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Quadriceps Neuromuscular Function During and After Exercise-Induced Fatigue in Patients With Patellofemoral Pain

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Context: Exercise-induced fatigue reduces muscle force production and motoneuron pool excitability. However, it is unclear if patients with patellofemoral pain (PFP) experience further loss in quadriceps neuromuscular function due to fatigue during exercise and postexercise.

Objective: To observe how quadriceps maximal strength, activation, and force-generating capacity change during and after repetitive bouts of isokinetic knee-extension exercise in patients with PFP.

Design: Cross-sectional study.

Setting: Laboratory.

Patients or Other Participants: Twenty-two patients with PFP (visual analog scale mean pain severity = 4.2 of 10 cm, mean symptom duration = 38.6 months) and 19 healthy control individuals matched on age and body mass index.

Main Outcome Measure(s): Quadriceps peak torque (PT), central activation ratio (CAR), and rate of torque development (RTD) were assessed at baseline and immediately after every 5 sets of knee-extension exercise (times 1–5). Participants continued knee-extension exercises until the baseline quadriceps PT dropped below 50% for 3 consecutive contractions.

Results: No group-by-time interaction was observed for quadriceps PT ($F_{5,195} = 1.03$, $P = .40$). However, group-by-time interactions were detected for quadriceps CAR ($F_{5,195} = 2.63$, $P = .03$) and RTD ($F_{5,195} = 3.85$, $P = .002$). Quadriceps CAR (−3.6%, $P = .04$, Cohen $d = 0.53$) and RTD (−18.9%, $P = .0008$, Cohen $d = 1.02$) decreased between baseline and time 1 in patients with PFP but not in their healthy counterparts (CAR −1.9%, $P = .86$; RTD −9.8%, $P = .22$). Quadriceps RTD also decreased between times 4 and 5 in patients with PFP (−24.9%, $P = .002$, Cohen $d = 0.89$) but not in the healthy group (−0.9%, $P = .99$).

Conclusions: Patients with PFP appeared to experience an additional reduction in quadriceps activation, force-generating capacity, or both during the early and late stages of exercise compared with healthy individuals. Clinicians should be aware of such possible acute changes during exercise and postexercise and use fatigue-resistant rehabilitation programs for patients with PFP.

Key Words: anterior knee pain, neuromuscular fatigue, strength, central activation, rate of torque development

Key Points

- Fatigue induced during and after isokinetic knee-extension exercises reduced quadriceps neuromuscular function, regardless of the presence or absence of patellofemoral pain.
- Compared with healthy individuals, patients with patellofemoral pain were more likely to be vulnerable to fatigue in their ability to maintain quadriceps activation and force-generating capacity.
- Clinicians should be cognizant of potential alterations in neuromuscular function during exercise and postexercise and use rehabilitation strategies that incorporate fatigue-resistance training when treating patients with patellofemoral pain.

Patellofemoral pain (PFP) is one of the most common lower extremity conditions among physically active individuals.[1,2] Although PFP accounts for 25% to 40% of all patients with knee-related disorders in sports medicine clinics,[2] it is still a challenge to manage because of its poorly identified pathogenesis. A nonspecific pain condition, PFP is characterized by diffuse peripatellar or retropatellar pain during daily activities, such as running, squatting, stair climbing, and jumping.[3] More than 90% of individuals complain of long-lasting pain and symptoms for up to 16 years after their initial PFP diagnosis.[4] Patellofemoral pain has also been suggested to be a precursor of patellofemoral osteoarthritis,[5] imposing a long-term substantial clinical and economic burden on both individuals and health care systems.[1] Approximately 3 in 4 athletes experiencing PFP will also limit or cease sport participation because of their symptoms.[6] However, despite persistent pain and impaired knee function,[7,8] patients with PFP still attempt to remain physically active in their activities of daily living.[9] Neuromuscular dysfunction in the quadriceps is frequently seen in individuals with PFP.[8,10] As a protective mechanism, this is termed *arthrogenic muscle*

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inhibition and can be deemed a natural response designed to protect the painful knee by discouraging its use and minimizing painful movements.[11] Still, prior researchers[12] suggested that prolonged adaptations may negatively affect joint stability and energy absorption during functional activities. Failure to maximally or rapidly generate force or to fully activate the quadriceps has also been theorized to alter lower extremity biomechanics during functional tasks,[13,14] increase the likelihood of subsequent pain or injury,[15] and accelerate early-onset joint degeneration.[16] As such, adequate quadriceps neuromuscular function would be essential for optimizing patellofemoral joint health in patients with PFP.

Neuromuscular fatigue due to continuous exercises and high-demand tasks leads to decreased lower extremity function (eg, quadriceps maximal strength and voluntary activation[17] or dynamic balance[18]), which is an immediate natural response of the body. However, individuals with chronic PFP (eg, $\geq$3 months) could be particularly vulnerable to the influences of neuromuscular fatigue compared with healthy individuals because they often return to functional activities despite having significant deficits in muscle strength, central activation, or both.[7,10,19] Although anterior cruciate ligament reconstruction is a different condition, investigators[20] found that postsurgery, individuals experienced greater hip-extensor strength loss after exercise than healthy people. Yet these authors[20,21] studied only a single bout of exercise, which provides limited information on the effects of fatigue from sustained and cumulative activities in active individuals. Despite this reasonable expectation, to our knowledge, no evidence of neuromuscular responses to exercise-induced fatigue over time in PFP cohorts is available. Tracking neuromuscular changes during and after repetitive exercises offers further insight into developing more tailored rehabilitation programs for patients with PFP. If trajectories are different than in a healthy population, for example, clinicians may need to suggest appropriate rest periods or interventions at specific time points to increase functional performance and reduce the risk of other injuries.

The primary purpose of our study was to observe changes in quadriceps peak torque (PT), central activation ratio (CAR), and rate of torque development (RTD) during and after repetitive bouts of isokinetic knee-extension exercise in patients with PFP compared with age- and body mass index (BMI)–matched healthy control individuals. The secondary purpose was to compare fatigue levels (ie, blood lactate concentration) and muscular endurance performance (ie, knee-extension repetitions and quadriceps total work during isokinetic exercise) between patients with PFP and a matched healthy control group. We hypothesized that patients with PFP would (1) exhibit additional reductions in all quadriceps neuromuscular function as exercise sets progressed and (2) display lower fatigue levels with worse muscular endurance performance during and after isokinetic exercise compared with the control group.

METHODS

A cross-sectional design with repeated measures was used in this study. The main outcome measures were quadriceps PT, CAR, and RTD at baseline and immediately after every 5 sets of isokinetic knee-extension exercise (times 1–5). Secondary outcome measures were blood lactate concentration (baseline and times 1–5) and knee-extension repetitions and quadriceps total work during isokinetic exercise (sets 1–5). *Times 1 to 5* are the time points at which data were obtained immediately after each exercise set, whereas *sets 1 to 5* are the time points at which data were obtained during each exercise set.

Participants

Twenty-two patients with PFP (age = 22.4 ± 2.9 years, BMI = 22.0 ± 2.1) and 19 healthy control individuals (age = 22.9 ± 1.9 years, BMI = 21.6 ± 2.2) matched on age and BMI were analyzed in this study (Table 1). All participants were between 18 and 35 years old and were recruited from a local university and community via flyers and social media posts (Figure 1). Inclusion criteria for PFP were defined according to the 2016 International Patellofemoral Research Retreat consensus statement.[22] Specific inclusion and exclusion criteria for both groups are presented in Table 2. All participants had to engage in $\geq$150 minutes of moderate-intensity (eg, walking, light jogging) or 60 minutes of vigorous-intensity (eg, running, weightlifting) exercise per week.[10] All participants provided written informed consent approved by the university's institutional review board (approval KHSIRB-17-030).

Procedures

Once participants had completed the eligibility screening and given informed consent, they self-reported their sex, age, amount of physical activity, and symptom duration. Using a bioelectrical impedance device (model InBody 770; Biospace Ltd), we measured participants' height, mass, and BMI. Afterward, we assessed the severity of their usual pain in the previous week using the visual analog scale (VAS; 0 = *no pain*; 10 = *worst pain imaginable*) and patient-reported outcomes using the Lower Extremity Functional Scale (LEFS); both are valid and reliable tools commonly used in the PFP literature.[7,8,10,13]

Testing procedures are described in Figure 2. After a 10-minute warm-up on a stationary bike at a self-selected pace, participants were seated on an isokinetic dynamometer (model 770 Norm; Cybex International Inc). The knee and hip joints were positioned at 90° and 85°, respectively. The chest, pelvis, and nontesting thigh were secured with straps to minimize accessory motions or assisting muscle contractions. Two 7- × 12.7-cm stimulating electrodes (model Dura-Stick II; Chattanooga Group Inc) were attached to the proximal vastus lateralis and the distal vastus medialis after the skin of the anterior thigh was shaved with a razor and cleaned with an alcohol swab. For the matched healthy control group, the *dominant leg* (defined as the leg used to kick a ball) was evaluated.[7]

Participants pursued a gradual warm-up session of 3-second isometric contractions (2 submaximal at 50% and 75% and 1 maximal at 100% of PT) coupled with a superimposed burst (SIB; 2 submaximal at 50% and 75% and 1 maximal at 100% of stimulation intensity) to familiarize themselves with the quadriceps neuromuscular assessments.[10] We then asked them to produce their maximal and explosive force ("as fast and hard as possible") and to maintain the contraction for at least 3 seconds. When knee-extension torque reached a plateau, an

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Table 1. Participant Characteristics[a]

Variable	Group		*P* Value
	Patellofemoral Pain (n = 22)	Healthy Control (n = 19)	
Sex, female/male	15/7	9/10	Not applicable
	Mean ± SD		
Age, y	22.4 ± 2.9	22.9 ± 1.9	.09
Height, cm	165.0 ± 8.6	170.7 ± 7.3	.03
Mass, kg	60.3 ± 10.2	63.2 ± 8.9	.35
Body mass index, kg/m^2	22.0 ± 2.1	21.6 ± 2.2	.55
Physical activity, min/wk	232.7 ± 88.9	241.6 ± 80.9	.74
Pain severity, cm on visual analog scale	4.2 ± 1.4	0.0 ± 0.0	**<.0001**
Symptom duration (range), mo	38.6 ± 32.0 (4–110)	0.0 ± 0.0	**<.0001**
Patient-reported outcome, Lower Extremity Functional Scale score	58.8 ± 9.1	79.2 ± 1.3	**<.0001**

[a] Values in bold represent statistical and clinical significance.

exogenous supramaximal electrical stimulus (100 pulses/s, 600-microsecond pulse duration, 10 train in 100-millisecond duration, 125 V with a peak output current of 450 mA) was manually delivered to the quadriceps via 2 stimulating electrodes to recruit any residual motor units.[23] The S48 Grass Stimulator with an SIU8T transformer stimulus isolation unit (Grass-Telefactor Inc) was used to generate the SIB. For quadriceps neuromuscular function, PT was evaluated, and then CAR and RTD were calculated using muscle force waveforms.

After 5 minutes of rest, the assessor collected a 0.7-μL blood sample using a lancet on the fingertip and lactate test strip[24] to ensure minimal quadriceps neuromuscular fatigue at baseline. Sample analysis time was 13 seconds by a portable lactate analyzer (model Lactate Plus Meter; Nova Biomedical Corp). Once we obtained the baseline blood lactate concentration (in millimoles), the participants performed the first set of continuous concentric knee extensions at 60°/s on the isokinetic dynamometer.[25] When 3 consecutive contractions were <50% of the baseline quadriceps PT, the individual ceased the contractions and finished the exercise set.[25] Immediately after each set of exercise, the blood lactate level was measured again to identify the fatigue level induced by the exercise. We then repeated the quadriceps function assessment. Five sets of knee-extension exercise and postexercise testing were conducted with both visual feedback and oral encouragement to elicit participants' maximal effort. Data collection

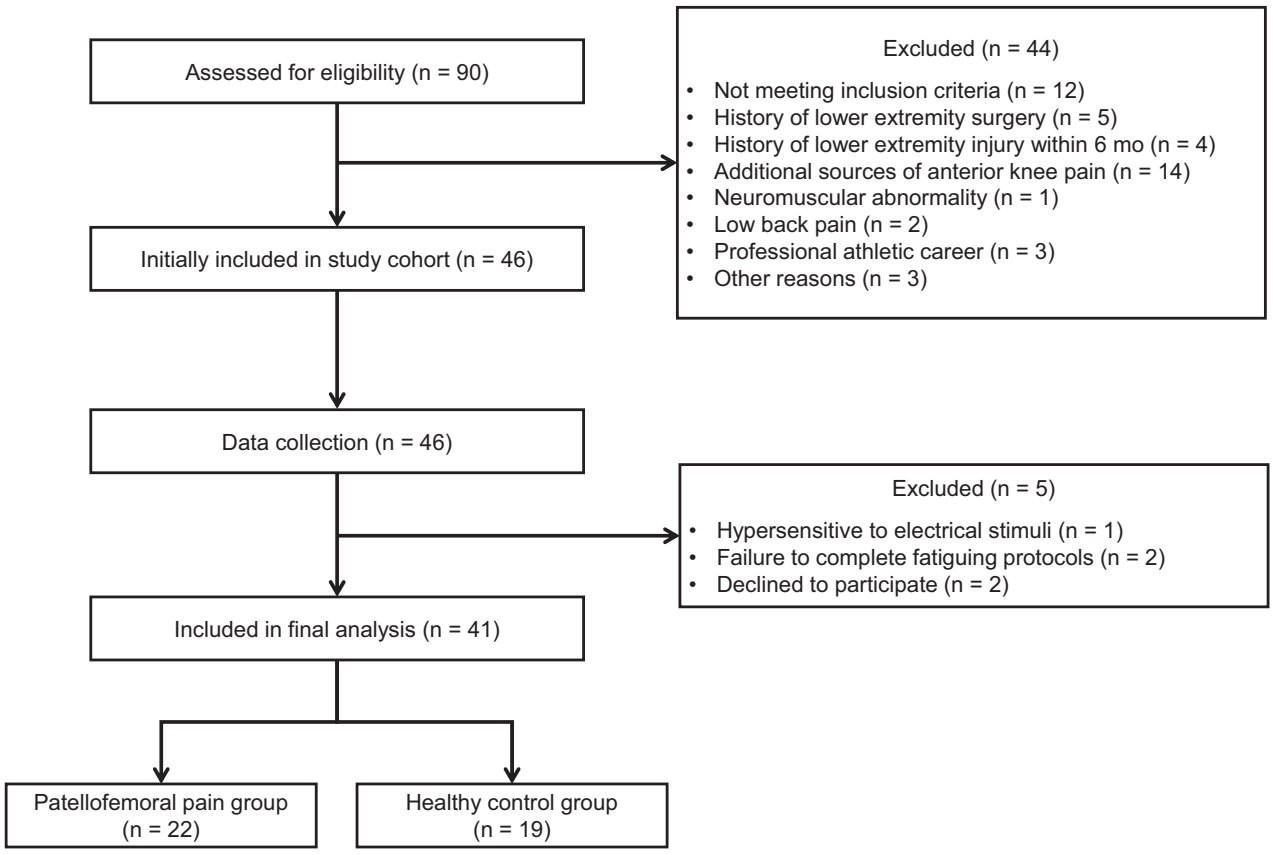

Figure 1. Participant recruitment and selection.

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Table 2. Inclusion and Exclusion Criteria

Inclusion criteria for patellofemoral pain group
- Insidious unilateral retropatellar or peripatellar pain ≥3 months
- Usual pain in the previous week of ≥3 of 10
- Pain ≥2 during or after
  - Prolonged sitting
  - Kneeling
  - Stair climbing
  - Running
  - Jumping
  - Squatting
  - Patellar compression
  - Quadriceps contraction

Inclusion criteria for healthy control group
- No history of lower extremity or spine surgery
- No history of lower extremity injury or pain within 6 mo

Exclusion criteria for both groups
- Previous knee injury and surgery
- Ligamentous instability
- Internal derangement
- Additional sources of anterior knee pain (eg, tendinopathy)
- Physician-confirmed diagnosis of knee osteoarthritis
- Low back pain
- Professional athletic career
- Contraindication to electrical stimulation:
  - Hypersensitivity to electrical stimulation
  - Neuromuscular abnormality
  - Infection of lower extremity
  - Implanted biomechanical device

was performed by a single investigator who was blinded to the presence or absence of PFP until all testing procedures were completed.

For each set of isokinetic exercises, the number of knee-extension repetitions was counted. In addition, quadriceps total work was calculated and normalized to body mass (joules per kilogram)[26] except for the last 3 consecutive concentric torques, which did not exceed 50% of the baseline quadriceps PT. For each time point, 3 trials of quadriceps PT were averaged and normalized to body mass (newton meters per kilogram). The quadriceps CAR was calculated by the ratio Force $_{PT}$/Force $_{PT+SIB}$.[23] The quadriceps RTD was calculated as the slope (Δtorque/Δtime) of the torque-time curve from 20% to 80% of PT and normalized to body mass and time interval (newton meters per kilogram per second).[10]

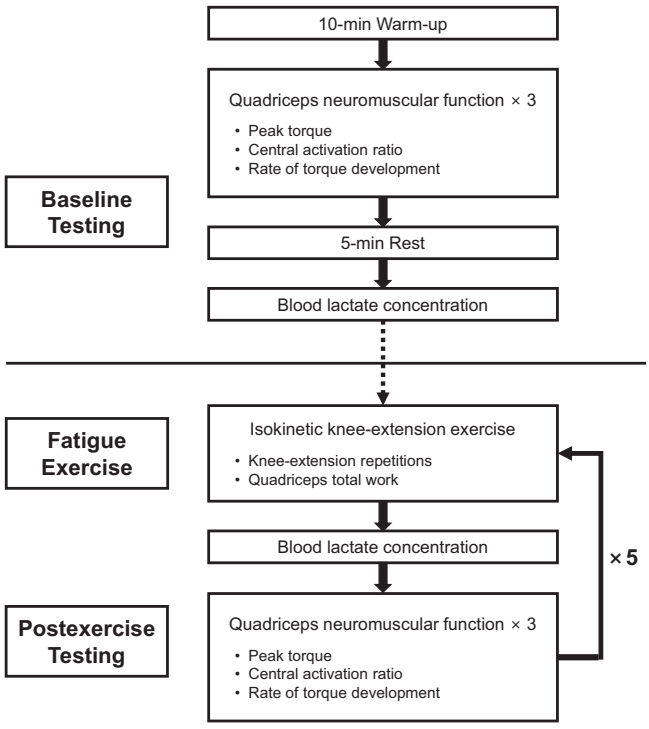

Figure 2. Testing procedures.

Statistical Analysis

Our sample size was determined using an expected mean difference in quadriceps CAR of 0.11 with an SD of 0.14, which yielded a Cohen *d* effect size (ES) of 0.8.[23] Using an α of .05 and a β of .2, we estimated that 14 participants were necessary for each group.

Age, height, mass, BMI, amount of physical activity, pain severity, symptom duration, and patient-reported outcomes were compared between groups using independent *t* tests. The mean and SD were computed from each dependent measurement at each time point. We conducted a 2-by-6 mixed-model analysis of variance for quadriceps neuromuscular function (PT, CAR, and RTD) and blood lactate concentration. A 2-by-5 mixed-model analysis of variance was also performed to investigate differences in knee-extension repetitions and quadriceps total work during isokinetic exercise. When statistical significance was present, the Tukey-Kramer post hoc tests were used for pairwise comparisons. Percentage changes were identified by subtracting the baseline (quadriceps neuromuscular function or blood lactate concentration) or set 1 (knee-extension repetitions or quadriceps total work during isokinetic exercise) value from each subsequent time point value, dividing that difference by the baseline or set 1 value, and multiplying by 100. To determine practical significance, between-times and between-groups Cohen *d* ESs[27] with 95% CIs were also calculated. Thresholds for ESs were set as *trivial* (<0.20), *small* (0.20–0.49), *moderate* (0.50–0.79), and *large* (≥0.80).[27] The statistical package SAS (version 9.4; SAS Institute) was used for all tests ($P < .05$).

RESULTS

Descriptive characteristics of the participants, including demographics, pain severity, symptom duration, and patient-reported outcomes, are shown in Table 1. Data related to quadriceps neuromuscular function and blood lactate concentration are supplied in Table 3. The trajectories of quadriceps PT, CAR, and RTD before, during, and after isokinetic knee-extension exercises are also visualized in Figures 3, 4, and 5, respectively. Data related to knee-extension repetitions and quadriceps total work during isokinetic exercise are provided in Table 4.

Quadriceps PT

At baseline, we did not observe a difference in quadriceps PT between groups ($P = .18$). No group-by-time interaction was present for quadriceps PT ($F_{5,195} = 1.09$, $P = .37$). Regardless of time (group main effect: $F_{1,195} = 7.35$, $P = .007$), patients with PFP displayed 19.8% less quadriceps PT compared with the matched healthy control individuals. Regardless of group (time main effect: $F_{5,195} = 134.95$,

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Table 3. Changes in Quadriceps Neuromuscular Function and Blood Lactate Concentration[a]

Outcome Measure	Time	Group: Patellofemoral Pain (n = 22) Mean ± SD	Patellofemoral Pain Baseline to Each Time Point Cohen *d* Effect Size (95% CI)[b]	Group: Healthy Control (n = 19) Mean ± SD	Healthy Control Baseline to Each Time Point Cohen *d* Effect Size (95% CI)[b]	Between-Groups *P* Value; Cohen *d* Effect Size (95% CI)[c]
Quadriceps peak torque, N·m/kg	Baseline	2.50 ± 0.57	NA	3.01 ± 0.78	NA	.18; **0.76 (0.12, 1.40)**
	1	1.95 ± 0.46[d]	**1.05 (0.42, 1.68)**	**2.51 ± 0.77**[d]	0.65 (0.00, 1.30)	.10; **0.89 (0.25, 1.53)**
	2	1.84 ± 0.43[d]	**1.30 (0.65, 1.95)**	**2.34 ± 0.69**[d]	0.91 (0.24, 1.58)	.21; **0.89 (0.25, 1.53)**
	3	1.80 ± 0.46[d]	**1.35 (0.70, 2.00)**	**2.20 ± 0.63**[d]	1.14 (0.45, 1.83)	.54; **0.74 (0.11, 1.37)**
	4	1.72 ± 0.45[d]	**1.52 (0.85, 2.19)**	**2.15 ± 0.60**[d]	1.24 (0.55, 1.93)	.42; **0.83 (0.19, 1.47)**
	5	1.65 ± 0.50[d]	**1.59 (0.91, 2.27)**	**2.08 ± 0.56**[d]	1.38 (0.69, 2.07)	.42; **0.82 (0.18, 1.46)**
Quadriceps central activation ratio	Baseline	0.949 ± 0.054	NA	0.978 ± 0.017	NA	.95; **0.71 (0.08, 1.34)**
	1	0.915 ± 0.072[d]	**0.53 (0.07, 1.13)**	0.960 ± 0.025	0.86 (0.20, 1.52)	.51; **0.81 (0.17, 1.45)**
	2	0.906 ± 0.067[d]	**0.69 (0.08, 1.30)**	**0.938 ± 0.033**[d]	1.53 (0.81, 2.25)	.91; 0.58 (−0.05, 1.21)
	3	0.879 ± 0.085[d]	**0.98 (0.35, 1.61)**	**0.937 ± 0.035**[d]	1.48 (0.76, 2.20)	.14; **0.87 (0.23, 1.51)**
	4	0.877 ± 0.090[d]	**0.96 (0.34, 1.58)**	**0.937 ± 0.036**[d]	1.46 (0.74, 2.18)	.12; **0.84 (0.20, 1.48)**
	5	0.869 ± 0.110[d]	**0.93 (0.31, 1.55)**	**0.939 ± 0.037**[d]	1.35 (0.65, 2.05)	.02; **0.84 (0.20, 1.48)**
Quadriceps rate of torque development, N·m/kg/s	Baseline	7.52 ± 1.38	NA	9.56 ± 1.86	NA	**.007; 1.26 (0.59, 1.93)**
	1	6.10 ± 1.41[d]	**1.02 (0.39, 1.65)**	8.63 ± 1.98	0.48 (−0.17, 1.13)	**.0002; 1.49 (0.80, 2.86)**
	2	6.04 ± 1.65[d]	**0.98 (0.35, 1.61)**	**8.03 ± 1.71**[d]	0.86 (0.20, 1.52)	**.009; 1.19 (0.52, 1.86)**
	3	5.66 ± 1.82[d]	**1.15 (0.51, 1.79)**	**7.46 ± 1.79**[d]	1.15 (0.46, 1.84)	**.03; 0.99 (0.34, 1.64)**
	4	5.46 ± 1.76[d]	**1.30 (0.65, 1.95)**	**7.60 ± 1.73**[d]	1.09 (0.41, 1.77)	**.003; 1.23 (0.56, 1.90)**
	5	4.10 ± 1.25[d,e]	**2.60 (1.80, 3.40)**	**7.67 ± 1.54**[d]	1.10 (0.42, 1.78)	**<.0001; 2.56 (1.73, 3.39)**
Blood lactate concentration, mmol	Baseline	1.65 ± 0.38	NA	1.94 ± 1.00	NA	.99; 0.33 (−0.29, 0.95)
	1	4.28 ± 1.41[d]	**2.27 (1.51, 3.03)**	**4.91 ± 1.65**[d]	2.17 (1.37, 2.97)	.99; 0.41 (−0.21, 1.03)
	2	5.21 ± 1.41[d]	**3.08 (2.21, 3.95)**	**6.43 ± 2.11**[d]	2.72 (1.84, 3.60)	.82; **0.69 (0.06, 1.32)**
	3	6.04 ± 2.31[d]	**2.53 (1.74, 3.32)**	**7.34 ± 2.27**[d]	3.08 (2.14, 4.02)	.75; 0.57 (−0.06, 1.20)
	4	6.40 ± 3.01[d]	**2.16 (1.42, 2.90)**	**7.35 ± 1.94**[d]	3.50 (2.49, 4.51)	.96; 0.37 (−0.25, 0.99)
	5	7.94 ± 3.52[d]	**2.46 (1.68, 3.24)**	**8.29 ± 2.74**[d]	3.08 (2.14, 4.02)	.99; 0.11 (−0.50, 0.72)

Abbreviation: NA, not applicable.

[a] Values in bold represent statistical and clinical significance.
[b] Effect sizes compared between baseline and each time point.
[c] *P* values and effect sizes compared groups at the same time point.
[d] Statistically different from baseline ($P < .05$).
[e] Statistically different from time 4 ($P < .05$).

$P < .0001$), quadriceps PT decreased at times 1 (−19.1%, $P < .0001$, ES = 0.75), 2 (−24.1%, $P < .0001$, ES = 1.00), 3 (−27.4%, $P < .0001$, ES = 1.16), 4 (−29.9%, $P < .0001$, ES = 1.28), and 5 (−32.4%, $P < .0001$, ES = 1.39) compared with baseline.

Quadriceps CAR

At baseline, we did not find a difference in quadriceps CAR between groups ($P = .95$). A group-by-time interaction was detected for quadriceps CAR ($F_{5,195} = 2.63$, $P = .03$). Compared with baseline, the control group maintained quadriceps CAR at time 1 (−1.9%, $P = .86$) and then demonstrated decreased quadriceps CAR at times 2 to 5 (−3.9% to −4.2%, $P \leq .02$, ES ≥ 1.35), whereas patients with PFP had decreased quadriceps CAR at all time points (−3.6% to −8.4%, $P \leq .04$, ES ≥ 0.53). Regardless of time (group main effect: $F_{1,195} = 7.84$, $P = .006$), the quadriceps CAR of patients with PFP was 5.2% less than that of the control group. Regardless of group (time main effect: $F_{5,195} = 20.08$, $P < .0001$), quadriceps CAR was decreased

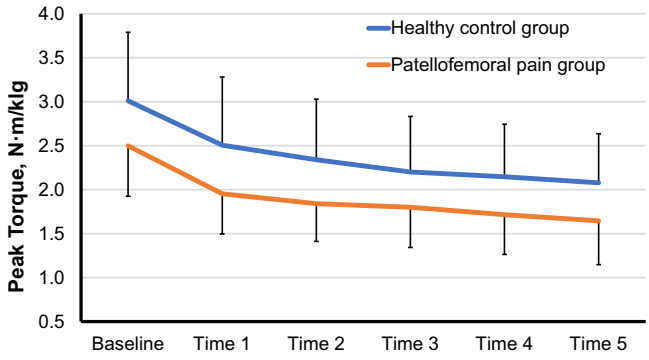

Figure 3. Trajectory of quadriceps peak torque before, during, and after isokinetic knee-extension exercises. Error bars indicate standard deviations. [a] Different from baseline ($P < .05$).

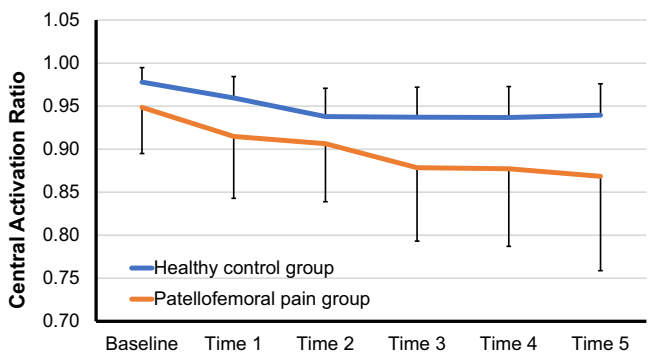

Figure 4. Trajectory of quadriceps central activation ratio before, during, and after isokinetic knee-extension exercises. Error bars indicate standard deviations. [a] Different from baseline ($P < .05$).

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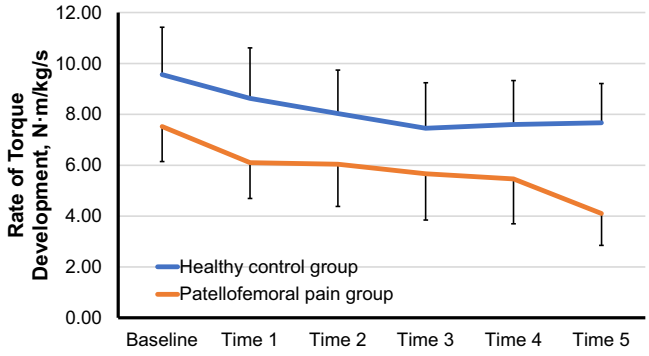

Figure 5. Trajectory of quadriceps rate of torque development before, during, and after isokinetic knee-extension exercises. Error bars indicate standard deviations. [a] Difference between groups at baseline ($P = .007$). [b] Different from baseline ($P < .05$). [c] Different from time 4 ($P = .002$).

at times 1 (−2.7%, $P = .006$, ES = 0.50), 2 (−4.3%, $P < .0001$, ES = 0.82), 3 (−5.8%, $P < .0001$, ES = 0.93), 4 (−5.8%, $P < .0001$, ES = 0.91), and 5 (−6.2%, $P < .0001$, ES = 0.84) compared with baseline.

Quadriceps RTD

At baseline, patients with PFP had less quadriceps RTD than the matched healthy individuals ($P = .007$). A group-by-time interaction was evident for quadriceps RTD ($F_{5,195} = 3.85$, $P = .002$). Compared with baseline, the control group maintained quadriceps RTD at time 1 (−9.8%, $P = .22$) and then displayed decreased quadriceps RTD at times 2 (−16.0%, $P = .0008$, ES = 0.86), 3 (−22.0%, $P < .0001$, ES = 1.15), 4 (−20.5%, $P < .0001$, ES = 1.09), and 5 (−19.8%, $P < .0001$, ES = 1.10), whereas patients with PFP had decreased quadriceps RTD at all time points (−18.9% to −45.5%, $P \leq .0008$, ES ≥ 0.98). We also observed a percentage reduction in quadriceps RTD between times 4 and 5 in patients with PFP (−24.9%, $P = .002$, ES = 0.89) but not in their healthy counterparts (−0.9%, $P = .99$). Regardless of time (group main effect: $F_{1,195} = 30.40$, $P < .0001$), patients with PFP exhibited 28.7% less quadriceps RTD compared with the matched healthy control group. Regardless of group (time main effect: $F_{5,195} = 30.59$, $P < .0001$), quadriceps RTD was decreased at times 1 (−13.8%, $P = .006$, ES = 0.59), 2 (−17.7%, $P < .0001$, ES = 0.79), 3 (−23.2%, $P < .0001$, ES = 1.02), 4 (−23.5%, $P < .0001$, ES = 1.9021), and 5 (−31.1%, $P < .0001$, ES = 1.27) compared with baseline.

Blood Lactate Concentration

No group main effect ($F_{1,195} = 2.32$, $P = .13$) or group-by-time interaction ($F_{5,195} = 0.81$, $P = .55$) was noted for blood lactate concentration. Regardless of group (time main effect: $F_{5,195} = 85.65$, $P < .0001$), blood lactate concentration was increased at times 1 (156.1%, $P < .0001$, ES = 2.21), 2 (224.5%, $P < .0001$, ES = 2.76), 3 (273.0%, $P < .0001$, ES = 2.74), 4 (283.2%, $P < .0001$, ES = 2.62), and 5 (352.6%, $P < .0001$, ES = 2.73) compared with baseline.

Knee-Extension Repetitions and Quadriceps Total Work During Isokinetic Exercise

No group main effects or group-by-time interactions were seen for knee-extension repetitions (group main effect: $F_{1,156} = 0.03$, $P = .86$; group-by-time interaction: $F_{4,156} = 0.03$, $P = .99$) or quadriceps total work (group main effect: $F_{1,156} = 2.37$, $P = .13$; group-by-time interaction: $F_{4,156} = 0.13$, $P = .97$) during isokinetic exercise. Regardless of group (time main effect: $F_{4,195} = 28.55$, $P < .0001$), knee-extension repetitions during isokinetic exercise were decreased during sets 2 (−27.6%, $P < .0001$, ES = 0.77), 3 (−35.5%, $P < .0001$, ES = 1.01), 4 (−41.5%, $P < .0001$, ES = 1.22), and 5 (−44.2%, $P < .0001$, ES = 1.20) compared with set 1. Regardless of group (time main effect: $F_{4,195} = 11.55$, $P < .0001$), quadriceps total work during isokinetic exercise was decreased during sets 2 (−5.9%, $P = .002$, ES = 0.24), 3 (−8.2%, $P < .0001$, ES = 0.33), 4 (−9.3%, $P < .0001$, ES = 0.39), and 5 (−8.5%, $P < .0001$, ES = 0.35) compared with set 1.

Table 4. Changes in Knee-Extension Repetitions and Quadriceps Total Work During Isokinetic Exercise[a]

		Group				
		Patellofemoral Pain (n = 22)		Healthy Control (n = 19)		
Outcome Measure	Set	Mean ± SD	Set 1 to Each Set Point Cohen *d* Effect Size (95% CI)[b]	Mean ± SD	Set 1 to Each Set Point Cohen *d* Effect Size (95% CI)[b]	Between-Groups *P* Value; Cohen *d* Effect Size (95% CI)[c]
Knee-extension repetitions, No.	1	41.2 ± 13.8	NA	41.0 ± 18.2	NA	.99; 0.01 (−0.60, 0.62)
	2	**30.4 ± 16.6[d]**	**0.71 (0.10, 1.32)**	**29.1 ± 8.8[d]**	**0.83 (0.17, 1.49)**	.99; 0.09 (−0.52, 0.70)
	3	**26.7 ± 13.9[d]**	**1.05 (0.42, 1.68)**	**26.3 ± 11.9[d]**	**0.95 (0.28, 1.62)**	.99; 0.03 (−0.58, 0.64)
	4	**24.6 ± 11.7[d]**	**1.30 (0.65, 1.95)**	**23.5 ± 12.6[d]**	**1.12 (0.44, 1.80)**	.99; 0.09 (−0.52, 0.70)
	5	**23.1 ± 14.3[d]**	**1.28 (0.63, 1.93)**	**22.7 ± 14.8[d]**	**1.10 (0.42, 1.78)**	.99; 0.02 (−0.59, 0.63)
Quadriceps total work, J/kg	1	62.0 ± 14.5	NA	68.3 ± 17.6	NA	.94; 0.40 (−0.22, 1.02)
	2	**57.4 ± 15.0[d]**	0.31 (−0.28, 0.90)	**63.2 ± 15.9[d]**	0.32 (−0.32, 0.96)	.83; 0.50 (−0.12, 1.12)
	3	**56.6 ± 14.3[d]**	0.37 (−0.23, 0.97)	**63.5 ± 14.2[d]**	0.30 (−0.34, 0.94)	.91; 0.50 (−0.12, 1.11)
	4	**55.4 ± 14.5[d]**	0.45 (−0.15, 1.05)	**62.7 ± 14.6[d]**	0.35 (−0.29, 0.99)	.88; 0.51 (−0.11, 1.12)
	5	**56.1 ± 15.3[d]**	0.39 (−0.21, 0.99)	**63.0 ± 15.9[d]**	0.32 (−0.32, 0.96)	.91; 0.44 (−0.18, 1.06)

Abbreviation: NA, not applicable.

[a] Values in bold represent statistical and clinical significance.

[b] Effect sizes compared set 1 and each set point.

[c] *P* values and effect sizes compared groups at the same set point.

[d] Statistically different from set 1 ($P < .05$).

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DISCUSSION

The aims of our study were to observe (1) changes in quadriceps neuromuscular function during and after repetitive bouts of exercise in patients with PFP and (2) fatigue level and muscular endurance performance during exercise in patients with PFP compared with their age- and BMI-matched healthy counterparts. We found that patients with PFP experienced rapid reductions in quadriceps central activation, force-generating capacity, or both in the early and late stages of exercise-induced fatigue, whereas neuromuscular function in the healthy control group gradually decreased, yet quadriceps maximal strength did not differ as the exercise sets progressed. Further, fatigue levels during and after repeated bouts of exercise and knee-extension repetitions and quadriceps total work during the exercise sets were similar between groups.

To our knowledge, this is the first investigation to identify trajectories of quadriceps neuromuscular function before, during, and after isokinetic knee-extension exercises in patients with PFP. Understanding neuromuscular alterations during continuous exercise sets and cumulative fatigue may lead to improvements in current treatment strategies to better prepare people with PFP for the return to physically demanding activities. All quadriceps neuromuscular function measures (PT, CAR, and RTD) decreased over time, regardless of the presence or absence of PFP, indicating that our fatiguing protocol was valid for inducing neuromuscular fatigue. It has been suggested[28] that combined central and peripheral processes may contribute to neuromuscular fatigue. Peripheral mechanisms arise from changes in the contractile elements within skeletal muscle fibers (ie, fatigue in the muscle itself).[28] On the other hand, central mechanisms arise from changes at any spinal and supraspinal levels, which may contribute to a further decline in muscle force production and force-generating capacity due to reduced neural drive to the motoneuron pool.[28,29]

Interestingly, whereas quadriceps central activation and force-generating capacity were maintained after the first set of fatiguing exercises in healthy individuals, these neuromuscular variables (CAR and RTD) were sharply reduced in patients with PFP. These results may indicate that patients with PFP were more susceptible to fatigue even from the first bout of exercise. Patellofemoral pain is a common cause of peripheral neuromuscular dysfunction linked to reduced lower extremity force production.[7,30] Chronic pain has been postulated to also influence the central nervous system,[8,31] making it difficult for individuals to fully depolarize all motor units in a motoneuron pool. Some researchers[32,33] suggested that chronic pain conditions lead to prolonged adaptations, possibly from long-lasting nociceptive activity in the peripheral joint, which may affect the extent of neural adaptations over time. In this regard, a long symptom duration (>3 years; Table 1) in our participants with PFP may have further contributed to the central activation failure during repeated muscle contractions. As the pain severity of PFP has been associated with quadriceps dysfunction,[7,8] a moderate pain level of 4.2 (of 10 on the VAS) in our patients could have influenced the magnitude of deficits in neuromuscular function.

Although authors[34] of a recent scoping review reported that RTD appears to be a valid and sensitive indicator of neuromuscular fatigue, RTD during the fatigued state in the PFP population has not been explored. Previous investigators[35] determined that 100 repetitions of quadriceps contraction decreased RTD by 36% in healthy individuals, whereas a 22% reduction was seen in our healthy control group after 3 sets (average of 96 knee-extension repetitions; Table 4) of exercise. Unfortunately, our results cannot be directly compared with those of the previous study[35] because details of the study design, such as fatigue protocols (eg, isometric versus isokinetic contractions) and rest periods (eg, fatigue level and neuromuscular assessments between exercise sets in our study), were not identical. In the present study, RTD was the most impaired function compared with other neuromuscular measurements in patients with PFP, with a reduction of nearly half (−46%) from baseline to the last set of exercise. This may suggest that RTD is a sensitive indicator of quadriceps dysfunction in both resting and fatigued states, whereas CAR seemed to indicate subsequent dysfunction only postexercise in our patient cohort. In addition to the significant decline between baseline and time 1 (−19%), RTD was reduced in patients with PFP between times 4 and 5 (−25%). An inability to generate force rapidly is associated with biomechanical deviations in the knee joint (eg, quadriceps-avoidance gait) and altered joint-loading patterns,[14] so we should focus on the nature and magnitude of changes in neuromuscular function. Further studies are needed to determine whether a greater loss in quadriceps RTD in the fatigued state is another contributing factor to deviations in lower extremity biomechanics or the risk for other injuries. This may provide clinicians with evidence for restoring neuromuscular function before patients return to a physically active lifestyle or participate in competitive sports events.

Because the lack of task specificity could lead to an underestimation of neuromuscular fatigue, we adopted a specific fatigue protocol for the same task (ie, knee extension) to induce isolated quadriceps fatigue.[34] Contrary to our hypothesis, the increased rates of fatigue based on blood lactate concentration were not different between groups. Also, we did not identify statistical differences in the reduced knee-extension repetitions or quadriceps total work during isokinetic exercise. Still, healthy individuals showed greater quadriceps total work with moderate ESs at times 2 (Cohen d [95% CI] = 0.50 [−0.12, 1.12]), 3 (Cohen d [95% CI] = 0.50 [−0.12, 1.11]), and 4 (Cohen d [95% CI] = 0.51 [−0.11, 1.12]), representing clinically meaningful differences. These outcomes may suggest that patients with PFP experience rapid declines in neuromuscular function even though the number of joint movements and the total muscle workloads are similar or lower. Our differences in quadriceps neuromuscular dysfunction, but not in repetition numbers and total work, may also be due to the different mechanisms of central and peripheral fatigue between patients with PFP and healthy individuals. Future studies are needed to confirm this hypothesis. Readers should also be cautious when interpreting these data because we used a laboratory-based fatiguing protocol, such as stopping continuous concentric contractions at 60°/s until the torque output dropped to <50% of the precalculated PT for 3 consecutive contractions.[25] A participant who produced an isokinetic PT of <50% of the baseline isometric PT during 2 consecutive contractions but >50% in the third was able to continue exercising and increase the

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number of knee-extension repetitions. Investigators should explore what level of repetition of muscle torque occurs during specific functional activities and apply it to fatigue research. Psychological fatigue levels (eg, determination or perseverance) should also be considered.

Our study was not without limitations. Although age and BMI were matched between the groups, their heights differed. This may have influenced the knee moment arm during testing, but we assumed that this would have a minimal effect on our results. Also, the sexes were not fully balanced between groups (females accounted for 32% of the PFP group and 53% of the healthy control group), which could have influenced our outcomes. We also tried to match the amount of physical activity (minutes per week) between groups using open-ended questions to screen participants for our physical activity–related inclusion criteria (ie, $\geq$150 minutes of moderate or 60 minutes of vigorous intensity exercise per week). Nonetheless, validated questionnaire tools (eg, International Physical Activity Questionnaire) should be used to obtain more accurate physical activity data in future research. Lastly, although pain information (eg, pain level and variability) or self-reported fatigue (eg, rating of perceived exertion) during and after a fatiguing protocol may play an important role in neuromuscular responses, we did not collect these data. To provide a better treatment approach, investigators should examine the relationship between changes in pain perception and neuromuscular dysfunction. In addition, future researchers should develop and evaluate effective treatment strategies for PFP that can improve the patient's ability to continue performing at a high level with a low risk of injury during and after a prolonged period of exercise (ie, fatigue resistance).

CONCLUSIONS

Patients with PFP were more likely to suffer from acute reductions in quadriceps neuromuscular function due to fatigue from the first single bout of knee-extension exercise. Furthermore, the ability to maintain force-generating capacity appeared to decrease sharply again after repeated bouts of exercise. Hence, when prescribing rehabilitation programs and integrating patients back into functional activities, exercise, and sport, clinicians should be aware of changes in neuromuscular function during exercise and postexercise.

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REFERENCES

1. Glaviano NR, Kew M, Hart JM, Saliba S. Demographic and epidemiological trends in patellofemoral pain. *Int J Sports Phys Ther*. 2015;10(3):281–290.
2. Smith BE, Selfe J, Thacker D, et al. Incidence and prevalence of patellofemoral pain: a systematic review and meta-analysis. *PLoS One*. 2018;13(1):e0190892. doi:10.1371/journal.pone.0190892
3. Crossley KM, Stefanik JJ, Selfe J, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, part 1: terminology, definitions, clinical examination, natural history, patellofemoral osteoarthritis and patient-reported outcome measures. *Br J Sports Med*. 2016;50(14):839–843. doi:10.1136/bjsports-2016-096384
4. Stathopulu E, Baildam E. Anterior knee pain: a long-term follow-up. *Rheumatology (Oxford)*. 2003;42(2):380–382. doi:10.1093/rheumatology/keg093
5. Wyndow N, Collins N, Vicenzino B, Tucker K, Crossley K. Is there a biomechanical link between patellofemoral pain and osteoarthritis? A narrative review. *Sports Med*. 2016;46(12):1797–1808. doi:10.1007/s40279-016-0545-6
6. Blønd L, Hansen L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg*. 1998;64(4):393–400.
7. Kim S, Park J. Impact of severity and duration of anterior knee pain on quadriceps function and self-reported function. *J Athl Train*. 2022;57(8):771–779. doi:10.4085/1062-6050-0647.21
8. de Oliveira Silva D, Magalhães FH, Faria NC, et al. Vastus medialis Hoffmann reflex excitability is associated with pain level, self-reported function, and chronicity in women with patellofemoral pain. *Arch Phys Med Rehabil*. 2017;98(1):114–119. doi:10.1016/j.apmr.2016.06.011
9. Glaviano NR, Holden S, Bazett-Jones DM, Singe SM, Rathleff MS. Living well (or not) with patellofemoral pain: a qualitative study. *Phys Ther Sport*. 2022;56:1–7. doi:10.1016/j.ptsp.2022.05.011
10. Kim S, Kim D, Park J. Knee joint and quadriceps dysfunction in individuals with anterior knee pain, anterior cruciate ligament reconstruction, and meniscus surgery: a cross-sectional study. *J Sport Rehabil*. 2021;30(1):112–119. doi:10.1123/jsr.2018-0482
11. Hopkins JT, Ingersoll CD. Arthrogenic muscle inhibition: a limiting factor in joint rehabilitation. *J Sport Rehabil*. 2000;9(2):135–159. doi:10.1123/jsr.9.2.135
12. Radin EL, Yang KH, Riegger C, Kish VL, O'Connor JJ. Relationship between lower limb dynamics and knee joint pain. *J Orthop Res*. 1991;9(3):398–405. doi:10.1002/jor.1100090312
13. Seeley MK, Son SJ, Kim H, Hopkins JT. Biomechanics differ for individuals with similar self-reported characteristics of patellofemoral pain during a high-demand multiplanar movement task. *J Sport Rehabil*. 2021;30(6):860–869. doi:10.1123/jsr.2020-0220
14. Kline PW, Jacobs CA, Duncan ST, Noehren B. Rate of torque development is the primary contributor to quadriceps avoidance gait following total knee arthroplasty. *Gait Posture*. 2019;68:397–402. doi:10.1016/j.gaitpost.2018.12.019
15. Neal BS, Lack SD, Lankhorst NE, Raye A, Morrissey D, van Middelkoop M. Risk factors for patellofemoral pain: a systematic review and meta-analysis. *Br J Sports Med*. 2019;53(5):270–281. doi:10.1136/bjsports-2017-098890
16. Øiestad BE, Juhl CB, Culvenor AG, Berg B, Thorlund JB. Knee extensor muscle weakness is a risk factor for the development of knee osteoarthritis: an updated systematic review and meta-analysis including 46 819 men and women. *Br J Sports Med*. 2022;56(6):349–355. doi:10.1136/bjsports-2021-104861
17. Zory R, Weist R, Malakieh J, Grenier S. Thigh muscles' responses caused by a single combined aerobic and resistance training session in healthy young men. *Int J Sports Med*. 2010;31(5):311–318. doi:10.1055/s-0030-1248329
18. Negahban H, Etemadi M, Naghibi S, et al. The effects of muscle fatigue on dynamic standing balance in people with and without patellofemoral pain syndrome. *Gait Posture*. 2013;37(3):336–339. doi:10.1016/j.gaitpost.2012.07.025
19. Van Cant J, Declève P, Garnier A, Roy JS. Influence of symptom frequency and severity on hip abductor strength and endurance in individuals with patellofemoral pain. *Phys Ther Sport*. 2021;49:83–89. doi:10.1016/j.ptsp.2021.02.001
20. Dalton EC, Pfile KR, Weniger GR, Ingersoll CD, Herman D, Hart JM. Neuromuscular changes after aerobic exercise in people with anterior cruciate ligament–reconstructed knees. *J Athl Train*. 2011;46(5):476–483. doi:10.4085/1062-6050-46.5.476

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21. Davis AG, Pietrosimone BG, Ingersoll CD, Pugh K, Hart JM. Quadriceps function after exercise in patients with anterior cruciate ligament–reconstructed knees wearing knee braces. *J Athl Train*. 2011;46(6):615–620. doi:10.4085/1062-6050-46.6.615
22. Crossley KM, van Middelkoop M, Callaghan MJ, Collins NJ, Rathleff MS, Barton CJ. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br J Sports Med*. 2016;50(14):844–852. doi:10.1136/bjsports-2016-096268
23. Park J, Hopkins JT. Induced anterior knee pain immediately reduces involuntary and voluntary quadriceps activation. *Clin J Sport Med*. 2013;23(1):19–24. doi:10.1097/JSM.0b013e3182717b7b
24. Hart S, Drevets K, Alford M, Salacinski A, Hunt BE. A method-comparison study regarding the validity and reliability of the Lactate Plus analyzer. *BMJ Open*. 2013;3(2):e001899. doi:10.1136/bmjopen-2012-001899
25. Gribble PA, Hertel J. Effect of lower-extremity muscle fatigue on postural control. *Arch Phys Med Rehabil*. 2004;85(4):589–592. doi:10.1016/j.apmr.2003.06.031
26. Norte GE, Hertel JN, Saliba SA, Diduch DR, Hart JM. Quadriceps and patient-reported function in ACL-reconstructed patients: a principal component analysis. *J Sport Rehabil*. 2019;28(1):8–16. doi:10.1123/jsr.2017-0080
27. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Rev ed. Academic Press; 1977:145–178.
28. Taylor JL, Amann M, Duchateau J, Meeusen R, Rice CL. Neural contributions to muscle fatigue: from the brain to the muscle and back again. *Med Sci Sports Exerc*. 2016;48(11):2294–2306. doi:10.1249/MSS.0000000000000923
29. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev*. 2001;81(4):1725–1789. doi:10.1152/physrev.2001.81.4.1725
30. Briani RV, de Oliveira Silva D, Ducatti MHM, et al. Knee flexor strength and rate of torque development deficits in women with patellofemoral pain are related to poor objective function. *Gait Posture*. 2021;83:100–106. doi:10.1016/j.gaitpost.2020.10.011
31. Ward S, Pearce AJ, Pietrosimone B, Bennell K, Clark R, Bryant AL. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve*. 2015;51(3):327–332. doi:10.1002/mus.24463
32. Apkarian AV, Bushnell MC, Treede R-D, Zubieta J-K. Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain*. 2005;9(4):463–484. doi:10.1016/j.ejpain.2004.11.001
33. Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. *Science*. 2000;288(5472):1765–1769. doi:10.1126/science.288.5472.1765
34. D'Emanuele S, Maffiuletti NA, Tarperi C, Rainoldi A, Schena F, Boccia G. Rate of force development as an indicator of neuromuscular fatigue: a scoping review. *Front Hum Neurosci*. 2021;15:701916. doi:10.3389/fnhum.2021.701916
35. Viitasalo JT, Komi PV. Effects of fatigue on isometric force- and relaxation-time characteristics in human muscle. *Acta Physiol Scand*. 1981;111(1):87–95. doi:10.1111/j.1748-1716.1981.tb06709.x

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