Neuromuscular Electrical Stimulation Superimposed on Movement Early after ACL Surgery

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ABSTRACT

LABANCA, L., J. E. ROCCHI, L. LAUDANI, R. GUITALDI, A. VIRGULTI, P. P. MARIANI, and A. MACALUSO. Neuromuscular Electrical Stimulation Superimposed on Movement Early after ACL Surgery. *Med. Sci. Sports Exerc.*, Vol. 50, No. 3, pp. 407–416, 2018. **Purpose**: Quadriceps weakness and asymmetrical loading of lower limbs are two major issues after anterior cruciate ligament reconstruction (ACLR). The aim of this study was to evaluate the effectiveness of a 6-wk training protocol involving neuromuscular electrical stimulations (NMES) of the quadriceps muscle superimposed on repeated sit-to-stand-to-sit exercises (STSTS), as an additional treatment to standard rehabilitation, from the 15th to the 60th day after ACLR. **Methods**: Sixty-three ACLR patients were randomly allocated to one of the three treatment groups: NMES superimposed on STSTS (NMES + STSTS), STSTS only, or no additional treatment (NAT) to standard rehabilitation. Maximal isometric strength of the knee extensor and flexor muscles was measured 60 and 180 d after surgery. Asymmetry in lower extremity loading was measured during a sit-to-stand movement at 15, 30, 60, and 180 d after surgery and during a countermovement jump 180 d after surgery by means of two adjacent force platforms placed under each foot. **Results**: The NMES + STSTS participants showed higher muscle strength of the knee extensors, which was accompanied by lower perception of pain and higher symmetry in lower extremity loading compared with STSTS-only and NAT participants after both 60 and 180 d from surgery. Participants in the STSTS-only treatment group showed higher symmetry in lower extremity loading compared with those in the NAT group 60 d after surgery. **Conclusions**: These results suggest that an early intervention based on NMES superimposed to repeated STSTS exercises is effective for recovering quadriceps strength and symmetry in lower extremity loading by the time of return to sport. **Key Words:** PATELLAR TENDON, REHABILITATION, SIT-TO-STAND, SELECTIVE MUSCLE STRENGTHENING, ELECTRICAL STIMULATION, ARTHROGENIC MUSCLE INHIBITION

The first 2 months after surgical reconstruction of the anterior cruciate ligament (ACL) are mainly aimed at recovering knee joint range of motion, managing pain and swelling, and recovering muscle strength (1–3). Interventions to counteract quadriceps muscle inhibition, which is an ongoing reflex inhibition of the knee extensor muscles, have to be started as early as possible in the rehabilitation process (4). The lack of activation leads the muscle to a persistent state of atrophy, which may affect further stages of rehabilitation and long-term recovery as well as the biomechanics of functional movements (5,6). For example, asymmetrical lower limb loading has been observed during various functional movement tasks and in all phases of rehabilitation after ACL reconstruction (6–10). In turn, the lack of loading on the operated limb represents a limitation for quadriceps muscle strength recovery, because the load on the operated limb is an important training stimulus for the recovery of strength (4,11). It is well known that full recovery of muscle strength is possible only when the load applied on the muscle is appropriate. However, it is difficult to create an adequate training stimulus for the quadriceps muscle when patients are unable to fully activate the muscle.

A number of rehabilitation approaches have been used to address this issue. Neuromuscular electrical stimulation (NMES) has been adopted in rehabilitation after ACL reconstruction as a tool to create externally generated muscle contractions for improving muscle strength either as single treatment or in combination with voluntary exercise (12–15). In addition, eccentric exercise has been shown to be an effective intervention for the recovery of muscle strength (16,17). Other interventions such as biofeedback therapy (18) or open and closed kinetic chain exercises (19) have given interesting results. Although these techniques may

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improve the postoperative recovery, a full recovery of quadriceps muscle strength was not achieved in most cases and patients showed deficits at the time of return to sport and for years after surgery.

To address this point, a recent review by Gokeler and colleagues (4) pointed out that motor learning principles should be incorporated into rehabilitation programs in addition to traditional strength training for a complete recovery of muscle strength, thus stressing the importance of enhancing voluntary control of movement.

The objective of this study was to investigate the effectiveness of introducing an additional rehabilitation exercise based on NMES of the quadriceps muscle superimposed on voluntary sit-to-stand-to-sit exercises (STSTS) during the early phase of rehabilitation after ACL reconstruction compared with a traditional rehabilitation protocol alone or a traditional protocol associated with STSTS exercises without NMES. It was hypothesized that the early introduction of voluntary double-limb functional movements, featured by both a concentric and an eccentric contraction of the quadriceps, with the superimposition of NMES, would create an effective training stimulus for the quadriceps starting in the early phase after surgery. This would lead to an earlier recovery of muscle strength, as well as a more symmetrical loading between the two limbs during functional movements, when compared with a traditional rehabilitation protocol alone or a traditional protocol associated with STSTS exercises without NMES. In addition, it was hypothesized that patients undergoing the novel NMES protocol will get better improvements than the other two groups of patients not only in the short term but also in the midterm.

MATERIALS AND METHODS

Patients and Intervention Protocols

The study was carried out on 63 male patients who underwent unilateral isolated ACL reconstruction at Villa Stuart Sports Clinic, FIFA Medical Center of Excellence, in Rome. Inclusion criteria were as follows: age between 18 and 40 yr, ACL reconstruction using ipsilateral autologous bone–patellar tendon–bone graft performed by the same surgeon, physical activity level defined as a Tegner Activity Scale level 7–10 (20), and knee flexion of at least 90° 15 d after surgery, following the same standardized rehabilitation protocol. Exclusion criteria were as follows: previous injury or surgery of the injured knee, concomitant injury to any other knee ligament, and levels of pain in the knee joint that did not allow to carry out an STSTS movement. Patients with associated meniscal repair were allowed to participate in the study.

The same standardized postoperative rehabilitation protocol was administered under supervision of physical therapists 5 $d \cdot wk^{-1}$. Briefly, all patients were asked to wear a postoperative immobilizer immediately after surgery and to bear weight on the second day. During the first 2 wk, the rehabilitation program consisted of continuous passive mobilizations combined with low-frequency and high-volume NMES of the quadriceps muscles to counteract activation failure (21). Isometric straight leg raises were carried out until the end of the first month. Squatting exercises were incorporated within the first 3–4 wk, as well as exercises in water, which involved cycling, walking, and stepping movements. During the second month, strengthening exercises were introduced into rehabilitation. From the third to the sixth months, the rehabilitation program was featured by progressive muscle strengthening and power training together with relearning of specific sport skills.

Patients were randomly assigned to one of the three groups: the NMES + STSTS group, the STSTS-only group, and the no additional treatment group (NAT).

Patients in the NMES + STSTS group (age, 23.2 ± 4.6 yr; stature, 1.80 ± 0.06 m; body mass, 75.9 ± 5.4 kg; Tegner level, 8.3 ± 1.1) received additional treatment based on a number of STSTS tasks with the superimposition of NMES in addition to the standard rehabilitation protocol (Fig. 1).

Training lasted from days 15 to 60 and consisted of five sessions a week. The NMES was given with a wireless portable battery-powered stimulator (Chattanooga Wireless Professional), which produced a rectangular, balanced monophasic pulse in response to a voluntary contraction of the muscle. Self-adhesive electrodes (Compex Dura-Stick plus) were placed on the operated limb over the motor points of vastus lateralis and vastus medialis muscles, which are the two muscle mostly affected by postsurgical atrophy (22). Motor points were identified at the start of each session in accordance with the electrical stimulator user's guide. Two frequencies of the

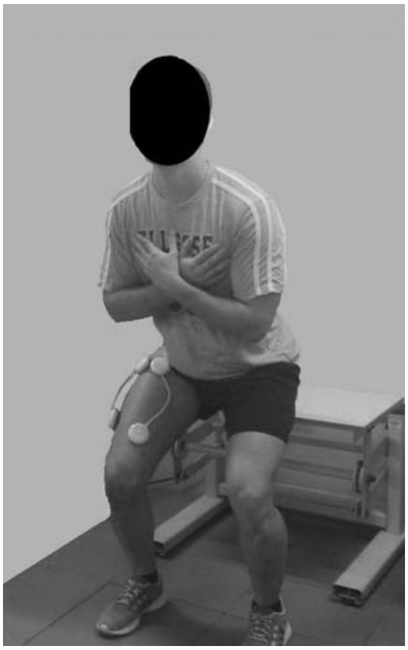

FIGURE 1—One of the patients of the NMES + STSTS group while performing the sit-to-stand phase of the STSTS task. Electrodes were applied over the vastus lateralis and medialis muscles of the operated limb.

NMES were used, 35 and 50 Hz, which were alternately applied at each session. These two frequencies were chosen to stimulate both slow- and fast-twitch muscle fibers while at the same time promoting the highest comfort during stimulation (23). The intensity of stimulation was increased by the trainer at each repetition of each session and throughout all the sessions, in accordance with patient tolerance, to maximize motor unit recruitment (24). Patients were encouraged to voluntarily activate their quadriceps muscle throughout the duration of movement. The maximal intensity given by the stimulator was 120 mA. All of the patients showed an adaptation throughout the sessions and were able to reach this intensity, usually during the last 2–3 wk of treatment.

During the STSTS training, patients were asked to sit and maintain a 90° knee flexion angle. The stimulation lasted 8 s and was initiated by the quadriceps muscle contraction caused by the setting of the electrical stimulator. Patients were asked to contract their quadriceps and, after the onset of the NMES, to perform the STSTS phase in 8 s, and then to rest for 8 s, thus creating a duty cycle of 16 s. The duration of the concentric (sit-to-stand) and the eccentric (stand-to-sit) contractions of the quadriceps muscle varied over the intervention, along with the number of sets and repetitions throughout the program. From the 15th to the 20th day, patients performed three sets of six repetitions. Concentric phase lasted 4 s and eccentric phase lasted 4 s. From the 20th to the 30th day, patients performed three sets of 10 repetitions. Concentric phase lasted 4 s and eccentric phase lasted 4 s. From the 30th to the 45th day, patients performed 3 sets of 10 repetitions. Concentric phase lasted 2 s and eccentric phase lasted 6 s. From the 45th to the 60th day, patients performed three sets of 12 repetitions. Concentric phase lasted 2 s and eccentric phase lasted 6 s.

During the first 2 wk, patients were allowed to start and finish the STSTS task in a sitting position with a lower degree of knee flexion (approximately 60°) for the comfort of the knee joint.

Before each NMES session, patients were asked to warm up on an exercise bicycle at low resistance for 10 min. During the first week of training (15th–20th day), if patients were not able to perform cycling movements, a passive and an active knee joint mobilization was supervised by a physical therapist.

Patients in the STSTS-only group (age, 21.1 ± 3.3 yr; stature, 1.79 ± 0.07 m; body mass, 73.9 ± 9.4 kg; Tegner level, 8.2 ± 1.1) received an additional treatment based on the same type, number of sets, and repetitions of STSTS tasks for the same number of sessions as the NMES + STSTS group, but without superimposition of NMES.

Patients in the NAT group (age, 22.0 ± 3.2 yr; stature, 1.78 ± 0.06 m; body mass, 76.3 ± 9.6 kg; Tegner level, 8.1 ± 1.0) received the standard rehabilitation program as previously described with no additional treatments.

An eligibility investigation was initially conducted on 75 male patients. Sixty-three patients were eligible for the study and were allocated in one of the three groups according to a randomization that was controlled for age and physical activity level. Thirteen patients dropped out of the study. Therefore, 50 patients completed all the rehabilitation and the testing sessions and were included in the data analysis (Fig. 2). The study was approved by the Ethics Committee of the University of Rome "La Sapienza." Informed consent was

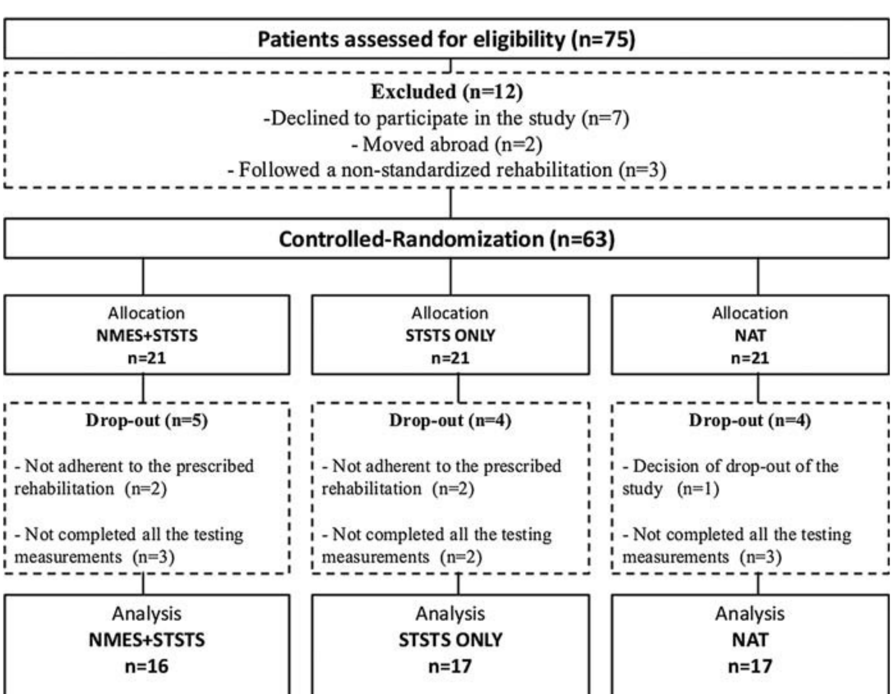

FIGURE 2—Flowchart of the patients recruited for the study.

obtained from the patients, and all the procedures were conducted in accordance with the Declaration of Helsinki.

Assessments

Knee extensor and flexor isometric muscle strength. Patients were asked to perform a maximal voluntary isometric contraction of the knee extensor and flexor muscles at 60 and 180 d after surgery. All participants were tested for maximal voluntary isometric contraction of the knee extensor muscles at 30° and 90° of knee flexion and of the knee flexor muscles at 90° of knee flexion in both limbs. During the assessment, participants were seated on a leg extension machine (Technogym, Forli-Cesena, Italy) for the knee extension maximal voluntary isometric contraction and on a leg curl machine (Technogym) for the knee flexion maximal voluntary isometric contraction. Patients were fastened using three crossing belts on both machines. Muscle force was recorded using a load cell connected to a computerized system unit (MuscleLab; Bosco-System Technologies, Rieti, Italy). The maximal voluntary isometric contraction task consisted of a progressive increase to a maximum force exerted by the leg muscles. Participants were able to follow their performance on a computer screen and were verbally encouraged to achieve a maximum and to maintain that maximum for at least 2 s before relaxing. Maximal voluntary isometric contraction was calculated as the largest 1-s average reached within any single force recording. Peak forces exerted by each limb were recorded. Side-to-side symmetry was quantified for peak forces using the limb symmetry index, which was calculated as the ratio between the involved and uninvolved limb expressed as a percentage. Absolute force was calculated by normalizing peak forces recorded during all maximal voluntary isometric contractions to the body weight of each patient. The side-to-side symmetry and absolute force values were used for further analysis.

Knee joint pain. Patients were asked to verbally quantify pain at the knee joint during the maximal voluntary isometric contractions by means of an 11 point (0–10) numerical rating scale. The numerical rating scale was numerically graded at each unit and additional explanatory information was reported as follows: 0, no pain; 2, light pain; 4, moderate pain; 6, high pain; 8, very high pain; and 10, the worst imaginable pain.

Symmetry of lower extremity loading. Patients were tested by recording ground reaction force on two force platforms during a sit-to-stand movement at 15, 30, 60, and 180 d after surgery and during a countermovement jump at 180 d after surgery. The sit-to-stand task was performed as described in the study by Laudani et al. (8) and consisted of rising from a seat as fast as possible. The height of the seat was adjusted to the shank length to obtain a 90° angle at the knee joint. The participants were asked to keep their trunk in a vertical position, their arms held across the chest, and their feet shoulder-width apart. Participants were verbally instructed to stand up as fast as possible and maintain the upright position for 5 s. A total of three sit-to-stand trials with 1-min rest in between them were performed for each session. The countermovement jump was performed as described in the study by Labanca et al. (6). Briefly, patients were asked to stand in an upright position and maintain their hands on their hips during performance of the whole movement. They were asked to quickly squat with knees flexed to approximately 90° and then jump immediately as high as possible without pausing. A total of three countermovement jump trials with 1-min rest in between were performed. Ground reaction forces during the sit-to-stand and the countermovement jump were measured by means of two, six-component force platforms (KISTLER, model 9281 B; Winterthur, Switzerland; 100-Hz sampling frequency), which were positioned below each foot. Vertical components of the ground reaction force were offline filtered using a digital, low-pass, second-order, Butterworth filter with a cutoff frequency set at 15 Hz. Peak values of the vertical components of the ground reaction force of the seat-off instant for the sit-to-stand and the highest before the take-off instant for the countermovement jump were calculated for both limbs. Side-to-side symmetry was quantified for peak forces using the limb symmetry index. The mean limb symmetry index of the three trials was calculated and was used for further analysis.

Anthropometric measurements. Thigh and knee circumferences were measured on both limbs at 15, 30, 60, and 180 d after surgery. Thigh circumference was measured with a tape measure placed perpendicular to the long axis of the femur around the midthigh, which was identified between the superior pole of the patella and the anterior inferior iliac spine. Knee circumference was measured with the knee joint in full extension at the middle of the patella. All the measurements were performed by the same examiner who had 4 yr of clinical experience and was confident with all the measurements. Circumferences were measured on both limbs. The difference between the operated and healthy limb was calculated and used for further analysis.

Randomization and Blinding

The allocation to each group was done by one of the authors who was unaware of patients' identity. The allocation was controlled for age and physical activity level to guarantee a homogeneous distribution between groups. Patients knew that they were involved in an experimental study, but they were unaware of the other experimental groups of the study. Physical therapists were informed about the two intervention protocols, which were conducted by two experimenters at the start of each physical therapy session. Assessments and data analyses were blinded. The assessor was blinded on patients' allocation and assigned a numerical code to all of the recorded tests, which were blindly processed by another of the investigators.

Sample Size and Statistical Power

Sample size was *a priori* calculated with a significance level of $\alpha = 0.05$ and a power of 90% on the basis of data of a preliminary pilot investigation on 12 patients who were

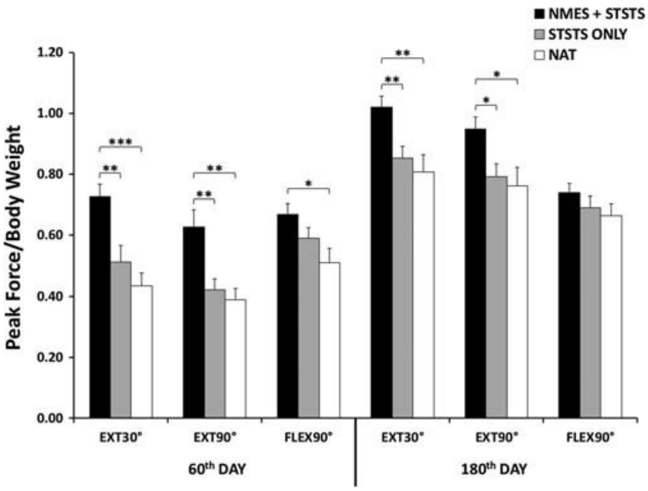

FIGURE 3—Peak forces normalized by body weight during maximal voluntary isometric contraction of knee extensor muscles at 30° (EXT30°) and 90° (EXT90°), and knee flexor muscles (FLEX90°) 60 and 180 d after surgery in the operated limb. Data are reported as mean and SE. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

randomly assigned to one of the three groups (NMES + STSTS, STSTS only, NAT). Effect size was calculated on the basis of the mean limb symmetry index of peak forces recorded during maximal voluntary isometric contraction of knee extensor muscles 60 d after surgery at 30°, which was 75% for the first group, 62% for the second, and 61% for the third. A minimum of 16 patients for each group were required for the study. Additional patients were recruited to allow for dropouts.

Data Analysis and Statistics

Descriptive statistics were used to summarize demographic data. The Shapiro–Wilk test was used to test the distribution of all variables. A two-way repeated-measures ANOVA was used to analyze the effect of rehabilitation treatment and time on absolute knee extensor and flexor muscles force and limb symmetry index of peak forces recorded during maximal voluntary isometric contractions and the sit-to-stand test, and on anthropometric variables. A one-way ANOVA was used to look at the differences between the three groups for the limb symmetry index of peak force recorded during the countermovement jump. If the main effect F value was significant, a Student's t-test with Bonferroni correction was used to locate the significant differences. The Kruskal–Wallis ANOVA and chi-square test were used to investigate the differences between the three groups for pain scores recorded during all of the maximal voluntary isometric contractions. All analyses were performed using SPSS version 20.0 (SPSS, Inc., Chicago, IL).

RESULTS

Knee extensor and flexor isometric muscles strength. Mean values of absolute force are reported in Figure 3. The ANOVA showed an effect of both treatment and time on absolute force of knee extensor muscles of the operated limb at 30° (treatment: $F = 17.194$, $P < 0.001$; time: $F = 84.450$, $P < 0.001$) and 90° (treatment: $F = 10.435$, $P < 0.01$; time, $F = 94.321$, $P < 0.001$). The ANOVA also showed an effect of time ($F = 21.977$, $P < 0.001$) on absolute force of knee flexor muscles of the operated limb. *Post hoc* analyses demonstrated that patients in the NMES + STSTS group showed a significantly higher knee extensor muscle strength when compared with patients in the other two groups at both 30° and 90°, at 60 and 180 d after surgery. Patients in the NMES + STSTS group showed significantly higher strength of knee flexor muscles than did the NAT group at 60 d after surgery. All of the groups showed a significant increase in knee extensor muscle strength from 60 to 180 d after surgery.

In Figure 4, mean values of limb symmetry index of peak forces recorded during maximal voluntary isometric contraction of knee extensor muscles are reported. The ANOVA showed an effect of treatment ($F = 11.429$, $P < 0.001$) and time ($F = 88.437$, $P < 0.001$) on the symmetry index of knee extensor muscles at 30°. An effect of treatment ($F = 12.631$, $P < 0.01$) and time ($F = 172.551$, $P < 0.001$) was also found for the limb symmetry index of knee extensor muscles at 90°. All patients showed a significantly higher limb symmetry index at 180 d after surgery when compared with 60 d, with patients in the NMES + STSTS group showing a significantly higher limb symmetry index compared with the other two groups at both 60 and 180 d after surgery.

The limb symmetry index of knee flexor muscle strength was 83.7% ± 10.9% in the NMES + STSTS group, 82.2% ± 17.9% in the STSTS-only group, and 79.3% ± 13.7% in the NAT group at 60 d after surgery, and 98.7% ± 14.1% in the NMES + STSTS group, 96.3% ± 16.9% in the STSTS-only group, and 98.5% ± 13.2% in the NAT group at 180 d after surgery. The ANOVA showed an effect of time ($F = 40.326$, $P < 0.001$). *Post hoc* analysis showed in all groups a

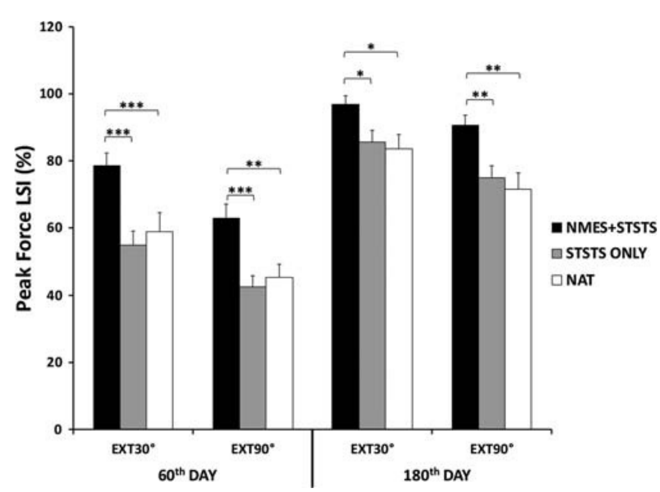

FIGURE 4—Limb symmetry index (LSI) of peak forces recorded during maximal voluntary isometric contraction of knee extensor muscle at 30° and 90° at 60 and 180 d after surgery. Data are reported as mean and SE. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

significantly higher limb symmetry index at 180 d compared with 60 d after surgery.

Knee joint pain. The Kruskal–Wallis ANOVA did not reveal any significant differences between groups. However, a further analysis was conducted on pain scores divided into two categories: "pain >4" and "pain <4." The score of 4 was selected because it stands for "moderate" knee pain. Evidence of a relationship between rehabilitation treatment and pain to the knee joint during maximal voluntary isometric contraction of knee extensor muscles was found at 30° at 60 d after surgery (chi-square = 6.724, $df = 2$, $P < 0.05$). Figure 5 shows the percentage of pain referred to the knee joint while performing maximal voluntary isometric contraction of knee extensor muscles at 30° and 90° at 60 and 180 d after ACL surgery.

Symmetry of lower extremity loading. Figure 6 shows mean values of the limb symmetry index of peak forces recorded during the sit-to-stand. The ANOVA showed a main effect of treatment ($F = 8.768$, $P < 0.01$) and time ($F = 67.380$, $P < 0.001$) on limb symmetry index of peak forces. The *post hoc* analysis showed that patients in the NMES + STSTS group had a significantly higher limb symmetry index in comparison with patients of the STSTS-only group at 60 d after surgery, and in comparison with the NAT group at 30, 60, and 180 d after surgery. All the groups showed significant differences between 30-, 60-, and 180-d assessments, thus showing an improvement over time. Only patients in the NMES group had a significantly ($P < 0.001$) higher limb symmetry index at 30 d compared with 15 d after surgery.

Mean value of the limb symmetry index calculated for peak forces recorded during the countermovement jump was 92.2% ± 4.8% for patients in the NMES + STSTS group, 87.7% ± 7.3% for patients in the STSTS-only group, and 83.1% ± 10.7% for patients in the NAT group. The ANOVA

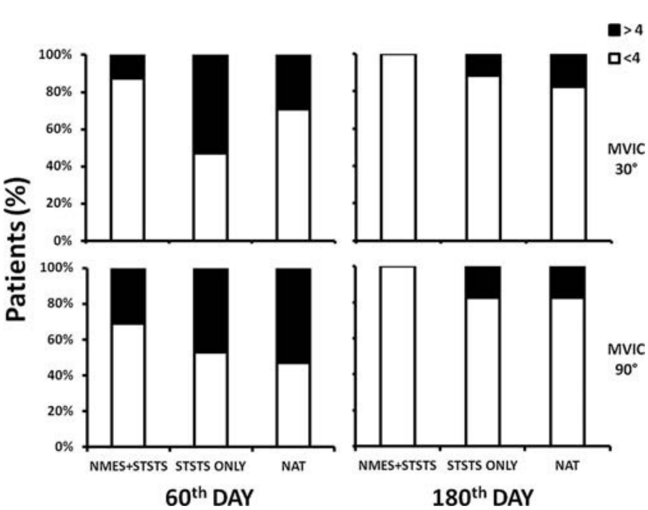

FIGURE 5—Percentage of patients in the NMES + STSTS, STSTS-only, and NAT groups who referred pain >4 or <4 while performing maximal voluntary isometric contraction of knee extensor muscles at 30° (*above*) and 90° (*below*), 60 d (on the *left*) and 180 d (on the *right*) days after surgery.

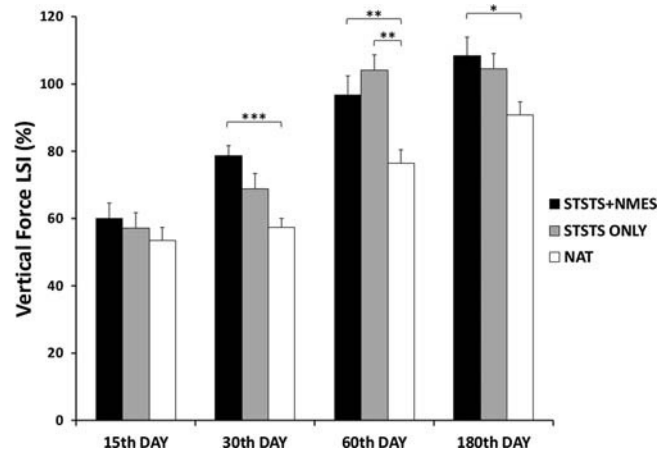

FIGURE 6—Limb symmetry index (LSI) of peak vertical forces recorded during the sit-to-stand test at 15, 30, 60, and 180 d after surgery. Data are reported as mean and SE. *P < 0.05, **P < 0.01, ***P < 0.001.

showed a main effect of treatment ($F = 4.688$, $P < 0.05$) on the limb symmetry index of peak forces during countermovement jump. *Post hoc* analysis showed that patients in the NMES group had a significantly ($P < 0.01$) higher limb symmetry index in comparison with patients in the NAT group.

Anthropometric measurements. The ANOVA showed an effect of treatment ($F = 5.941$, $P < 0.05$) and time ($F = 24.581$, $P < 0.001$) on between-limb differences of the thigh, and an effect of time for the knee joint ($F = 101.490$, $P < 0.001$). The *post hoc* analysis showed that patients in the NMES + STSTS group had a significantly ($P < 0.001$) lower between-limb difference of thigh circumference in comparison with patients in the STSTS-only and NAT groups at 30 d (−1.8 ± 1.3, −3.3 ± 1.4, and −3.8 ± 1.7 cm), 60 d (−0.5 ± 0.8, −2.5 ± 1.1, and −2.3 ± 1.8 cm), and 180 d (0 ± 0.6, −1.1 ± 0.9, and −1.5 ± 1.1 cm) after surgery. No differences were found between the STSTS-only and NAT groups. All the groups showed significant differences across the four assessment time points for both thigh and knee joint between-limb differences, thus showing an improvement across time.

DISCUSSION

The main finding of this study was that a novel early intervention based on NMES superimposed on a number of STSTS movements, in addition to a traditional rehabilitation protocol, has been shown to be more effective than a traditional rehabilitation protocol alone or a traditional protocol associated with functional exercises without NMES, in fully recovering quadriceps muscle strength after ACL reconstruction using bone–patellar tendon–bone graft. Moreover, adding either NMES + STSTS or STSTS only to traditional rehabilitation in the first 2 months after surgery was effective for the recovery of symmetrical loading on lower limbs while performing functional movements.

Patients in the NMES + STSTS group showed higher quadriceps muscle strength than did the other two groups from the 60th day after surgery onward, which corresponded to the end of the intervention protocol. Remarkably, NMES patients were still the strongest patients of the study at 6 months after surgery, thus showing that an early intervention is effective for the midterm recovery of quadriceps muscle strength. This was supported by the observation that only patients in the NMES group reached values of symmetry near 100%, both at 30° and 90° knee angle. It is important to point out that the other two groups reached values of symmetry lower than 85%, which is the threshold suggested by previous studies to guarantee a safe return to sport activities (25). These results could be explained by the fact that strengthening exercises in the early phases after surgery do not create an effective training stimulus for the quadriceps muscle because of two main factors: first, it is not possible to overload the operated knee joint with high external loads, and second, there is an ongoing arthrogenic muscle inhibition. Because patients are not able to fully activate quadriceps muscle, it is difficult to achieve high-intensity quadriceps muscle contractions. It is well known from neuromuscular physiological principles that if a muscle is atrophied and not used, it progressively loses its function due to molecular alterations (26). The longer a muscle is left in an atrophy condition, the longer it takes for an atrophy reversal. This point is particularly important in ACL patients because atrophy is not only due to molecular alterations related to disuse and immobilization but also due to neural factors (27). Therefore, it is not surprising that long-term impairments in quadriceps muscle function are frequently reported after ACL reconstruction (4).

It is difficult to compare the results of our study with those of previous investigations, because many factors vary, such as type of surgical graft for ACL reconstruction, time of rehabilitation in which NMES is applied, pretreatment and posttreatment assessments, NMES frequency and intensity used, and how NMES is applied, that is, alone, superimposed to a voluntary contraction of the muscle or in combination with exercises (13,15,28–31). It is not surprising that reviews on the topic claim inconsistencies in the application of NMES as well as the need for evidence-based structured approaches (21,32,33). It is also crucial to consider that ACL rehabilitation has shown a continuous evolution through the course of time.

To the best of the authors' knowledge, NMES has never been superimposed on a functional voluntary movement, such as the STSTS, starting from as early as 15 d after ACL reconstruction, for the purpose of evaluating its effects on muscle strength and asymmetrical lower extremity loading. It has been shown that NMES leads to an improvement in maximal strength (34,35), but often does not translate into an improvement in functional movements (14,17,36), perhaps because of the synchronous motor unit recruitment that is not achieved in real functional movements (24). The results of the present study (e.g., higher symmetry of both maximal strength and lower extremity loading in NMES + STSTS participants compared with STSTS-only and NAT participants) show that the superimposition of NMES to a functional movement may have addressed the issue. Moreover, it is likely that not only has NMES superimposed on STSTS led to muscle hypertrophy, but also it has improved the voluntary control of the muscle activation during a functional movement.

There are many other reasons to believe that the NMES superimposed on the STSTS task adopted in this study was successful, as it addressed many of the issues related to knee extensor muscles training in the early phase after ACL reconstruction. First, it is a simple task. Perhaps it is the only double-limb functional movement that patients are able to perform 15 d after surgery. Second, it is a safe movement. It is a closed-kinetic chain movement and no external loads were applied. Thus, patients could focus on the correct execution of the movement and exercise intensity was increased by increasing the intensity of stimulation and the number of repetitions. Third, since the 15th day after surgery, NMES enabled a selective muscle strengthening together with the activation of both slow- and fast-twitch motor units by adopting two specific stimulation frequencies. Otherwise, it would not have been possible to selectively strengthen atrophied muscles and activate fast-twitch motor units, because high-intensity or fast exercises are not possible at this stage of rehabilitation owing to arthrogenic muscle inhibition. Fourth, the STSTS movement includes an eccentric contraction of the quadriceps during the stand-to-sit phase, the duration of which was progressively increased throughout the protocol. It has been shown that eccentric exercise is one of the best ways to increase muscle strength after ACL reconstruction (4). However, without the superimposition of NMES, it would have been impossible to create an effective eccentric exercise as early as 15 d after surgery. Patients in the STSTS-only group performed the same exercise and thus the same eccentric contraction without the superimposition of the NMES and did not improve their strength as much as those in the NMES + STSTS group. Lastly, it is also a safe and effective exercise for the patellar tendon, which is damaged by the surgical graft during the ACL reconstruction procedure. It has been shown that eccentric exercise is effective for the healing of damaged tendons (37) and gives an effective load to the tendon. In addition, it is also known that muscle and tendon adaptations are related to each other (38). Thus, the early recovery of quadriceps muscle function allowed for an adequate load to the patellar tendon for healing.

It was a unique finding that patients in the NMES group had less knee joint pain, or no pain at all with respect to the other two groups during the two maximal voluntary isometric contraction assessments of knee extensor muscles considering that it is a high-demanding and stressful task for the knee joint extensor mechanism. The pain noted while performing this type of task after ACL reconstruction is mainly located anteriorly in the knee joint and is due to a variety of surgical-related consequences: deficit of knee joint full extension, patellar tendon healing, inflammation, or tendinopathy. In our study, the full extension was recovered within the first 2 months and none of the patients showed knee extension deficits 6 months after surgery. However, pain to the knee joint was still noted by 20% of patients at this time point. It is likely that pain was mainly related to patellar tendon damage rather than to knee extension deficits. Although pain mechanisms related to tendon are extremely complex (39), the observation of a reduced knee joint pain could be related to the healing process of the patellar tendon and the decrease in tendon inflammation.

It should also be noted that patients of the NMES + STSTS group had less pain than did the other two groups during maximal voluntary isometric contraction of knee extensor muscles, particularly at the knee angle of 30°. This result may be due to two main reasons: first, performing exercises at 30° knee angle is biomechanically less stressful on the extensor mechanism and on the patellar tendon than at 90°, and second, muscular and tendon adaptations are coordinated and dependent on the joint angle at which they are trained (40). Because the STSTS exercise stopped at 90° of knee flexion, when patients were asked to sit before starting the next repetition, it is likely that the beneficial effects of exercise were less evident as the patellar tendon was not "trained" at this angle.

Both the intervention protocols of this study, NMES + STSTS and STSTS only, were effective for the recovery of symmetry in lower extremity loading during functional movement during the first 2 months. More interestingly, the symmetry was maintained at 6 months after surgery, which was 4 months after the end of the protocol, both during an easy task like the sit-to-stand and a higher-demanding task like the countermovement jump. This is an important result because it means that adding simple double-limb functional movements in the early rehabilitation phase helps in the recovery of symmetry, which is essential in light of the deleterious effect of asymmetrical loading or lack of early weight bearing (41). In addition, the symmetry in lower extremity loading is not fully dependent on the symmetry in quadriceps muscle strength. This is supported by the fact that patients of the STSTS-only group showed a perfect symmetry in lower extremity loading but poor results in muscle strength assessments. Previous literature also supports this finding because it has been shown that the asymmetry in lower extremity loading early after surgery was predictive of long-term asymmetry more than asymmetry in knee extensor muscles strength (6). Thus, it could be argued that long-term asymmetrical loading during functional movements after ACL reconstruction may be related to the lack of a motor learning principles–based training in the early rehabilitation phase.

Some limitations need to be mentioned for this study. NMES produces muscle activation that is not physiological, and in this study, it was applied to a voluntary movement in a nonphysiological manner. For example, NMES at a high frequency aimed at activating high-threshold motor units was superimposed during a slow movement. Surely, this condition is not physiological. However, it is the only way to activate high-threshold motor units without overloading the knee joint or performing unsafe exercises. Another limitation of this study was that thigh muscle volume and knee joint swelling were assessed by measuring thigh and knee circumferences using a tape, which is not a direct measure of muscle volume and joint swelling. Future studies should investigate the effects of these treatments by using more direct measurements, such as magnetic resonance imaging. Only male patients were recruited for this study, which is another limitation. Because neuromuscular adaptations to strength training are different between male and female patients, future studies should investigate the effects of the novel training interventions proposed in the present study also in female patients. It should also be mentioned that in this study, no negative control group of healthy participants was included. This would have provided normative values of some parameters, as thigh and knee circumferences. In addition, the use of limb symmetry index has been frequently questioned as it may conceal results on the functional status of the operated limb, because neuromuscular alterations, such as atrophy, have been observed also in the nonoperated limb. Therefore, the ratio between the operated and the nonoperated limb may overestimate the function of the operated limb. This may not apply to the sit-to-stand task adopted in this study, because the objective was not to assess function of the single limb but the ability to manage the load between the two limbs. Lastly, the protocol proposed in this study requires the continuous monitoring of the exercises by a trainer or a physical therapist who is familiar with the structured use of NMES and cannot be self-applied by the patients themselves. Although this point may be a limitation from a general use perspective, it is also a strength of the protocol, because it guarantees the quality and effectiveness of the training that was carried out.

In conclusion, to the best of the authors' knowledge, this is the first study in which NMES, superimposed to a functional movement, was adopted in ACL-reconstructed patients as early as 15 d after surgery. This early intervention was shown to be effective to fight quadriceps muscle atrophy early after surgery and completely restore quadriceps muscle strength before the time of return to sport activities. In addition, the results of this study show that it is possible to restore symmetry in lower extremity loading by introducing double-limb functional movements early after surgery. The recovery of strength and symmetry in lower limb loading may represent an important factor for the prevention of further injuries on both the operated and the healthy limb. On the basis of these findings, the use of NMES in the early rehabilitation phase after ACL reconstruction should be revised together with the commonly used nonfunctional strengthening exercises. Future studies should monitor the effects of such an early intervention on strength and functional outcomes in the long term and when returning to sport activities. In addition, further investigations are needed to understand which physiological mechanisms underpin the improvements in muscle strength and lower limb loading.

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REFERENCES

1. Adams D, Logerstedt DS, Hunter-Giordano A, Axe MJ, Snyder-Mackler L. Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression. *J Orthop Sports Phys Ther*. 2012;42(7):601–14.
2. Palmieri-Smith RM, Thomas AC, Wojtys EM. Maximizing quadriceps strength after ACL reconstruction. *Clin Sports Med*. 2008;27(3): 405–24.
3. Wilk KE, Macrina LC, Cain EL, Dugas JR, Andrews JR. Recent advances in the rehabilitation of anterior cruciate ligament injuries. *J Orthop Sports Phys Ther*. 2012;42(3):153–71.
4. Gokeler A, Bisschop M, Benjaminse A, Myer GD, Eppinga P, Otten E. Quadriceps function following ACL reconstruction and rehabilitation: implications for optimisation of current practices. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(5):1163–74.
5. Labanca L, Laudani L, Casabona A, Menotti F, Mariani PP, Macaluso A. Early compensatory and anticipatory postural adjustments following anterior cruciate ligament reconstruction. *Eur J Appl Physiol*. 2015;115(7):1441–51.
6. Labanca L, Laudani L, Menotti F, et al. Asymmetrical lower extremity loading early after anterior cruciate ligament reconstruction is a significant predictor of asymmetrical loading at the time of return to sport. *Am J Phys Med Rehab*. 2016;95(4):248–55.
7. Gokeler A, Hof AL, Arnold MP, Dijkstra PU, Postema K, Otten E. Abnormal landing strategies after ACL reconstruction. *Scand J Med Sci Sports*. 2010;20(1):e12–9.
8. Laudani L, Giombini A, Mariani PP, Pigozzi F, Macaluso A. Application of the sit-to-stand movement for the early assessment of functional deficits in patients who underwent anterior cruciate ligament reconstruction. *Am J Phys Med Rehabil*. 2014;93(3): 189–99.
9. Lewek M, Rudolph K, Axe M, Snyder-Mackler L. The effect of insufficient quadriceps strength on gait after anterior cruciate ligament reconstruction. *Clin Biomech (Bristol, Avon)*. 2002;17(1): 56–63.
10. Neitzel JA, Kernozek TW, Davies GJ. Loading response following anterior cruciate ligament reconstruction during the parallel squat exercise. *Clin Biomech (Bristol, Avon)*. 2002;17(7):551–4.
11. Chmielewski TL. Asymmetrical lower extremity loading after ACL reconstruction: more than meets the eye. *J Orthop Sports Phys Ther*. 2011;41(6):374–6.
12. Delitto A, Rose SJ, McKowen JM, Lehman RC, Thomas JA, Shively RA. Electrical stimulation versus voluntary exercise in strengthening thigh musculature after anterior cruciate ligament surgery. *Phys Ther*. 1988;68(5):660–3.
13. Fitzgerald GK, Piva SR, Irrgang JJ. A modified neuromuscular electrical stimulation protocol for quadriceps strength training following anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther*. 2003;33(9):492–501.
14. 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 (Bristol, Avon)*. 2015;30(7):738–47.
15. Snyder-Mackler L, Delitto A, Stralka SW, Bailey SL. Use of electrical stimulation to enhance recovery of quadriceps femoris muscle force production in patients following anterior cruciate ligament reconstruction. *Phys Ther*. 1994;74(10):901–7.
16. Gerber JP, Marcus RL, Dibble LE, Greis PE, Burks RT, LaStayo PC. Effects of early progressive eccentric exercise on muscle structure after anterior cruciate ligament reconstruction. *J Bone Joint Surg Am*. 2007;89(3):559–70.
17. Lepley LK, Wojtys EM, Palmieri-Smith RM. Combination of eccentric exercise and neuromuscular electrical stimulation to improve quadriceps function post-ACL reconstruction. *Knee*. 2015;22(3):270–7.
18. Draper V, Ballard L. Electrical stimulation versus electromyographic biofeedback in the recovery of quadriceps femoris muscle function following anterior cruciate ligament surgery. *Phys Ther*. 1991;71(6):455–61.
19. Mikkelsen C, Werner S, Eriksson E. Closed kinetic chain alone compared to combined open and closed kinetic chain exercises for quadriceps strengthening after anterior cruciate ligament reconstruction with respect to return to sports: a prospective matched follow-up study. *Knee Surg Sports Traumatol Arthrosc*. 2000;8(6): 337–42.
20. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res*. 1985;(198):43–9.
21. Spector P, Laufer Y, Elboim Gabyzon M, Kittelson A, Stevens Lapsley J, Maffiuletti NA. Neuromuscular electrical stimulation therapy to restore quadriceps muscle function in patients after orthopaedic surgery: a novel structured approach. *J Bone Joint Surg Am*. 2016;98(23):2017–24.
22. Konishi Y, Fukubayashi T, Takeshita D. Mechanism of quadriceps femoris muscle weakness in patients with anterior cruciate ligament reconstruction. *Scand J Med Sci Sports*. 2002;12(6):371–5.
23. Glaviano NR, Saliba S. Can the use of neuromuscular electrical stimulation be improved to optimize quadriceps strengthening? *Sports Health*. 2016;8(1):79–85.
24. Maffiuletti NA. Physiological and methodological considerations for the use of neuromuscular electrical stimulation. *Eur J Appl Physiol*. 2010;110(2):223–34.
25. Myer GD, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior cruciate ligament reconstruction: criteria-based progression through the return-to-sport phase. *J Orthop Sports Phys Ther*. 2006;36(6):385–402.
26. Jackman RW, Kandarian SC. The molecular basis of skeletal muscle atrophy. *Am J Physiol Cell Physiol*. 2004;287(4):C834–43.
27. Hopkins JT, Ingersoll CD. Arthrogenic muscle inhibition: a limiting factor in joint rehabilitation. *J Sport Rehabil*. 2000;9:135–59.
28. Eriksson E, Häggmark T. Comparison of isometric muscle training and electrical stimulation supplementing isometric muscle training in the recovery after major knee ligament surgery. A preliminary report. *Am J Sports Med*. 1979;7(3):169–71.
29. Feil S, Newell J, Minogue C, Paessler HH. The effectiveness of supplementing a standard rehabilitation program with superimposed neuromuscular electrical stimulation after anterior cruciate ligament reconstruction: a prospective, randomized, single-blind Study. *Am J Sports Med*. 2011;39(6):1238–47.
30. Hasegawa S, Kobayashi M, Arai R, Tamaki A, Nakamura T, Moritani T. Effect of early implementation of electrical muscle stimulation to prevent muscle atrophy and weakness in patients after anterior cruciate ligament reconstruction. *J Electromyogr Kinesiol*. 2011;21(4):622–30.
31. Snyder-Mackler L, Ladin Z, Schepsis AA, Young JC. Electrical stimulation of the thigh muscles after reconstruction of the anterior cruciate ligament. Effects of electrically elicited contraction of the quadriceps femoris and hamstring muscles on gait and on strength of the thigh muscles. *J Bone Joint Surg Am*. 1991;73(7):1025–36.
32. Herzig D, Maffiuletti NA, Eser P. The application of neuromuscular electrical stimulation training in various non-neurologic patient populations: a narrative review. *PM R*. 2015;7(11):1167–78.
33. Kim K, Croy T, Hertel J, Saliba S. Effects of neuromuscular electrical stimulation after anterior cruciate ligament reconstruction

on quadriceps strength, function, and patient-oriented outcomes: a systematic review. *J Orthop Sports Phys Ther*. 2010;40(7):383–91.
34. Hortobágyi T, Maffiuletti NA. Neural adaptations to electrical stimulation strength training. *Eur J Appl Physiol*. 2011;111(10):2439–49.
35. Vanderthommen M, Duchateau J. Electrical stimulation as a modality to improve performance of the neuromuscular system. *Exerc Sport Sci Rev*. 2007;35(4):180–5.
36. Mathes S, Lehnen N, Link T, Bloch W, Mester J, Wahl P. Chronic effects of superimposed electromyostimulation during cycling on aerobic and anaerobic capacity. *Eur J Appl Physiol*. 2017;117(5):881–92.
37. Enwemeka CS. Functional loading augments the initial tensile strength and energy absorption capacity of regenerating rabbit Achilles tendons. *Am J Phys Med Rehab*. 1992;71(1):31–8.
38. Miller BF, Olesen JL, Hansen M, et al. Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. *J Physiol*. 2005;567(Pt 3):1021–33.
39. Kjaer M. Role of extracellular matrix in adaptation of tendon and skeletal muscle to mechanical loading. *Physiol Rev*. 2004;84(2): 649–98.
40. Kubo K, Ohgo K, Takeishi R, et al. Effects of isometric training at different knee angles on the muscle-tendon complex in vivo. *Scand J Med Sci Sports*. 2006;16(3):159–67.
41. Wright RW, Preston E, Fleming BC, et al. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part II: open versus closed kinetic chain exercises, neuromuscular electrical stimulation, accelerated rehabilitation, and miscellaneous topics. *J Knee Surg*. 2008;21(3):225–34.