercise programme.

Results

Although pain did not significantly improve all patients were pain-free after the six-week exercise programme (NPRS: $p = 0.074$). Function, kinesiophobia and quadriceps AMI improved significantly after the six-week exercise programme (KUJALA: $p = 0.001$, KOOS: $p = 0.0001$, Tampa: $p = 0.017$, AMI: $p = 0.018$). Running biomechanics during stance phase did not change after the exercise intervention. Quadriceps strength was not different after the six-week exercise programme (isometric: $p = 0.992$, concentric: $p = 0.075$, eccentric: $p = 0.351$).

Conclusion

The results of this study demonstrate that the current exercise recommendations can improve function and kinesiophobia and reduce pain and AMI in individuals with PFP. There is a need for reconsideration of the current exercise guidelines in stronger individuals with PFP.

Keywords

Patellofemoral pain, exercises, strength, treatment, pain, function

INTRODUCTION

Patellofemoral pain (PFP) describes pain around or behind the patella, which is commonly aggravated by activities that load the patellofemoral joint, such as stair stepping, squatting or running [16]. PFP is a common overuse injury in young and physically active people and can lead to limitations in sport and recreational activities [16]. Alarmingly, the results of long term follow up studies have reported that the majority of individuals with PFP still suffered from pain four to eight years later despite initially receiving treatment and education [41, 58, 59]. Such findings underline that PFP is not self-limiting and the gold standard strategy for managing PFP is yet to be identified [38]. It also indicates that the majority of patients with PFP do not respond to treatment and might be at risk of developing chronic pain [69]. Despite this, there are few published guidelines to help clinicians choose the appropriate evidence-based treatment for patellofemoral pain [17]. To address this gap, guidelines for a comprehensive rehabilitation programme were developed by international researchers during a consensus meeting at the 5th International Patellofemoral Pain Research Retreat in Manchester 2015 [17].

The consensus meeting was held to update the current evidence base and produce consensus-based recommendations regarding treatment for PFP. The participants of the consensus meeting were all active researchers in PFP[17]. The following six evidence-based recommendations to guide medical and health practitioners were established:

1. Exercise-therapy is recommended to reduce pain and improve function, regardless of the type of exercise (such as weight-bearing or not, targeting hip or knee).
2. The combination of hip and knee exercises is recommended to reduce pain and improve function and should be used in preference to knee exercises alone.
3. Combined interventions consisting of exercise therapy, targeting hip and knee musculature, patellofemoral taping, mobilisation and foot orthoses are recommended to reduce pain in adults with PFP.
4. Foot orthoses are recommended to reduce pain in the short term.
5. Patellofemoral, knee and lumbar mobilisations are not recommended.
6. Electrophysical agents are not recommended [17].

The experts at the consensus meeting also concluded that there is a lack of clarity regarding the taxonomy and reporting of exercise programmes and reported that the measurement of effectiveness of interventions to achieve a target, such as improved strength was rarely undertaken. To solve these problems, they recommended that future trials should publish the intervention in sufficient detail to enable clinicians to apply these in clinical practice. Furthermore, the potential mechanisms underpinning

the treatment effects are still not understood enough which to date hinders the optimisation of treatments [17].

The experts at the consensus meeting concluded: "Exercise therapy is the intervention of choice for PFP, with the largest body of evidence supporting its use to improve pain and function in the short, medium and long terms" [17]. Previously, researchers reported that multimodal interventions, such as the gluteal and quadriceps strengthening resulted in the strongest and most consistent evidence[3, 16, 63]. Hip and knee strengthening programmes were effective in the management of PFP, especially when open and closed kinetic chain exercises were applied [21, 63].

This study aimed to investigate the effect of a multi-modal rehabilitation programme, based on these guidelines. Therefore, the authors aimed to developed and delivered a six- week exercise programme, based on the published recommendations, and investigated the effect on pain, function, kinesiophobia, running biomechanics, quadriceps strength and inhibition in individuals with PFP.

It was hypothesised that pain, function, kinesiophobia, running biomechanics and quadriceps strength and inhibition would improve after the six- week exercise programme in individuals with PFP.

METHODS

Ethical approval was obtained from the University Research and Governance committee (HSCR 15–142) and the HRA (16/NW/0497). The trial was registered at ClinicalTrials.gov (NCT02786784).

Participant recruitment

Twenty-seven participants, aged 22 to 43 years, were recruited by physiotherapists of the Salford Royal Hospital NHS Foundation Trust (Figure 1).

The eligibility criteria for patients with PFP were: 1) aged 18-45 years; 2) antero- or retro-patellar pain with at least two of these activities: ascending or descending stairs or ramps, squatting, kneeling, prolonged sitting, hopping/ jumping, isometric quadriceps contraction or running 3) duration of current PFP symptoms >1 month.

The exclusion criteria for patients with PFP were: (1) any history of previous lower limb surgery or patellar instability and dislocation, (2) lower limb deformities or any history of traumatic, inflammatory, or infectious pathology in the lower extremities or any internal derangements, (3) not able to perform running during the measurement.

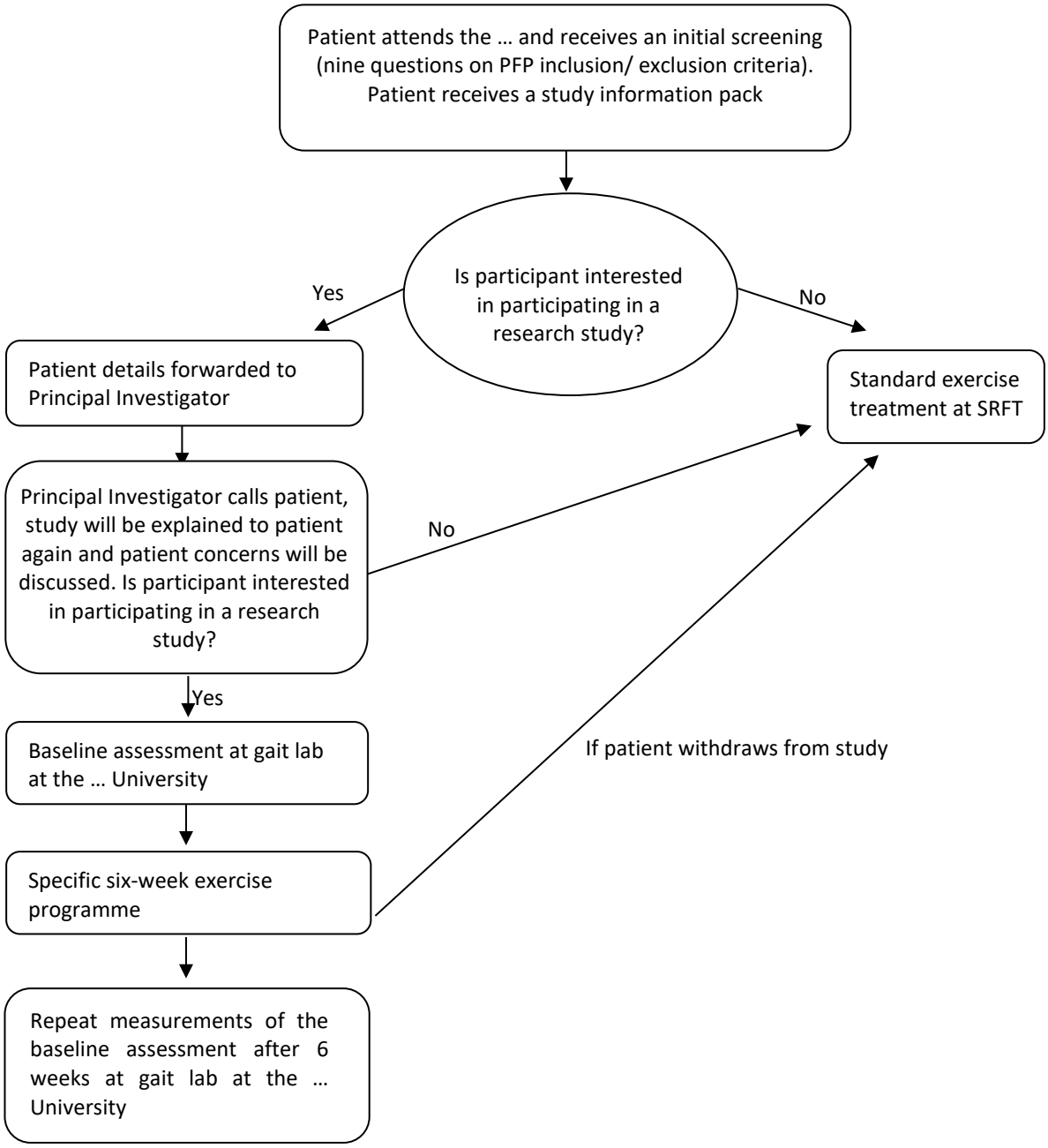

Figure 1: *Recruitment process for this study*

Procedure

Upon arrival at the laboratory, the patients were asked to fill in the numeric pain rating scale corresponding to their current pain, the knee injury and osteoarthritis outcome score (KOOS), the anterior knee pain scale KUJALA score and the Tampa scale for kinesiophobia. All patients were fitted with standard running shoes (New Balance, model M639SA UK), to control the interface of the shoe and the surface. Before the test, the body mass and height of each participant was measured. Only the lower limb where participants experienced PFP was assessed. If the participant experienced PFP in both limbs the more painful limb was assessed in this study.

An intra-rater reliability study on running kinematics, quadriceps inhibition and strength assessment was carried prior to this study. Therefore, 9 healthy individuals were tested in two separate sessions within two weeks. This unpublished study reported good reliability for all parameters[30].

Lower limb biomechanics assessment

Three-dimensional kinematic data were collected with ten Qualisys OQUS7 cameras (Qualisys AB, Sweden) sampling at 250 Hz. Forty retro-reflective markers, with a diameter of 14.5 mm, were placed on the lower limb of the participants. Kinetic data were calculated based on the GRF data collected with three force plates (BP600900, Advanced Mechanical Technology, Inc. USA), sampling at 1500 Hz, which were synchronised with the Qualisys system. The calibrated anatomical system technique (CAST) model, which included anatomical landmarks (markers on anatomical bony landmarks) and anatomical frames (segment mounted marker clusters), was used [12].

The retro-reflective markers were placed at the following anatomical landmarks: the anterior superior iliac spine, the posterior superior iliac spine, the iliac crest, the greater trochanter, the medial and lateral femoral epicondyle, the medial and lateral malleolus, the posterior calcanei, and the head of the first, second and fifth metatarsals[31]. The movement of the shank and thigh were tracked using a rigid 4-marker cluster, which were attached on the lateral side of shank and thigh with elastic wraps. A reference trial was collected to specify the location of the anatomical landmark markers in relation to the clusters and to approximate the joint center. The ankle and knee joint centers were calculated as midpoints between the medial and lateral malleolus and femoral epicondyles, respectively. The hip joint center was calculated using the regression model of Bell[5].

After the static trial, each subject was asked to run on a 15 m walkway at his/her own self-selected speed until 5 successful trials were collected. Unsuccessful trials were ones whereby less than three markers per segment were visible, or where a partial/double contact with the force platforms occurred. The self-selected running speed was collected and reported (Brower timing lights, Draper, UT).

After finishing all the tasks, the exercise programme was introduced to the patients, whereby each exercise was explained and shown to the patients. The booklet was explained to the patient and he/she was instructed how to document the exercises for the upcoming 6 weeks. They were informed that they should contact the researcher if they required advice or if they develop pain.

Within one week after finishing the six-week exercise programme a second assessment session was arranged to reassess the treatment effect.

Biomechanical data processing

The kinematic and kinetic outcomes were calculated with a 6 degrees of freedom model in Visual3D (Version 5, C-motion Inc, USA), which included six components to define the joint angle and joint moment. The joint angle was the rotation angle of the shank about the femur in a Cardan sequence of XYZ. The joint moment was calculated with inverse dynamics based on the kinematic data and GRF. The joint moments were normalised to body mass to ensure that the observed differences resulted from the body mass. The joint moments were presented as external moments referenced to the proximal segment. Marker movement and GRF data were filtered with a 4th order Butterworth filter with cut-off frequencies of 12 Hz. The kinematic and kinetic data were normalised to 100% of the stance phase during running. Stance phase was normalised from the force platform data when the forces exceeded 10 N for heel strike and went below 10 N for toe-off. The stance phase was sub-grouped into early (0-24% of stance phase), mid (25-62%) and late-stance phase (63%-100%) [44]. The peaks of the hip and knee flexion, adduction and internal rotation angles and moments were calculated for the early, mid, and late-stance phase.

Strength measurement

The isometric, eccentric and concentric (angular velocity of 60 degrees/second) peak torque of the quadriceps were assessed with an isokinetic dynamometer (Kin-Com, Chattanooga, USA). Participants were seated with 90° hip flexion on an isokinetic dynamometer and secured to the test chair with a chest and pelvic belt. The resistance pad was attached 1 cm proximal to the malleoli of the ankle and a gravity correction was performed prior to the strength test in line with previously described procedures [62]. The participant was verbally encouraged throughout the strength tests to ensure their attempt to a maximal voluntary effort.

The arthrogenic muscular inhibition (AMI) of the quadriceps was assessed, during the maximal voluntary isometric contraction (MVIC) of the quadriceps with the interpolated twitch technique. Therefore, the participants were seated in an isokinetic dynamometer and positioned in 90° hip flexion and 60° knee flexion. This position had been chosen as previous studies demonstrated that peak torques and flexor-to-extensor torque ratios were only symmetrical at 60° knee flexion[36]. Two electrodes (Axelgaard, Fallbrook, Ca, USA) were placed on the quadriceps muscle at one-third and two-thirds from the distance between the anterior superior iliac spine and the upper border of the patella [31]. A single twitch was triggered by the assessor manually on the relaxed muscles prior to the MVC (resting twitch torque (RTT). During the MVIC another single twitch with a pulse duration of 200 ms and a stimulus amplitude of 125mA (DS7AH Digitimer Ltd, Hertfordshire, England) was triggered manually by the investigator when the MVIC force had plateaued on the monitor (interpolated twitch torque - ITT). AMI was quantified

with the following equation: AMI = (ITT/ RTT)*100. An inhibition of 0% meant that the subject was able to fully recruit the muscle without showing any signs of inhibition[11, 28] (Figure S1).

Prior to the test a warm-up session of 4 submaximal isometric, eccentric and concentric quadriceps contractions was performed. Each participant was tested during the concentric and eccentric contraction at the angular velocity of 60°/second through the full available range of motion (ROM) from 90° knee flexion to maximal knee extension. Each individual performed three repetitions of both the isometric and isokinetic knee extensor strength tests with resting times of 30 seconds in between each maximal isometric and isokinetic assessments [10]. The order of the strength tests was randomized between isometric, concentric and eccentric testing.

Development of a six-week exercise programme

A six-week exercise programme, which patients could follow on their own at home, was developed based on the current recommendations, since the current guidelines recommend an exercise programme as a stand-alone treatment [17]. An exercise booklet was created, which described the correct execution of the exercises, with videos of all exercises uploaded to a password-protected website (Vimeo) to permit participants to undertake the programme without the supervision of a therapist.

Experts recommended that not more than 3-4 exercises should be prescribed to ensure the compliance of the patient with the treatment [3, 17]. Thus, the main exercise programme consisted of four strengthening exercises. In addition, two stretches for the hamstrings and gastrocnemius muscles were included.

The current PFP treatment guidelines emphasised that there was a need to individualise the treatments to each patient, as not all patients will require the same treatment [3, 17]. To meet these needs, each exercise included a progressive loading in six steps. The participants were instructed to progress individually for each exercise. They could enter a higher progression stage, if they did not experience any pain and if they felt only light or no exertion. If patients experienced pain during an exercise, they were instructed to either progress to the next lower level of the exercise or to contact the Principal Investigator of the study.

The first exercise was a squatting exercise, which has shown to strengthen and activate successfully the quadriceps and gluteal muscles with a relative low hamstrings co-activation [4, 14, 39, 50, 56, 67]. If the participant experienced pain, they were instructed to lean their trunk more forward or place their feet wider [25, 37].

The second exercise was a bridging exercise to strengthen the gluteus medius and maximus muscle [13, 50]. Unilateral bridging was chosen to increase gluteus maximus activity [50]. The execution of the exercise with a thera-band and on unstable surface has shown to generate more gluteus medius activity [13, 50].

To improve the control of the lower limb alignment, side band and rotational walks were included as a third exercise [33], which demonstrated to produce high levels of gluteus medius and maximus activity [2, 8, 20].

The last strength exercise was an open kinetic chain exercise to strengthen the quadriceps. This exercise was included since studies have shown that the combination of open and closed kinetic chain strength exercises seem to be the most effective method to strengthen the quadriceps [32, 68].

Reduced ankle dorsiflexion range of motion has shown to increase dynamic knee valgus during functional tasks [45]. Thus, mobilisations to address dorsiflexion restrictions are recommended as part of an exercise programme [17]. To ensure optimised knee and ankle biomechanics, the integration of a hamstrings stretch exercise has also been recommended [17, 66]. The integration of these two stretching exercises also served the purpose of planned rests for the participants in between their exercises.

The exercise programme was organised as a circuit training strategy of maximal 30 minutes, with three sets of 10 to 25 repetitions. The exercise booklet involved an exercise schedule. The participants were asked to note daily his/her level of progression and the number of repetitions for each exercise. They were asked to bring the booklet back after the six-week exercise programme to examine the individual progression (supplement: Exercise booklet).

Ankle weights and thera-bands were given to the participants and were returned after the six-week exercise programme.

Statistical analyses

The statistical analysis was performed using SPSS (v. 20). Normality was assessed by applying the Shapiro-Wilk's test and by the investigation of the normal q-q plots. For the data that was normally distributed, two-tailed paired sample t-tests and 95% confidence intervals were calculated to determine whether the six-week exercise programme significantly influenced the lower limb biomechanics. Data that was not normal distributed, as well as ordinal data (pain scale) was tested by using the Wilcoxon's rank test with an *a priori* alpha level set at $p < 0.05$. Furthermore, the mean change, SD of the mean change and the 95% confidence intervals of the difference were calculated.

Cohen's *d* effect sizes were calculated to determine the magnitude of the effect of the intervention (>0.8 large effect, 0.3-0.8 moderate effect, <0.3 small effect) [15].

Power calculation

A post hoc power calculation was performed on participants with PFP, using G-Power (Version 3.1.9.2), for pain (KOOS-pain), function (KUJALA), kinesiophobia (Tampa), quadriceps strength (isometric), quadriceps inhibition and hip adduction angle during stance phase by using a two-tailed t-test for two dependent means. The calculated effect size for the pain was dz=1.31 with a power of 99%, for function it was dz=1.2 with a power of 99%, for kinesiophobia (Tampa) it was dz= 0.48 with a power of 44%, quadriceps strength it was dz= 0.29 with a power of 19%, for inhibition it was dz=0.57 with a power of 56% and for hip adduction angle during stance phase it was dz=0.17 with a power of 9%.

RESULTS

Twenty-seven participants were recruited to the study and undertook the first examination. However, there was a drop-out of individuals who completed the six-week exercise programme with only 16 participants successfully completing the programme (Figure 2, Table 1). There were no significant differences in NPRS between participants that completed and participants that did not complete the study.

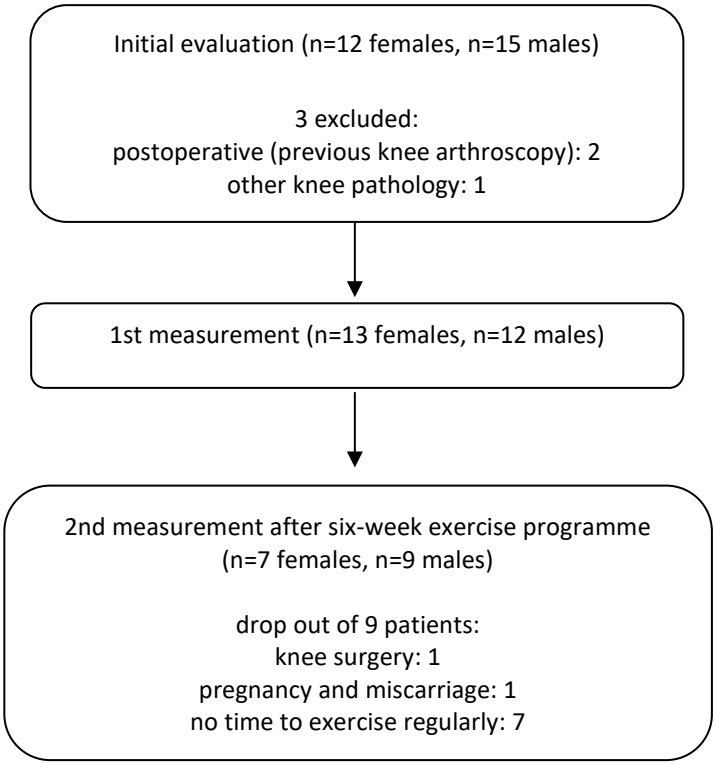

Figure 2: *Study flow diagram*

Pain was assessed with the NPRS and the KOOS-pain. Pain did not improve significantly on the NPRS (p = 0.074) but did significantly improve by 13.2 points from 79.7 to 92.9 points on the KOOS pain scale (p = 0.0001) (Table 2).

Function was assessed by the the KOOS and the KUJALA scores which improved significantly in patients with PFP after the six-week exercise programme. The KUJALA improved by 10.06 points (p = 0.001) and the KOOS by 16.26 points (p = 0.0001) with large effect sizes (Table 2, Figures 2 and 3). The Tampa scale of kinesiophobia improved by 3.44 points (p = 0.017) after the treatment with a moderate effect size (Table 2).

Running speed before and after the exercise treatment was not significantly different (p = 0.717, before the treatment: 3.42 ± 0.12 m/s, after the treatment: 3.43 ± 0.12 m/s). The peak joint angles and moments of hip and knee during the stance phase did not significantly change after the exercise intervention (Table 3 & 4).

Quadriceps strength was not significantly different after the six-week exercise programme (isometric: p = 0.992, concentric: p = 0.075, eccentric: p = 0.351, Supplements Figure S3). However, the concentric strength demonstrated the tendency to increase with a moderate effect size. Quadriceps AMI decreased by 4.69% after the six-week exercise programme with a moderate effect size (p = 0.018, Table 2, Supplements Figure S2).

Table 1: *Baseline characteristics of participants who successfully completed the six-week exercise programme. Values are mean (SD) unless stated otherwise.*

No of women (%)	Age in years	Height in m	Body mass in kg	Body mass index (kg/m^2)	Unilateral PFP (%)
7 (43.8%)	30.8 (6.34)	1.73 (0.08)	69.04 (9.07)	22.9 (1.64)	6 (37.5%)

Table 2: *Function, Kinesiophobia, pain, quadriceps strength and arthrogenic muscle inhibition (AMI)*

		Before the exercise treatment		After the exercise treatment		*P* value: (T-test, sig 2-tailed)	Effect size	Mean change	Std. Deviation of mean change	95% Confidence Interval of the Difference	
		Mean	SD	Mean	SD					Lower	Upper
Strength (Nm/kg)[a]	Quadriceps isometric torque	2.91	0.67	2.91	0.57	0.992	0.11	0.00	0.61	-0.34	0.33
	Quadriceps concentric torque	1.92	0.48	2.05	0.38	0.075	0.60	0.13	0.24	-0.26	-0.01
	Quadriceps eccentric torque	3.34	1.33	3.00	0.73	0.351	0.29	0.34	1.35	-0.43	1.13
Quadriceps AMI[b] in %		12.75	7.93	8.07	5.38	0.018*	0.62	4.68	7.04	0.93	8.43
Pain	numeric pain rating scale (NPRS)	0.88	0.46	0	0	0.074	2.71	0.88	1.82	-0.10	1.85
	KOOS[c] pain	79.70	11.19	92.88	8.42	0.001*	1.33	13.18	11.40	-19.26	-7.10
Tampa scale of kinesiophobia		32.63	6.34	29.19	7.70	0.017*	0.46	3.44	5.10	0.72	6.15
Function	KUJALA scale	81.69	9.23	91.75	7.23	0.001*	1.21	10.06	10.29	-15.55	-4.58
	KOOS[c] sum	73.50	10.54	89.76	8.89	0.0001*	1.67	16.26	12.81	-23.09	-9.44
	KOOS[c] symptoms	79.62	13.11	87.72	9.40	0.064	0.71	8.10	16.21	-16.73	0.54
	KOOS[c] ADL	87.08	12.91	96.34	6.46	0.024*	0.91	9.26	14.73	-17.11	-1.41
	KOOS[c] Sport/ Rec	65.31	16.88	91.00	11.25	0.0001*	1.79	25.69	15.88	-34.15	-17.22
	KOOS[c] QOL	57.42	17.26	80.86	18.88	0.002*	1.30	23.44	25.05	-36.79	-10.09

[a]*= Torque in Nm/kg normalised to body mass;* [b]*= Arthrogenic muscle inhibition;* [c]= knee injury and osteoarthritis outcome score; **= indicated the results were significantly different after the intervention*

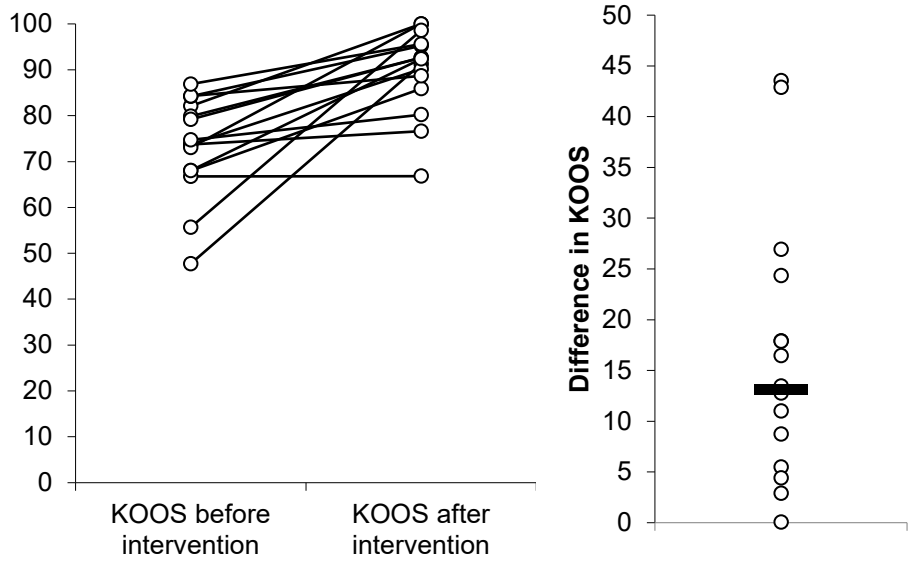

Figure 3: Changes in the knee injury and osteoarthritis outcome score (KOOS) after the six-week exercise programme. The thick black bar represents the mean change.

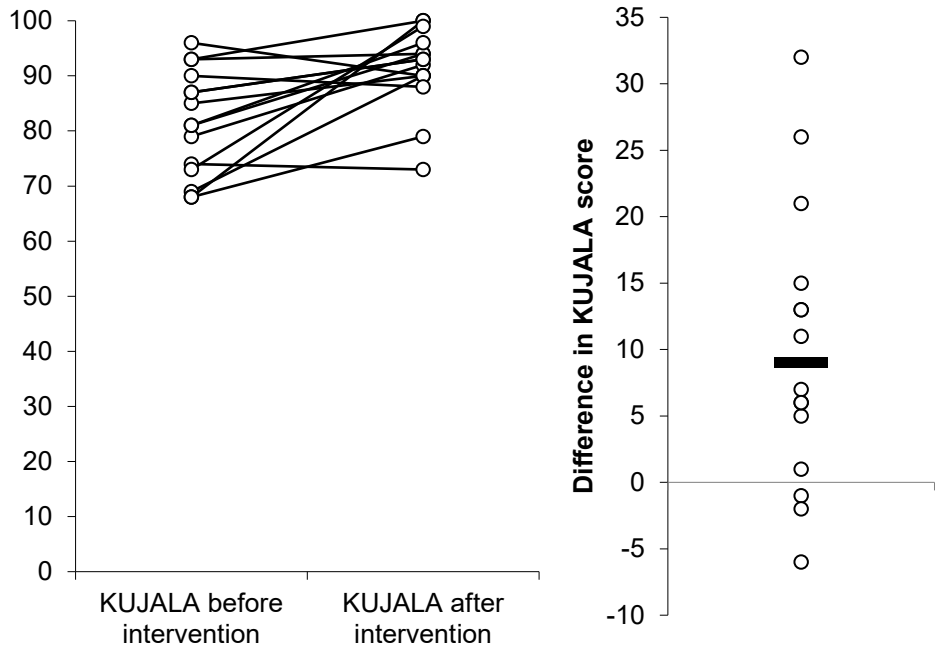

Figure 4: Changes in the anterior knee pain scale KUJALA score after the six-week exercise programme. The thick black bar represents the mean change.

Table 3: *The lower extremity kinematics during the stance phase in running. Flexion, adduction, internal rotation are positive and extension, abduction, external rotation are negative.*

The kinematic variables (º) during stance phase	Before the exercise treatment		After the exercise treatment		*P* value: (T-test, sig 2-tailed)	Effect size	Mean change	Std. Deviation of mean change	95% Confidence Interval of the Difference	
	Mean	SD	Mean	SD					Lower	Upper
Hip flexion angle ESP[a]	36.2	5.7	35.5	6.3	0.427	0.15	0.7	4.9	-2.1	3.5
Hip flexion angle MSP[b]	35.5	6.9	34.4	6.3	0.233	0.23	1.1	4.5	-1.5	3.7
Hip flexion angle LSP[c]	21.6	5.9	20.5	5.0	0.233	0.23	1.1	4.8	-1.6	3.9
Hip adduction angle ESP[a]	6.2	5.1	6.3	3.9	0.609	0.11	0.0	3.2	-1.9	1.8
Hip adduction angle MSP[b]	9.5	4.9	9.3	5.2	0.570	0.25	0.2	4.1	-2.2	2.6
Hip adduction angle LSP[c]	5.9	4.8	5.8	4.6	0.394	0.11	0.1	2.2	-1.1	1.4
Hip internal rotation angle ESP[a]	4.1	7.6	2.5	7.1	0.910	0.15	1.6	7.4	-2.6	5.9
Hip internal rotation angle MSP[b]	0.2	8.8	-1.7	8.3	0.570	0.18	1.9	7.1	-2.2	6.0
Hip internal rotation angle LSP[c]	1.2	8.7	-1.3	8.1	0.233	0.23	2.4	5.5	-0.7	5.6
Knee flexion angle ESP[a]	32.2	3.2	31.0	3.2	0.173	0.40	1.2	3.1	-0.6	3.0
Knee flexion angle MSP[b]	45.6	4.5	43.2	6.0	0.125	0.41	2.4	4.1	0.0	4.7
Knee flexion angle LSP[c]	42.3	4.8	40.7	4.8	0.334	0.26	1.6	3.7	-0.5	3.7
Knee adduction angle ESP[a]	3.1	4.2	2.8	3.4	0.691	0.17	0.3	3.3	-1.6	2.2
Knee adduction angle MSP[b]	2.5	4.1	1.9	3.4	0.609	0.26	0.7	4.4	-1.9	3.2
Knee adduction angle LSP[c]	2.0	3.3	1.5	2.5	0.609	0.20	0.5	3.6	-1.6	2.6

*[a]= Early stance phase (ESP); [b]= Mid stance phase (MSP); [c]= Late stance phase (LSP); *= indicated the results were significantly different after the intervention*

Table 4: *The lower extremity kinetics during stance phase in running. Flexion, adduction, internal rotation are positive and extension, abduction, external rotation are negative.*

The kinematic variables (º) during stance phase	Before the exercise treatment		After the exercise treatment		*P* value: (T-test, sig 2-tailed)	Effect size	Mean change	Std. Deviation of mean change	95% Confidence Interval of the Difference	
	Mean	SD	Mean	SD					Lower	Upper
Hip flexion moment ESP[a]	2.01	0.37	1.94	0.46	0.776	0.16	0.07	0.41	-0.17	0.30
Hip flexion moment MSP[b]	1.19	0.35	1.23	0.33	0.460	0.14	-0.04	0.39	-0.26	0.19
Hip flexion moment LSP[c]	0.04	0.10	0.07	0.16	0.532	0.24	-0.03	0.15	-0.12	0.06
Hip adduction moment ESP[a]	1.46	0.24	1.44	0.17	0.125	0.47	0.05	0.17	-0.05	0.14
Hip adduction moment MSP[b]	0.55	0.27	0.52	0.24	0.334	0.16	0.03	0.28	-0.13	0.19
Hip adduction moment LSP[c]	0.85	0.37	0.84	0.36	0.820	0.18	0.01	0.41	-0.23	0.25
Hip internal rotation moment ESP[a]	1.92	0.38	1.93	0.35	0.691	0.14	-0.01	0.34	-0.21	0.19
Hip internal rotation moment MSP[b]	-0.28	0.21	-0.30	0.17	0.281	0.10	0.02	0.15	-0.07	0.10
Hip internal rotation moment LSP[c]	2.52	0.57	2.77	0.53	0.460	0.28	-0.24	0.93	-0.78	0.29
Knee flexion moment ESP[a]	0.55	0.23	0.61	0.26	0.865	0.12	-0.06	0.35	-0.25	0.14
Knee flexion moment MSP[b]	-0.03	0.23	-0.11	0.23	0.570	0.17	0.08	0.24	-0.06	0.21
Knee flexion moment LSP[c]	1.43	0.44	1.45	0.35	0.570	0.10	-0.03	0.30	-0.20	0.15
Knee adduction moment ESP[a]	0.02	0.04	0.03	0.03	0.532	0.28	-0.01	0.04	-0.03	0.01
Knee adduction moment MSP[b]	1.73	0.46	1.97	0.35	0.233	0.43	-0.24	0.51	-0.53	0.06
Knee adduction moment LSP[c]	0.37	0.14	0.42	0.25	0.532	0.10	-0.05	0.25	-0.20	0.09

*[a]= Early stance phase (ESP); [b]= Mid stance phase (MSP); [c]= Late stance phase (LSP); *= indicated the results were significantly different after the intervention*

DISCUSSION

This study aimed to investigate the effect of a six- week exercise programme, based on the published recommendations. The hypothesis that pain, function, kinesiophobia, and quadriceps inhibition would improve could be confirmed. However, running biomechanics and quadriceps strength did not improve after the six- week exercise programme. Pain was assessed with the NPRS and this did not improve significantly. However, the patients had very low pain scores to begin (0.9 ± 0.5 on the numeric pain rating scale) and thus only little room for improvement (p = 0.074). Although, pain did not significantly improve all patients were pain-free after the six-week exercise programme (0 ± 0 on the NPRS).

Participants with PFP demonstrated a significant and meaningful improvement in reported function after the six-week exercise programme. Function, measured by the KOOS was improved by 16.3 points which is greater than the meaningful difference of 8- 10 [51]. Thus, the result of this study shows a clinically meaningful improvement of function after the exercise treatment. These improvements of the KOOS are comparable to the improvements reported by Rathleff et. al. (2019), who investigated the outcomes of activity modification and load management in patients with PFP [60]. Rathleff outlined that a potential explanation for this success might be the structured approach to build up the tolerance of aggravating activities and guidance back to sports in a graded manner, which might explain the improvements in this study as well. The KOOS for sports in this study was 100 and for ADLS 97.1 which means that these patients had no limitations in their sporting activities and ADLs after the exercise programme, although

they still reported symptoms (KOOS symptoms: 67.9). These large improvements in function are strong clinical indicators for the effectiveness of the six-week exercise programme in participants with PFP. Function was also measured by the KUJALA score which improved by 10.1 points after the exercise programme. This is lower than the clinically meaningful difference in the KUJALA score (14 points) and thus it is questionable whether the change is meaningful [65]. The patients in this study had relatively high KUJALA scores (before: 81.7 and after: 91.8 the exercise treatment treatment), which might be also an explanation why the patients only improved by 10 points.

The Tampa scale demonstrated a significant reduction of kinesiophobia by 3.4 points after the exercise treatment ($p = 0.021$). Previous studies reported that a change of 5.5 points should be reported to define a clinical meaningful difference for the Tampa Scale of Kinesiophobia and thus it should be critically questioned whether these differences are clinical meaningful [40]. Previous studies showed a correlation of greater kinesiophobia with reduced peak knee flexion during stair descending[19]. Although kinesiophobia in this study improved the running biomechanics remained unchanged. However, it should be noted that the overall Tampa score was mild to moderate in the recruited group and thus, kinesiophobia appeared to not be a main problem of these patients.

These participants with PFP did not show differences in running biomechanics after the six-week exercise programme. These findings are in accordance with previous studies that demonstrated that hip muscle strengthening resulted in decreased pain but did not change running kinematics in individuals with PFP [24, 26, 67]. The observed improvements were believed to be caused by an increase in strength and improved neuromuscular control [7, 24, 26, 67]. Earl et al (2011) described that an explanation for the absent changes in kinematics might be that not all participants had a dynamic malignment at the onset of the study and that PFP might have been caused by other factors. Participants in this study did not show lower limb abnormalities before the exercise programme, which might be an explanation why no kinematic or kinetic changes of the sagittal and transverse plane of the hip and the sagittal plane of the knee after the intervention programme were found.

No improvement in quadriceps strength was achieved even though the strengthening protocol of this study was comparable to the strengthening protocols in previous studies [6, 46, 48, 52]. The lower loads combined with a higher amount of repetitions compared to a traditional hypertrophy/ strength training was chosen to reduce the flare up of symptoms [1]. However, such a strength endurance programme has been shown to increase muscle endurance and muscle power in relatively untrained / weak individuals, but only increased muscle strength slightly [1]. Previous exercise training in participants with PFP were still successful in increasing muscle strength might be related to the training status and quadriceps strength of the recruited individuals as weaker individuals adapt more rapidly. The American College of Sports

Medicine outlined that a training outlined above is recommended for novice training[1]. Compared to participants with PFP in previous studies, the participants with PFP in this study produced higher isometric quadriceps strength [22, 23, 43, 47, 64]. Thus, the participants with PFP in this study appeared to be stronger than subjects in previous studies and the strength endurance training was very likely not demanding enough to improve quadriceps strength. For intermediate to advance training, the American College of Sports Medicine recommends to use a wider loading range from 1 to 12 RM in a periodized fashion, with eventual emphasis on heavy loading[1]. So, it seems that participants with PFP that are stronger, as in this study, might require a strength training with higher loads and reduced repetitions and not a strength endurance training stimuli [55] to enhance their quadriceps strength. To ensure that an increased loading does not flare up the PFP, modifications of traditional strength training should be applied. Previous studies investigated the application of a blood flow restriction (BFR) training in participants with PFP, which aims to induce muscle hypertrophy and increase strength more than the same programme without BFR [29, 34, 35, 55]. These studies demonstrated promising outcomes in improvements in quadriceps strength and might be a potential solution to improve strength in stronger participants with PFP [29, 34, 35]. Thus, there might be a need for a reconsideration of the current available exercise guidelines in strong participants with PFP and further studies are required to investigate forms of modified hypertrophy and strength training in stronger patients with PFP. Another explanation for the absence of strength improvements might be that other factors that contribute to muscle function such as force steadiness or the rate to force development which might be impaired. These factors of muscle function might require a different treatment approach and might not respond to strengthening exercises[9, 27, 42]. Furthermore, factors related to the muscle physiology, such as a reduced thickness of the muscle or a reduced amount of non-contractile tissue of the muscle might also result in reduced muscle function and strengthening exercises might not be able to address these impairments[42].

In previous literature researchers have described that the magnitude of strength improvements decrease with high strength levels, which might be another explanation for no strength changes after this intervention [61].

Since the recruited individuals appeared to be a very strong patient group, it becomes difficult to compare this patient group results to previously published findings. The diversity of patients with PFP emerged during the International Patellofemoral Research Retreat [18]. Selfe et al. (2013) addressed this challenge and developed a framework of subgroups of participants with PFP by defining three main subgroups: 1. "Weak and tighter", 2. "Weak and pronated", 3. "strong" participants with PFP [53, 54]. The strength results, the trend towards less pain, higher function and better quality of life indicate that the recruited participants with PFP in this study could be categorised as "strong" [54]. It seems that the

recruited study group also demonstrated a different biomechanical movement than previously described in participants with PFP, likely due to the higher strength levels, although further research is required to confirm this.

Furthermore, the quadriceps inhibition reduced from 12.8% before to 8.1% after the treatment with a moderate effect size (p = 0.018). Previous studies established that a normative AMI value was 8.8% (SD 6.1) meaning that an activation level above 91.2% could be classed as within normal limits[11]. This means that after the six-week exercise programme the participants with PFP had a quadriceps activation that fell within normal limits. The reduced quadriceps inhibition might be one explanation why participants with PFP improved significantly in function and pain without observed improvements in quadriceps strength or lower limb biomechanics. These results are in accordance with previous research reporting that an increase in pain caused no alterations of lower limb biomechanics or strength but resulted in an improved quadriceps AMI [31]. Thus, it seems that quadriceps AMI might be a key factor in participants with PFP. However, to date studies investigating quadriceps AMI in participants with PFP are rare and more research is needed.

LIMITATIONS TO THE STUDY

One limitation of this study is the high-drop-out rate of 33.3%, which indicated that the exercise programme should be amended to increase compliance with the exercise programme. The reduced sample size also prevented division of the subjects into sub-groups. Smith et al. (2019) reported a loss of follow up of 21 of 30 patients in their loaded self-managed group, which emphasises that further research should focus on how compliance could be improved [57].

Another limitation is the absence of an apriori power calculation. Furthermore, the post hoc power calculation demonstrated that the study did not reach power of 80% for the assessment of kinesiophobia (Tampa), quadriceps strength, quadriceps inhibition and hip adduction angle and emphasises that a larger sample size would be required.

Another limitation is that no data on symptom duration and level of physical activity of the participants were collected and analysed in this study. This might have helped to give a further insight into which participants with PFP might have benefitted most and should be incorporated in future research. Furthermore, no minimum NPRS score for inclusion was required, which resulted in a very low baseline NPRS of only 0.9±0.5.

The improvements in function and pain might be related to neuromuscular improvements, which might not be reflected in the running biomechanics. Furthermore, the improvements in function and pain might also result from improved gluteal strength, which was not assessed in this study. Future research should incorporate these measurements.

The participants with PFP in this study did not improve quadriceps strength which indicates that the resistance training was not demanding enough. The strengthening programme in this study consisted of lower loaded exercises with a higher amount of repetitions. The American college of sports medicine outlines that this is a recommended approach for novice training. However, intermediate to advance training requires a wider loading range in a periodized fashion which was not applied in this study. Thus, future exercise programmes should ensure an adequate progressive overload training in stronger participants with PFP.

The participants in this study were part of a mixed-sex cohort which can lead to biased outcomes, especially in regard to quadriceps strength deficits[49]. The study sample was not divided into subgroups of females and males to avoid a further reduction in sample size, but this should be addressed in future research.

Lastly, the individuals in this study underwent a follow-up directly after finishing the six-week exercise programme but were not followed up at later time points. It would be worthwhile to investigate further follow-up timelines to assess the medium and long-term effects of an evidence-based exercise programme in patients with PFP.

CONCLUSION

The participants with PFP demonstrated a significantly improved function, reduced quadriceps inhibition and showed improvements in pain after the six-week exercise programme. Despite the strength training the quadriceps strength did not increase and there were no differences in running biomechanics after the exercise treatment. The reduced quadriceps inhibition might be a key factor in individuals with PFP and might have resulted in improved function and pain in the absence of improvements in quadriceps strength or changes in lower limb biomechanics. This study also showed that the quadriceps strengthening programme was not demanding enough for strong individuals with PFP to result in increased quadriceps strength, which suggests that strong individuals with PFP might require a strength training with higher loads and reduced repetitions to enhance quadriceps strength.

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