Sports Medicine and Health Science 8 (2026) 185–192

Contents lists available at ScienceDirect

Sports Medicine and Health Science

journal homepage: www.keaipublishing.com/smhs

Original Article

The effect of exercise rehabilitation on bone mineral density, muscle strength, and physical function outcomes in ACL ruptures: A randomized controlled clinical trial

Yue Wu [a,b,c,d,1], Ruilan Dai [b,c,d,1], Yunan Zhou [a,b,c,d], Wenqiang Yan [b,c,d], Shuang Ren [b,c,d], Xi Gong [b,c,d,*], Yingfang Ao [a,b,c,d,**]

[a] Tianjin Key Laboratory of Exercise Physiology and Sports Medicine, Institute of Sport, Exercise & Health, Tianjin University of Sport, Tianjin 300381, China
[b] Department of Sports Medicine, Peking University Third Hospital, Institute of Sports Medicine of Peking University, Beijing, China
[c] Beijing Key Laboratory of Sports Injuries, Beijing, China
[d] Engineering Research Center of Sports Trauma Treatment Technology and Devices, Ministry of Education, Beijing, China

ARTICLE INFO

Keywords:
Anterior cruciate ligament
Rehabilitation
Bone mineral density
Joint function

ABSTRACT

The purpose is to explore the effects of Exercise rehabilitation (ER) on bone mineral density (BMD) of the knee, muscle strength (MS), and physical function (PF) after ACL rupture. Finally, A total of 58 patients were randomized into 2 groups (Control Group [CON]: conventional treatment, male = 16, female = 13, age = [31.63 ± 8.01] years; Exercise rehabilitation group [ER]: 6-week ER on CON basis, male = 17, female = 12, age = [31.26 ± 7.07] years). At baseline and 6 weeks, the knee BMD was measured using DEXA, MS and PF measures were recorded by isokinetic strength test, IKDC, Lysholm, and VAS score. T-tests, analysis of variance (ANOVA), and Mann-Whitney tests were used for comparisons. The BMD outcomes: after a 6-week period, the BMD of the CON ([1.47 ± 0.24] g·cm^{-2}) was significantly lower than that of the ER ([1.65 ± 0.37] g·cm^{-2}) at lateral condyle of femur (LCF) ($p = 0.041$). MS outcomes: at 6 weeks, the relative peak torque (RPT) of the quadriceps and hamstrings during concentric contractions in ER group were significantly higher than that in CON group ($p < 0.001$, $p = 0.017$). Similarly, during eccentric contractions in ER group, the RPT of the quadriceps and the H/Q ratio revealed significant variations from the CON group ($p = 0.033$, $p = 0.043$). PF outcomes: the IKDC, Lysholm, and VAS scores of the ER group were significantly improved compared to the CON group ($p < 0.001$, $p < 0.001$, $p = 0.002$). The conclusion is that 6 weeks of ER intervention for patients with ACL rupture can effectively delay the decline of BMD in the LCF of the knee joint, and enhance the restoration of MS and PF. This provides guidance for clinical rehabilitation.

1. Introduction

Anterior cruciate ligament (ACL) rupture is one of the most common and serious knee injuries in sports medicine,[1] with an annual incidence of approximately five per 10 000 persons in the general population.[2] ACL rupture is usually accompanied by meniscus injury, cartilage injury, bone contusion, and other injuries.[3] In addition, patients experienced instability concerns, had pain during activity, lost bone mineral density (BMD) of the knee, which could affect the healing of tendon-bone after surgery, thereby increasing the risk of re-rupture of the graft.[4] Furthermore, patients would decrease muscle strength (MS), which could affect daily activities, physical activity, and even quality of life, especially for athletes.[5]

Exercise has the effect of increasing BMD and enhancing MS.[6] Exercise rehabilitation (ER) is used physical activity to promote recovery.[7] The rehabilitation therapy mainly includes improving joint range of motion (ROM), increasing MS, raising equilibrium, and so on.[8,9] Some studies found that ER can improve physical function (PF), relieve muscle atrophy, enhance muscle strength, speed up the rehabilitation process, and allow for an early return to sports.[10] ER has the advantages of convenient operation, low cost, and popularization. As a result, ER has

* Corresponding author. Department of Sports Medicine, Peking University Third Hospital, Institute of Sports Medicine of Peking University, Beijing, China.
** Corresponding author. Tianjin Key Laboratory of Exercise Physiology and Sports Medicine, Institute of Sport, Exercise & Health, Tianjin University of Sport, Tianjin 300381, China.
E-mail addresses: gongxi518@163.com (X. Gong), aoyingfang@163.com (Y. Ao).
[1] Yue Wu and Ruilan Dai contributed to the work equally and should be regarded as co-first authors.

https://doi.org/10.1016/j.smhs.2025.03.002
Received 29 June 2024; Received in revised form 7 March 2025; Accepted 12 March 2025
Available online 27 March 2025

Abbreviations

ACL	Anterior cruciate ligament
ER	Exercise rehabilitation
BMD	bone mineral density
PCL	Posterior Cruciate Ligament
LCL	Lateral Collateral Ligaments
MCL	Medial Collateral Ligament
BMI	Body Mass Index
RPE	the Borg Rating of Perceived Exertion
MCF	the medial condyle of the femur
LCF	the lateral condyle of the femur
MCT	the medial condyle of the tibia
LCT	the lateral condyle of the tibia
ROM	range of motion
MS	muscle strength
PF	physical function
CC	concentric contraction
EC	eccentric contraction
RPT	relative peak torque
H/Q	the hamstring-to-quadriceps ratio
IKDC	the International Knee Documentation Committee score
VAS	Visual analogue scale

become popular in rehabilitation.[11]

However, the impact of ER on clinical outcomes such as local knee joint BMD, MS, and PF measures after ACL rupture is not well known. Currently, there is no research on the impact of ER on BMD after ACL rupture. The objective of this study was to explore the changes in knee BMD, MS, and PF after 6 weeks in ACL rupture patients within 6 months of ER. We hypothesize that ER may mitigate the rate at which BMD diminishes in the knee joint, bolster MS, and enhance PF.

2. Methods

2.1. Trial design

This study was a randomized controlled superiority trial design with parallel intervention groups, balanced randomization (1:1), and patient-blinded. The ethics committee at Peking University Third Hospital approved the study (202303303). This study adheres to the ethical guidelines outlined in the Helsinki Declaration for human research.

This study was registered at www.clinicaltrials.gov (NCT05924178). Informed consent was obtained from all participants prior to enrollment and baseline testing.

2.1.1. Participant involvement

Patients were not directly involved in the design of the trial but actively participated in the experiments. A recruitment advertisement was posted in the outpatient department of Peking University Third Hospital to attract the attention of patients with ACL rupture.

2.1.2. Participants

Inclusion criteria were:[12–14]

① Patients aged 18–45 years diagnosed with ACL rupture via MRI.
② Patients with first-time unilateral ACL rupture would undergo ER at our hospital.
③ Time from injury was greater than 4 weeks and within 6 months (sub-chronic phase).
④ The affected knee joint passed the acute stage, with no significant swelling, pain, inflammation, limited joint movement, and had basically recovered to normal joint range of motion.
⑤ No injuries to the Posterior Cruciate Ligament (PCL), or Lateral Collateral Ligaments (LCL). No injuries or only minor injuries (no more than grade I: mild injury/contusion, slight elongation of the ligament, possible morphological changes, but normal ligament MRI signal) to Medial Collateral Ligament (MCL).

Exclusion criteria were:

① Body Mass Index (BMI) less than 18.5 or greater than 35 $kg \cdot m^{-2}$.
② Aged over 45 years old or under 18 years old.
③ Injury occurred within 4 weeks or more than 6 months.
④ Serious injury to the PCL, MCL, or LCL (grades II or III). Grade II is a partial tear, ligament thickening, tortuous, partial fiber interruption, with surrounding soft tissue swelling; Grade III is a complete rupture.
⑤ History of knee joint trauma.
⑥ Other knee joint diseases, such as knee osteoarthritis, knee joint tumor, rheumatoid, tuberculosis, etc.

Data collection was performed at the Sports Medicine of Peking University Third Hospital between April 2023 and May 2024.

2.1.3. Randomization and blinding

Patients were consecutively numbered from 1 to 60 and then randomly assigned to 2 groups, each comprising 30 patients, using a computer-generated randomization sequence. Upon inputting the range of 1–60, the computer-generated randomization sequence automatically generated 2 sets of random numbers to allocate participants into the respective groups. The groups were designated as the control group (CON) and the exercise rehabilitation group (ER). The sequence of patients visiting our hospital was marked with numbers 1–60. After baseline assessments, the patients were enrolled and underwent different intervention schemes. The CON group received only routine medical treatment, while the ER group underwent a 6-week ER program in addition to the CON group's treatment. This study utilized a single-blind design, ensuring that the testers and data analysts were unaware of the participants' group assignments.

2.1.4. Intervention

After enrollment, the patients in the ER group underwent an exercise program for 6 weeks, three times a week, lasting approximately 45–60 min each session, with a rest day between sessions.[9,15–20] Prior to each formal training session, patients were prepared for 3–5 min, followed by stretching and relaxation for another 3–5 min after the training. Ice application was administered appropriately after the training. When engaging in exercise, it was advisable to keep the intensity at a moderate level. By presenting the Borg Rating of Perceived Exertion (RPE) scale to patients, their subjective feeling should ideally fall within the range of 13–14 (Somewhat hard, but still able to talk).[21] The ER training program is outlined in Table 1 (or Protocol 1). In the knee range of motion (ROM) section, it was about 4 min. In the muscle strength exercises section, it was about 25–30 min; in the balance training section, it was about 4–6 min; and in the sclerotin training section, it was about 5–10 min. The time allocation of each training session is detailed in protocol 1.

Patients in the CON group received only conventional treatment, including ROM, daily activities, and conventional topical medications. Patients in both the CON and ER groups maintained their original lifestyle habits and schedules. Both groups underwent the same examinations, tests, and assessments.

Table 1
Exercise rehabilitation program.

Exercise Movement		1st week	2nd week	3rd week	4th week	5th week	6th week
ROM	Knee Extension	✓	✓	✓	✓	✓	✓
	Knee Flexion	✓	✓	✓	✓	✓	✓
Muscle Strength	Wall Squats	✓	✓	✓			
	Deep Squat				✓	✓	✓
	Lunge				✓	✓	✓
	Seated Knee Extension Resistance Exercise	✓	✓	✓	✓	✓	✓
	Prone Position Knee Flexion Resistance Exercise	✓	✓	✓	✓	✓	✓
Balance Training	Catch and throw with legs standing under the balance Cushion	✓	✓	✓			
	Catch and throw with Single-leg standing under the balance Cushion				✓	✓	✓
Sclerotin Training	Low Leg Raise	✓	✓				
	Leg Lift			✓	✓	✓	✓
	Skipping Rope	✓	✓	✓	✓	✓	✓

ROM: Range of Motion.

2.2. Sample size

The centripetal peak torque of quadriceps at 60°/s in the knee isokinetic dynamometer was used as the observation index. According to the calculation formula, $n_2 = \frac{(z_{1-\alpha/2}+z_{1-\beta})^2(sd_1^2+sd_2^2)(1+1/k)}{2(mean_1-mean_2)^2}$, $n_1 = k \times n_2$, and $z_{1-\alpha/2} = 1.96$, $z_{1-\beta} = 0.84$. We calculated that a sample size of 24 patients in each group would provide 80% power to detect a mean difference of 28.86 Nm (113.42–84.56 Nm) between groups, assuming standard deviations of 36 Nm for the experimental group and 34 Nm for the control group, with a two-sided alpha of 0.05.[22,23] Given an anticipated dropout rate of 20%, the total sample size required was 60 patients (30 in the experimental group; 30 in the control group).

2.3. Outcomes

2.3.1. Bone mineral density

BMD was measured using a Lunar iDXA (GE Healthcare, Milwaukee, WI, USA).[24,25] Lumbar BMD is first measured to rule out primary osteoporosis, and then the injured knee BMD is tested. All standard clinical scans (lumbar bone mineral density and knee) were acquired and analyzed in the standard clinical manner per manufacturer recommendations.[26]

However, the BMD of the knee joint was measured by manually outlining regions of interest (ROIs). A 5 cm vertical line was drawn from the intercondylar pit of the femur, and a 4 cm vertical line was drawn from the middle of the intercondylar spine of the tibia. This allowed the knee joint to be divided into 4 distinct areas: the medial condyle of the femur (MCF), the lateral condyle of the femur (LCF), the medial condyle of the tibia (MCT), and the lateral condyle of the tibia (LCT) (Fig. 1).

2.3.2. Muscle strength

In addition, the isokinetic MS of the injured knee extensor and flexor were measured using an isokinetic dynamometer (Con-Trex MJ; Germany) at 60°/s for concentric contraction (CC) and eccentric contraction (EC). The indicators utilized were: relative peak torque (RPT) of quadriceps and hamstrings, as well as the hamstring-to-quadriceps ratio (H/Q).

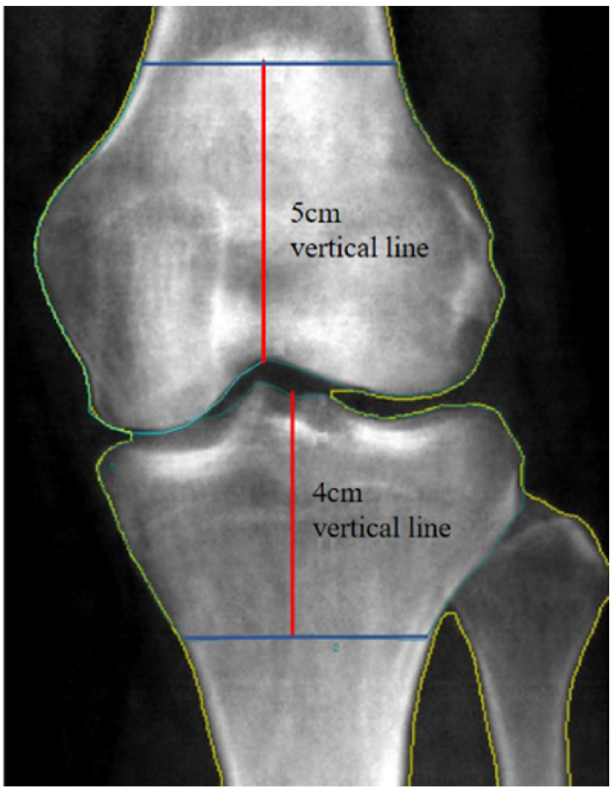

Fig. 1. Custom regions of interest. A 5 cm vertical line was drawn from the intercondylar pit of the femur, and a 4 cm vertical line was drawn from the lateral intercondylar ridge of the tibia, and the knee joint was divided into 4 regions (Medial condyle of femur, MCF; Lateral condyle of femur, LCF; Medial condyle of tibia, MCT; Lateral condyle of tibia, LCT), and 4 ROIs are formed with the boundary line. ROI; region of interest.

2.3.3. Knee physical function

Subjective knee function evaluation encompassed the International Knee Documentation Committee (IKDC) score, Lysholm score, Tegner Activity Scale level and Visual analogue scale (VAS).[27]

2.3.4. Kneelax

The KT-2000 knee laxity tester (KNEELAX3, MONITORED REHAB SYSTEMS B.V.; Netherlands) was used to assess knee joint laxity. In this test, the patient was positioned supine with the quadriceps muscle fully relaxed. The difference in tibial advancement distance between the affected side and the healthy side was measured at 30° flexion of both knee joints under 30 P tension.

2.4. Statistical analysis

SPSS 21.0 statistical software was utilized for statistical analysis. When the test index is normally distributed, it was expressed as mean ± standard deviation and analyzed using the Two-Way Analysis of Variance. If the detection indexes did not follow a normal distribution, they were described by the median (P25, P75) and tested using a non-parametric test (Friedman test). $p < 0.05$ was considered statistically significant. When variances were equal, Cohen's *d* was used to calculate the effect size. When variances were unequal, Hedges' *g* was used. A small effect is indicated by a *d* or *g* value less than 0.2, a medium effect by a *d* or *g* value greater than 0.2 but less than 0.5, and a large effect by a *d* or *g* value greater than 0.8.[28]

3. Results

3.1. Participants

From March 2023 to April 2024, a total of 75 ACL rupture patients from the Sports Medicine Department of Peking University Third Hospital were screened. Among them, 15 participants were excluded (11 patients had injuries longer than 6 months, and 4 patients had severe MCL injuries), resulting in 60 participants being eligible for inclusion. However, 2 participants (1 participant in the ER group and 1 participant in the CON group) were lost to follow-up due to their failure to adhere to the intervention program. Ultimately, 58 patients (29 participants in the ER group and 29 participants in the CON group) completed the experiment and opted for surgical treatment after 6 weeks. Intraoperatively, the diagnosis of an ACL rupture was reaffirmed for all patients. (Fig. 2).

The CON group participants ($n = 29$; 44.83% women) had a mean age of 31.63 years, a mean BMI of 23.49 kg·m^{-2}, a kneelax of 5.05 mm, a pre-injury Tegner score of 5.94, and a post-injury Tegner score of 2.22. The ER group participants ($n = 29$; 41.38% women) had a mean age of 31.26 years, a BMI of 23.61 kg·m^{-2}, a kneelax of 5.28 mm, a pre-injury Tegner score of 6.03, and a post-injury Tegner score of 2.26. Both groups included participants (16 and 14, respectively) with meniscus injury. There were no significant differences in baseline characteristics between the groups ($p > 0.05$) (Table 2).

Table 2
Baseline characteristics of the control group (CON) and exercise rehabilitation group (ER).

Characteristics	CON ($n = 29$) Mean (*SD*)	ER ($n = 29$) Mean (*SD*)
Age (years)	31.63 (8.01)	31.26 (7.07)
Male/Female (*n*/*n*)	16/13	17/12
Right/Left (*n*/*n*)	16/13	13/16
Height (cm)	172.17 (7.48)	171.56 (9.37)
Weight (kg)	69.8 (10.73)	69.89 (13.54)
BMI (kg·m^{-2})	23.49 (2.90)	23.61 (3.33)
Time from rupture to intervention(days)	58.06 (49.94)	49.23 (45.67)
Meniscus injury (*n*)	14	16
Kneelax (mm)	5.05 (2.37)	5.28 (2.21)
Pre-injury Tegner Activity Scale level score	5.94 (0.87)	6.03 (1.07)
Post-injury Tegner Activity Scale level score	2.2 (0.55)	2.26 (0.64)

3.2. Outcomes

3.2.1. BMD measurement

The patients did not suffer from primary osteoporosis. At the MCF, LCF, MCT, and LCT, the group × time effect was not significant ($F = 1.062, 0.371, 1.252, 0.065$) ($p = 0.307, 0.545, 0.268, 0.8$). At baseline, there was no significant difference in BMD at the MCF, LCF, MCT, and LCT between the CON and ER groups ($p > 0.05$). However, after 6 weeks, the BMD at the LCF in the CON group ([1.47 ± 0.24] g·cm^{-2}) was significantly lower than that in the ER group ([1.65 ± 0.37] g·cm^{-2}) ($p = 0.041$). However, the effect size of BMD at LCF was small ($d = 0.093$). Additionally, the BMD of the MCF and LCF in the CON group decreased significantly compared to baseline ($p < 0.05$). In both the CON and ER groups, the BMD of the MCT and LCT was significantly lower than the baseline ($p < 0.01$) (Fig. 3).

3.2.2. Muscle strength measurement

Only at RPT of quadriceps CC and hamstrings EC had a significant group × time effect ($p < 0.05$). In addition, there was no significant difference in MS between the CON and ER groups at baseline ($p > 0.05$). After 6 weeks, the RPT of CC and EC of quadriceps and hamstring muscles in both CON and ER groups increased significantly ($p < 0.05$). During CC, the RPT of quadriceps and hamstring muscles in the ER group was significantly higher than that in the CON group ($p < 0.001, p = 0.017$), at the same time, the effect size was large ($d = 1.01$) and medium ($d = 0.636$), respectively. During EC, the RPT of quadriceps muscle in the ER group was significantly higher than that in the CON group ($p = 0.033$), and the H/Q ratio in the ER group was significantly lower than that in the CON group ($p = 0.043$). The isokinetic MS measurements are presented in Table 3.

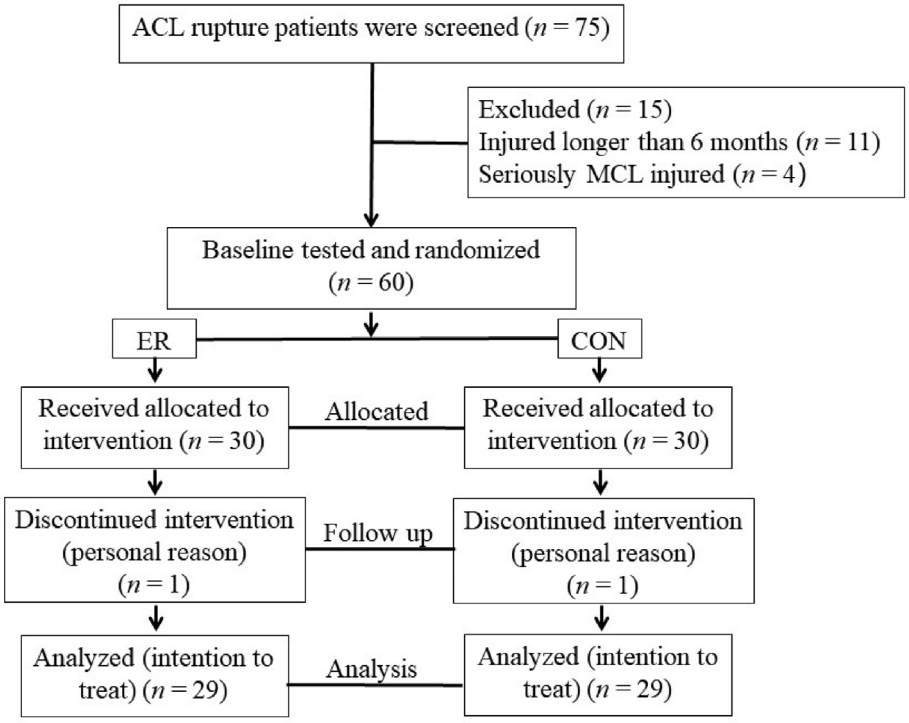

Fig. 2. Flow diagram of eligible and included participants. Abbreviations: CON, control group; ER, exercise rehabilitation group.

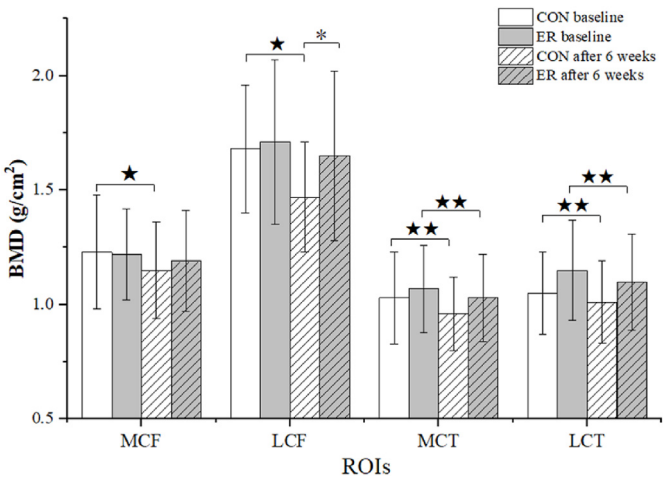

Fig. 3. BMD of Knee Baseline and After 6 weeks (g/cm^2) BMD, bone mineral density; ROIs, regions of interest; ER, exercise rehabilitation group; CON, control group; MCF, Medial condyle of femur; LCF, Lateral condyle of femur; MCT, Medial condyle of tibia; LCT, Lateral condyle of tibia. * Significant difference compared with CON groups $p < 0.05$, $^{**}p < 0.01$. ★ Significant difference compared with baseline $p < 0.05$, ★★ $p < 0.01$. Main result: After 6 weeks, the BMD at LCF in CON group was lower than ER group, and the BMD at MCF and TCF was lower than baseline.

3.2.3. *Knee physical function measurement*

In Table 4, a significant group × time effect ($p < 0.05$) was observed at the scores of IKDC, Lysholm, and VAS ($p < 0.05$). After 6 weeks, the CON and ER groups were significantly improved compared to baseline. The IKDC and Lysholm knee scores in ER group were higher than those in CON group ([78.89 ± 3.97] vs [60.17 ± 7.57], $p < 0.01$, $d = 3.10$; [78.55 ± 9.13] vs [60.24 ± 9.56], $p < 0.01$, $d = 1.96$), and the VAS scores were lower than those in CON group ([1.5 ± 1.2] vs [2.59 ± 1.33], $p < 0.01$, $d = -0.86$).

4. Discussion

After an ACL rupture, there is a decrease in BMD in the knee joint, which is not conducive to the healing of the graft-bone junction after reconstruction surgery.[29,30] Consequently, sustaining or enhancing BMD in the knee joint after an ACL injury is crucial for the healing process. ER is instrumental in improving BMD, yet there is currently a lack of research on the effects of ER on BMD in the knee joints of patients with ACL ruptures. Our paper is the first randomized controlled clinical study to explore the impact of ER on BMD in the knee joints of patients with ACL rupture, and it boasts a high level of evidential quality. Our study clarifies the importance of early ER intervention for patients with ACL rupture in effectively delaying the decline in BMD which may facilitate the postoperative healing of tendon-bone in those undergoing surgery, and enhancing the restoration of MS and PF.

Our hypothesis, that ER may mitigate the rate at which BMD diminishes in the knee, was partially supported. Given that the BMD of the knee joint after reconstruction may impact the tendon-to-bone healing, the ROIs for BMD assessment is specifically designated based on the sites where the bone tunnels are created by our department's surgeons during the procedure. This approach lays a solid foundation for future research. Our study found that after a six-week period, the BMD of the MCF and LCF in the ER group remained relatively stable compared to the baseline measurements, while a significant reduction in BMD was observed in the CON group for the same regions. Additionally, the results of our study demonstrate that after 6 weeks, the BMD at the LCF was significantly lower in the CON group than in the ER group. These results indicate that a continuous 6-week program of ER can effectively slow down the rate of BMD loss in the LCF. The possible reasons for this may be as follows: The

Table 3
Isokinetic MS in the quadriceps and hamstrings.

Variables	Groups	CON	ER	*p*
CC 60°/s Ext RPT(Nm/kg)	baseline	0.93 ± 0.47★★	1.08 ± 0.45★	0.329
	After 6 weeks	1.16 ± 0.46	1.63 ± 0.47**	< 0.001
	p	0.001	0.012	
group × time effect		$F = 7.705$, $p = 0.007$		
CC 60°/s Fle RPT(Nm/kg)	baseline	0.73 ± 0.24 ★★	0.72 ± 0.29 ★★	0.143
	After 6 weeks	0.88 ± 0.32	1.10 ± 0.37*	0.017
	p	< 0.001	< 0.001	
group × time effect		$F = 3.658$, $p = 0.061$		
CC 60°/s H/Q(%)	baseline	0.74 ± 0.24	0.68 ± 0.17	0.359
	After 6 weeks	0.79 ± 0.22	0.69 ± 0.11	0.175
	p	0.754	0.255	
group × time effect		$F = 0.048$, $p = 0.828$		
EC 60°/s Ext RPT(Nm/kg)	baseline	1.34 ± 0.45 ★	1.40 ± 0.45 ★★	0.54
	After 6 weeks	1.58 ± 0.56	1.95 ± 0.74*	0.033
	p	0.028	< 0.001	
group × time effect		$F = 2.120$, $p = 0.151$		
EC 60°/s Fle RPT(Nm/kg)	baseline	0.96 ± 0.25 ★★	0.92 ± 0.29 ★★	0.575
	After 6 weeks	1.15 ± 0.35	1.26 ± 0.51	0.345
	p	< 0.001	0.001	
group × time effect		$F = 4.66$, $p = 0.035$		
EC 60°/s H/Q(%)	baseline	0.75 ± 0.26	0.69 ± 0.17	0.092
	After 6 weeks	0.75 ± 0.27	0.66 ± 0.15*	0.043
	p	0.538	0.246	
group × time effect		$F = 0.004$, $p = 0.948$		

CC: concentric contraction; EC: eccentric contraction; Ext: extensor; Fle: flexor; RPT: relative peak torque; H/Q: hamstring-to-quadriceps ratio; *p*, *p*-value.
*Significant difference compared with CON groups $p < 0.05$, $^{**}p < 0.01$.
★Significant difference compared with baseline $p < 0.05$, ★★ $p < 0.01$.
Main result: After 6 weeks, the MS at CON and ER group was higher than baseline, but ER group was higher than CON group.

BMD at LCF is prone to decrease, and the LCF bears less weight compared to MCF in the knee joint. Mechanical loading is a crucial factor in promoting bone growth. Additionally, after ACL rupture, patients typically experience reduced physical activity, which further diminishes the mechanical stimuli to the bone. Consequently, this leads to decreased bone growth and remodeling at the LCF, resulting in lower BMD. Moreover, ER training can enhance bone stimulation through muscle contraction. However, the ER training employed in our study may have been of relatively low intensity, thus only serving to delay the decline in BMD rather than fully counteracting it. Currently, there are studies that align with our findings, indicating a decrease in BMD in the knee joint following an ACL rupture. A decrease in BMD of the medial femoral condyle is noted within the first 4 weeks post-injury, with a pronounced reduction in overall knee joint bone density by the 10th week.[31] Furthermore, research has shown that BMD on the injured leg is markedly reduced compared to the uninjured leg, regardless of whether ligament reconstruction has been performed, 26 months after the reconstruction, the BMD of the affected knee is still 16% lower than before the operation,[32] and the decline in BMD may persist for more than 10 years.[33] When patients undergo reconstruction surgery following an ACL rupture, the local BMD in the knee is diminished, leading to increased osteoclastic activity and compromised bone formation at the tendon-bone attachment site. This results in weakened tendon-bone interface strength, a reduction in the transitional structure of the tendon-bone interface, and an enlargement of the bone tunnel, which is

Table 4
Effect of exercise rehabilitation on knee function score (mean [95% *CI*]).

Variables	Groups	CON	ER	*p*
IKDC knee score	baseline	49.72 ± 6.05★★	51.11 ± 5.97★★	0.128
	After 6 weeks	60.17 ± 7.57	78.89 ± 3.97**	< 0.001
	p	< 0.001	< 0.001	
group × time effect		$F = 99.793$, $p < 0.001$		
Lysholm knee score	baseline	46.93 ± 9.54★★	50.3 ± 10.83★★	0.103
	After 6 weeks	60.24 ± 9.56	78.55 ± 9.13**	< 0.001
	p	< 0.001	< 0.001	
group × time effect		$F = 27.36$, $p < 0.001$		
VAS score	baseline	3.21 ± 1.14★	3 ± 1.14★★	0.466
	After 6 weeks	2.59 ± 1.33	1.5 ± 1.2**	0.002
	p	0.025	< 0.001	
group × time effect		$F = 6.313$, $p = 0.015$		

IKDC, International Knee Documentation Committee; VAS, Visual analogue scale. *p*, *p*-value.
*Significant difference compared with CON groups $p < 0.05$, **$p < 0.01$.
★Significant difference compared with baseline $p < 0.05$, ★★ $p < 0.01$.
Main result: After 6 weeks, the scores of IKDC, Lysholm and VAS at CON and ER groups were better than baseline, but the ER group was better than the CON group.

detrimental to the healing of the reconstructed ligament and the integration of the tendon-bone junction, ultimately affecting the clinical outcomes.[34] However, current research findings have not delved into the specific interventions for the decline in BMD in the knee joint post-ACL rupture, nor have they explored the effects of these interventions. Our findings indicate that ER can mitigate the rate of BMD decline after an ACL rupture. In particular, it significantly slows down the rate of BMD decrease at the LCF, which may promote local bone formation in the knee joint. Some findings did not align with the initial hypothesis; after 6 weeks, the BMD of the tibial condyles (MCT and LCT) in both the ER group and the CON group significantly decreased compared to the baseline. This outcome could be attributed to the relatively short duration of the exercise intervention. Excluding the LCF, after the 6-week period, there were no significant differences in BMD between the ER and CON groups at the MCF, MCT, and LCT regions. However, past research has suggested that a 6-week exercise intervention can increase the overall BMD in the elderly.[35] Therefore, this study suggests that for individuals with an ACL rupture, enhancing tibial BMD may require ER beyond 6 weeks. Moreover, muscle contractions can apply stress to the bones, thereby promoting the growth of BMD.[36] Anatomically, the ER strength training primarily targets the quadriceps and hamstring muscles. After 6 weeks, there was no significant change in the BMD of the femoral condyles (MCF and LCF) in the ER group from the baseline. Hence, relative to the tibia, this rehabilitation program is more effective in decelerating the reduction of BMD in the femur. These results indicate that adding calf muscle training to the rehabilitation program for ACL rupture patients may be beneficial in mitigating the decline in tibial BMD or even enhancing it. The mechanisms underlying the changes in BMD in different regions of the knee joint following ACL rupture will need to be further investigated. Furthermore, because the effect size of ER on changes in BMD is small, future studies would also consider extending the observation period and increasing the sample size to better evaluate long-term effects.

Our hypothesis, that ER could bolster MS and enhance PF, was fully supported. Our study demonstrates that following our rehabilitation program, there is a marked enhancement in the MS of the quadriceps and hamstrings, along with an enhancement in PF, when compared to CON group. In addition, patients in the CON group also experienced a significant improvement in MS and PF after 6 weeks compared to baseline, likely due to the gradual resumption of daily activities after a 6-week period of rest. This is consistent with previous research findings that an ACL rupture results in reduced stability of the knee joint, characterized by the anterior shift of the tibia and loss of joint stability. This prevents patients from resuming their pre-injury sports activities and from executing movements that impose significant stress on the knee, resulting in limited knee joint function. Concurrently, influenced by factors such as joint trauma, immobilization, stress, and inflammatory reactions, the muscles surrounding the knee joint experience a decline in strength and undergo atrophy.[37] Furthermore, our earlier studies have shown that following an ACL rupture, there is a 38% reduction in the peak torque of the quadriceps during EC and a 15% decrease in the peak torque of the hamstrings during EC.[22] Even after reconstruction surgery, by the first postoperative year, the quadriceps strength and the H/Q ratio of the patients' knees had not completely returned to normal; by the fourth postoperative year, the quadriceps strength on the affected side was still weaker compared to that of a healthy population.[38] Nevertheless, this study provides compelling evidence that ER is beneficial for the recovery of MS and PF following an ACL rupture. Similarly, research indicates that a systematic 9-session ER program for ACL rupture patients can increase the cross-sectional area (CSA) of the knee muscles and improve the strength of the extensors.[39] Moreover, an array of rehabilitation approaches, suggestions, and guidelines have been successively introduced for post-ACL injury recovery in clinical practice.[10] ER should be a continuous component of the entire treatment regimen, delivering advantages such as increased MS, reduced muscle atrophy, enhanced PF, expedited recovery, and an earlier return to sports.[38] Whether it is conservative treatment or surgical treatment, ER can facilitate post-injury recovery. Studies have shown that ACL rupture patients who underwent a 5-week preoperative RE exhibited increased knee ROM, enhanced thigh MS, and improved PF.[18] Likewise, post-reconstruction quadriceps strengthening exercises contribute to an increase in quadriceps torque and an improvement in the alignment of the lower limb's force line.[40]

Consequently, ER holds a significant role throughout the comprehensive treatment of ACL injuries. Our research represents a preliminary exploration into the effects of early ER on the BMD of the knee joint in patients with ACL ruptures. This rehabilitation protocol not only facilitated the restoration of PF in those opting for conservative management but also established a foundation for the postoperative recuperation of BMD and PF, including the enhancement of tendon-bone healing in those who eventually underwent surgery.

5. Limitations

The primary limitation of our study is the considerable variation in the enrollment period following injury among patients, which spans from 1 to 6 months. Nonetheless, the time elapsed from injury to study entry did not significantly differ between the CON and ER groups. Consequently, the influence of injury timing on the comparative outcomes between the CON and ER groups is minimal. Future studies could benefit from tailoring individualized rehabilitation programs based on the time elapsed since injury and the degree of BMD loss. Moreover, the follow-up period of this study was relatively short; it was a preliminary investigation into the impact of ER on BMD. However, the study has already revealed that 6 weeks of ER can slow down the decline of BMD and improve PF, laying a foundation for subsequent long-term research. We have also formulated a long-term research plan, which will further explore the long-term effects of ER on BMD and PF in patients with ACL rupture.

6. Conclusion

6 weeks of ER intervention for patients with ACL rupture can effectively delay the decline of BMD in the LCF of the knee joint which may facilitate the postoperative healing of tendon-bone, and enhance the restoration of MS and PF.

CRediT authorship contribution statement

Yue Wu: Writing – original draft. **Ruilan Dai:** Data curation. **Yunan Zhou:** Formal analysis. **Wenqiang Yan:** Data curation. **Shuang Ren:** Methodology. **Xi Gong:** Data curation, Conceptualization. **Yingfang Ao:** Data curation, Conceptualization.

Registrations

This study was registered at www.clinicaltrials.gov (NCT05924178).

Ethical approval statement

All participants have provided their written informed consent. The study has been reviewed and approved by the Ethics Committee of Peking University Third Hospital, with the assigned approval number 202303303. This study adheres to the ethical guidelines outlined in the Helsinki Declaration for human research.

Funding

Funding for this study was provided by the Joint Fund for Regional Innovation and Development (U23A20471), Beijing Natural Science Foundation (L242161, L241073, and 7232354).

Declaration of competing interest

Yingfang Ao is an Editorial Board Member for Sports Medicine and Health Science and was not involved in the editorial review or the decision to publish this article. All authors have agreed to publish the present article and declare no conflict of interest.

Acknowledgments

The authors extend their heartfelt thanks to the participants for their invaluable contributions to this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smhs.2025.03.002.

References

1. Liu H, Liu J, Wu YW, Ma YH, Gu SJ, Rui YJ. Changes in local bone mineral density can guide the treatment plan for patients with rupture of the anterior cruciate ligament. *Ann Palliat Med*. 2021;10(6):6388–6398. https://doi.org/10.21037/apm-21-741.
2. Moses B, Orchard J, Orchard J. Systematic review: annual incidence of ACL injury and surgery in various populations. *Res Sports Med*. 2012;20(3–4):157–179. https://doi.org/10.1080/15438627.2012.680633.
3. Bray RC, Dandy DJ. Meniscal lesions and chronic anterior cruciate ligament deficiency. Meniscal tears occurring before and after reconstruction. *J Bone Joint Surg Br*. 1989;71(1):128–130. https://doi.org/10.1302/0301-620x.71b1.2914982.
4. Boyd SK, Matyas JR, Wohl GR, Kantzas A, Zernicke RF. Early regional adaptation of periarticular bone mineral density after anterior cruciate ligament injury. *J Appl Physiol(1985)*. 2000;89(6):2359–2364. https://doi.org/10.1152/jappl.2000.89.6.2359.
5. Stropnik D, Sajovic M, Kacin A, Pavlič-Založnik S, Drobnič M. Early clinical and neuromuscular properties in patients with normal or sub-normal subjective knee function after anterior cruciate ligament reconstruction. *Arch Orthop Trauma Surg*. 2020;140(9):1231–1239. https://doi.org/10.1007/s00402-020-03436-0.
6. O'Bryan SJ, Giuliano C, Woessner MN, et al. Progressive resistance training for concomitant increases in muscle strength and bone mineral density in older adults: a systematic review and meta-analysis. *Sports Med*. 2022;52(8):1939–1960. https://doi.org/10.1007/s40279-022-01675-2.
7. Kuntze G, Nesbitt C, Whittaker JL, et al. Exercise therapy in juvenile idiopathic arthritis: a systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2018;99(1):178–193. e1. https://doi.org/10.1016/j.apmr.2017.05.030.
8. Chmielewski TL, Hurd WJ, Rudolph KS, Axe MJ, Snyder-Mackler L. Perturbation training improves knee kinematics and reduces muscle co-contraction after complete unilateral anterior cruciate ligament rupture. *Phys Ther*. 2005;85(8):740–754.
9. van der Graaff SJA, Meuffels DE, Bierma-Zeinstra SMA, et al. Why, when, and in which patients nonoperative treatment of anterior cruciate ligament injury fails: an exploratory analysis of the compare trial. *Am J Sports Med*. 2022;50(3):645–651. https://doi.org/10.1177/03635465211068532.
10. Kotsifaki R, Korakakis V, King E, et al. Aspetar clinical practice guideline on rehabilitation after anterior cruciate ligament reconstruction. *Br J Sports Med*. 2023;57(9):500–514. https://doi.org/10.1136/bjsports-2022-106158.
11. Taylor NF, Dodd KJ, Damiano DL. Progressive resistance exercise in physical therapy: a summary of systematic reviews. *Phys Ther*. 2005;85(11):1208–1223.
12. de Bakker CMJ, Knowles NK, Walker REA, Manske SL, Boyd SK. Independent changes in bone mineralized and marrow soft tissues following acute knee injury require dual-energy or high-resolution computed tomography for accurate assessment of bone mineral density and stiffness. *J Mech Behav Biomed Mater*. 2022;127:105091. https://doi.org/10.1016/j.jmbbm.2022.105091.
13. Failla MJ, Logerstedt DS, Grindem H, et al. Does extended preoperative rehabilitation influence outcomes 2 years after acl reconstruction? A comparative effectiveness study between the moon and Delaware-oslo acl cohorts. *Am J Sports Med*. 2016;44(10):2608–2614. https://doi.org/10.1177/0363546516652594.
14. Grindem H, Granan LP, Risberg MA, Engebretsen L, Snyder-Mackler L, Eitzen I. How does a combined preoperative and postoperative rehabilitation programme influence the outcome of acl reconstruction 2 years after surgery? A comparison between patients in the Delaware-oslo acl cohort and the Norwegian national knee ligament registry. *Br J Sports Med*. 2015;49(6):385–389. https://doi.org/10.1136/bjsports-2014-093891.
15. Mages M, Shojaa M, Kohl M, et al. Exercise effects on bone mineral density in men. *Nutrients*. 2021;13(12):4244. https://doi.org/10.3390/nu13124244.
16. Mosti MP, Carlsen T, Aas E, Hoff J, Stunes AK, Syversen U. Maximal strength training improves bone mineral density and neuromuscular performance in young adult women. *J Strength Condit Res*. 2014;28(10):2935–2945. https://doi.org/10.1519/jsc.0000000000000493.
17. Nilsson M, Ohlsson C, Mellstrom D, Lorentzon M. Sport-specific association between exercise loading and the density, geometry, and microstructure of weight-bearing bone in young adult men. *Osteoporos Int*. 2013;24(5):1613–1622. https://doi.org/10.1007/s00198-012-2142-3.
18. Eitzen I, Moksnes H, Snyder-Mackler L, Risberg MA. A progressive 5-week exercise therapy program leads to significant improvement in knee function early after anterior cruciate ligament injury. *J Orthop Sports Phys Ther*. 2010;40(11):705–721. https://doi.org/10.2519/jospt.2010.3345.
19. Zhang X, Huang H, Yu Y, Yang J, Liang Z, Chang C. Impact of whey protein isolate and eccentric training on quadriceps mass and strength in patients with anterior cruciate ligament rupture: a randomized controlled trial. *J Rehabil Med*. 2020;52(3):jrm00035. https://doi.org/10.2340/16501977-2664.
20. Hartigan E, Axe MJ, Snyder-Mackler L. Perturbation training prior to acl reconstruction improves gait asymmetries in non-copers. *J Orthop Res*. 2009;27(6):724–729. https://doi.org/10.1002/jor.20754.
21. Bok D, Rakovac M, Foster C. An examination and critique of subjective methods to determine exercise intensity: the talk test, feeling scale, and rating of perceived exertion. *Sports Med*. 2022;52(9):2085–2109. https://doi.org/10.1007/s40279-022-01690-3.
22. Shi H, Huang H, Ren S, et al. The relationship between quadriceps strength asymmetry and knee biomechanics asymmetry during walking in individuals with anterior cruciate ligament reconstruction. *Gait Posture*. 2019;73:74–79. https://doi.org/10.1016/j.gaitpost.2019.07.151.
23. Ren S, Yu Y, Shi H, et al. Three dimensional knee kinematics and kinetics in acl-deficient patients with and without medial meniscus posterior horn tear during level walking. *Gait Posture*. 2018;66:26–31. https://doi.org/10.1016/j.gaitpost.2018.08.007.
24. Blaty T, Krueger D, Illgen R, et al. Dxa evaluation of femoral bone mineral density and cortical width in patients with prior total knee arthroplasty. *Osteoporos Int*. 2019;30(2):383–390. https://doi.org/10.1007/s00198-018-4682-7.
25. Choi KY, Lee SW, In Y, et al. Dual-energy ct-based bone mineral density has practical value for osteoporosis screening around the knee. *Medicina (Kaunas)*. 2022;58(8):1085. https://doi.org/10.3390/medicina58081085.
26. Borchardt G, Nickel B, Andersen L, et al. Femur and tibia bmd measurement in elective total knee arthroplasty candidates. *J Clin Densitom*. 2022;25(3):319–327. https://doi.org/10.1016/j.jocd.2022.01.004.
27. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International knee documentation committee (ikdc) subjective knee evaluation form, knee injury and osteoarthritis outcome score (koos), knee injury and osteoarthritis outcome score physical function short form (koos-ps), knee outcome survey activities of daily living scale (kos-adl), lysholm knee scoring scale, oxford knee score (oks), western ontario and mcmaster universities osteoarthritis index (womac), activity rating scale (ars), and tegner activity score (tas). *Arthritis Care Res*. 2011;63(S11):S208–S228. https://doi.org/10.1002/acr.20632.
28. Goulet-Pelletier J-C, Cousineau D. A review of effect sizes and their confidence intervals, part {i}: the cohen's d family. *Quantit Methods Psychol*. 2018;14:242–265. https://doi.org/10.20982/tqmp.14.4.p242.
29. Rothrauff BB, Tuan RS. Cellular therapy in bone-tendon interface regeneration. *Organogenesis*. 2014;10(1):13–28. https://doi.org/10.4161/org.27404.
30. Osti L, Papalia R, Del Buono A, Leonardi F, Denaro V, Maffulli N. Surgery for acl deficiency in patients over 50. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(3):412–417. https://doi.org/10.1007/s00167-010-1242-x.
31. Wohl GR, Shymkiw RC, Matyas JR, Kloiber R, Zernicke RF. Periarticular cancellous bone changes following anterior cruciate ligament injury. *J Appl Physiol(1985)*. 2001;91(1):336–342. https://doi.org/10.1152/jappl.2001.91.1.336.

32. Ejerhed L, Kartus J, Nilsen R, Nilsson U, Kullenberg R, Karlsson J. The effect of anterior cruciate ligament surgery on bone mineral in the calcaneus: a prospective study with a 2-year follow-up evaluation. *Arthroscopy*. 2004;20(4):352–359. https://doi.org/10.1016/j.arthro.2004.01.030.
33. Coggan AR, Coyle EF. Reversal of fatigue during prolonged exercise by carbohydrate infusion or ingestion. *J Appl Physiol(1985)*. 1987;63(6):2388–2395. https://doi.org/10.1152/jappl.1987.63.6.2388.
34. Lui PP, Ho G, Shum WT, et al. Inferior tendon graft to bone tunnel healing at the tibia compared to that at the femur after anterior cruciate ligament reconstruction. *J Orthop Sci*. 2010;15(3):389–401. https://doi.org/10.1007/s00776-010-1460-6.
35. Herda AA, Nabavizadeh O. Effect of six weeks of resistance training on bone preservation in older adults: a randomized control trial. *Aging Clin Exp Res*. 2023;35(11):2633–2641. https://doi.org/10.1007/s40520-023-02575-9.
36. Dudley-Javoroski S, Saha PK, Liang G, Li C, Gao Z, Shields RK. High dose compressive loads attenuate bone mineral loss in humans with spinal cord injury. *Osteoporos Int*. 2011;23(9):2335–2346. https://doi.org/10.1007/s00198-011-1879-4.
37. Toth MJ, Tourville TW, Voigt TB, et al. Utility of neuromuscular electrical stimulation to preserve quadriceps muscle fiber size and contractility after anterior cruciate ligament injuries and reconstruction: a randomized, sham-controlled, blinded trial. *Am J Sports Med*. 2020;48(10):2429–2437. https://doi.org/10.1177/0363546520933622.
38. Shi H, Ren S, Huang H, et al. Bilateral alterations in isokinetic strength and knee biomechanics during side-cutting 1 year after unilateral acl reconstruction. *Am J Sports Med*. 2022;50(11):2961–2971. https://doi.org/10.1177/03635465221112940.
39. Kacin A, Drobnic M, Mars T, et al. Functional and molecular adaptations of quadriceps and hamstring muscles to blood flow restricted training in patients with acl rupture. *Scand J Med Sci Sports*. 2021;31(8):1636–1646. https://doi.org/10.1111/sms.13968.
40. Lepley LK, Wojtys EM, Palmieri-Smith RM. Combination of eccentric exercise and neuromuscular electrical stimulation to improve biomechanical limb symmetry after anterior cruciate ligament reconstruction. *Clin BioMech*. 2015;30(7):738–747. https://doi.org/10.1016/j.clinbiomech.2015.04.011.