Research Report

Early Neuromuscular Electrical Stimulation to Improve Quadriceps Muscle Strength After Total Knee Arthroplasty: A Randomized Controlled Trial

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Background. The recovery of quadriceps muscle force and function after total knee arthroplasty (TKA) is suboptimal, which predisposes patients to disability with increasing age.

Objective. The purpose of this investigation was to evaluate the efficacy of quadriceps muscle neuromuscular electrical stimulation (NMES), initiated 48 hours after TKA, as an adjunct to standard rehabilitation.

Design. This was a prospective, longitudinal randomized controlled trial.

Methods. Sixty-six patients, aged 50 to 85 years and planning a primary unilateral TKA, were randomly assigned to receive either standard rehabilitation (control) or standard rehabilitation plus NMES applied to the quadriceps muscle (initiated 48 hours after surgery). The NMES was applied twice per day at the maximum tolerable intensity for 15 contractions. Data for muscle strength, functional performance, and self-report measures were obtained before surgery and 3.5, 6.5, 13, 26, and 52 weeks after TKA.

Results. At 3.5 weeks after TKA, significant improvements with NMES were found for quadriceps and hamstring muscle strength, functional performance, and knee extension active range of motion. At 52 weeks, the differences between groups were attenuated, but improvements with NMES were still significant for quadriceps and hamstring muscle strength, functional performance, and some self-report measures.

Limitations. Treatment volume was not matched for both study arms; NMES was added to the standard of care treatment. Furthermore, testers were not blinded during testing, but used standardized scripts to avoid bias. Finally, some patients reached the maximum stimulator output during at least one treatment session and may have tolerated more stimulation.

Conclusions. The early addition of NMES effectively attenuated loss of quadriceps muscle strength and improved functional performance following TKA. The effects were most pronounced and clinically meaningful within the first month after surgery, but persisted through 1 year after surgery.

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Osteoarthritis (OA) is a chronic degenerative joint disease that compromises the quality of life of more than 50 million Americans.[1] To alleviate pain and disability associated with knee OA, more than 687,000 total knee arthroplasties (TKAs) are performed each year in the United States.[2] Future projections suggest that by the year 2030, 3.48 million TKAs will be performed yearly.[3] Although TKA reliably reduces pain and improves function in older adults with knee OA, the recovery of quadriceps muscle force and function is suboptimal and predisposes patients to disability with increasing age.[4–6]

One month after TKA, quadriceps muscle strength drops 50% to 60% of preoperative levels, despite the initiation of rehabilitation within 48 hours after surgery.[7–9] Even 6 to 13 years after surgery, quadriceps muscle weakness persists in people with TKA compared with people who are healthy.[10] Lower-extremity muscle weakness, particularly in the quadriceps muscle, has profound functional consequences, especially in older individuals. Quadriceps muscle weakness has been associated with decreased gait speed, balance, stair-climbing ability, and ability to rise from a seated position, as well as with an increased risk for falls.[11–17]

Effective rehabilitation strategies to address quadriceps muscle weakness after TKA should target the sources underlying early quadriceps muscle weakness. One month after TKA, impairments in quadriceps muscle strength are predominantly due to deficits in voluntary activation (also referred to as "reflex inhibition"), but also are influenced, to a lesser degree, by muscle atrophy.[7] Although the neurophysiologic mechanisms for quadriceps muscle voluntary activation deficits are not fully understood, spinal reflex activity from swelling or pain in the knee joint may alter afferent input from the injured joint and result in diminished efferent motor drive to the quadriceps muscle that reduces muscle strength. Neuromuscular electrical stimulation (NMES) offers an innovative approach to potentially mitigate quadriceps muscle voluntary activation deficits and prevent muscle atrophy early after surgery to restore normal quadriceps muscle function more effectively than voluntary exercise alone.[18–21] Severe voluntary activation deficits may limit improvements in muscle strength in response to rehabilitation that utilizes voluntary exercise,[22] possibly because of the inability to generate muscle contractions of sufficient intensity to promote strength gains. Neuromuscular electrical stimulation has the potential to override voluntary activation deficits and may even help re-educate the quadriceps muscle to contract normally. Yet, previous investigations of NMES application in an outpatient setting (2–3 times per week) have resulted in conflicting evidence in favor of[20–23] and against[24,25] benefits of treatment. Early intervention with intensive NMES may offer greater benefits than the initiation of NMES 1 month after TKA[26] because it may be easier to prevent the decline of muscle function after surgery than to reverse losses after they occur.

The purpose of this investigation was to evaluate the efficacy of quadriceps muscle NMES, initiated 48 hours after TKA, as an adjunct to standard rehabilitation in a randomized controlled trial. We hypothesized that NMES would attenuate quadriceps muscle strength loss by decreasing voluntary activation deficits and result in better functional performance outcomes when compared with standard rehabilitation.

Method

Design Overview

This was a randomized, controlled, parallel-group intervention trial to

The Bottom Line

What do we already know about this topic?

Quadriceps femoris muscle weakness after total knee arthroplasty is profound and often persists years after surgery. Early quadriceps weakness is largely attributed to deficits in muscle activation. This weakness has major functional consequences, especially in older patients.

What new information does this study offer?

According to this randomized controlled trial, daily application of neuromuscular electrical stimulation can help override deficits in quadriceps femoris muscle activation and attenuate loss of quadriceps strength when initiated within the first week after total knee arthroplasty.

If you're a patient or a caregiver, what might these findings mean for you?

Using neuromuscular electrical stimulation early after total knee arthroplasty surgery may improve your ability to perform activities such as walking and stair climbing. Although you may require a few sessions to get used to the stimulation, many people learn to tolerate the stimulation well.

evaluate the benefits of adding NMES to a postoperative rehabilitation program. Eligible patients were randomly assigned with concealed allocation to either an NMES intervention arm or a control intervention. Randomization included stratification for sex and decade of age. Participants were assessed 1 to 2 weeks preoperatively and at 3.5, 6.5, 13, 26, and 52 weeks postoperatively at the Clinical Translational Research Center of the University of Colorado. Informed consent was obtained from all participants.

Setting and Participants

Patients who underwent a primary unilateral TKA by 3 orthopedic surgeons at the University of Colorado Hospital were consecutively recruited between June 2006 and June 2010. Volunteers were recruited by referral or advertisement at preoperative educational sessions. All patients underwent a tricompartmental, cemented TKA with a medial parapatellar surgical approach.

Patients were included if they were aged 50 to 85 years. Exclusion criteria were uncontrolled hypertension, uncontrolled diabetes, body mass index (BMI) greater than 35 kg/m^2, significant neurologic impairments, contralateral knee OA (as defined by pain greater than 4/10 with activity), or other unstable lower-extremity orthopedic conditions.

Randomization and Interventions

Blocked randomization was used to ensure balanced assignment of participants to the 2 intervention groups by sex and decade of age, with random block sizes of 4, 6, or 8. Group assignment occurred after enrollment criteria were met and prior to the preoperative testing session. Testers were not blinded to group assignment because resources did not permit the hiring of separate personnel for testing and subsequent evaluation of NMES dose to ensure proper use of the NMES device. Standardized scripts and methods were used to eliminate bias with testing.

Following surgery, standard inpatient rehabilitation began on postoperative day 1 (Fig. 1) and continued twice daily for 3 days. All patients were provided the same standard rehabilitation protocol for TKA, consisting of a defined set of core exercises, as previously described.[27]

Following hospital discharge, participants received 6 treatments at home over 2 weeks and then received 10 to 12 outpatient physical therapy visits (Fig. 1). All home health and outpatient physical therapists followed a standardized rehabilitation protocol as previously described[27] and were not aware of group assignment (Appendix). Exercises consisted of knee passive range of motion (PROM) stretching; patellofemoral mobilization (as needed); incision mobility; cycling for range of motion (ROM); lower-extremity flexibility exercises for the quadriceps, calf, and hamstring muscles; modalities (ice or heat as needed); gait training; and functional training for transfers and stair climbing. For strengthening, both weight-bearing and non–weight-bearing exercises were initiated with 2 sets of 10 repetitions and progressed to 3 sets of 10 repetitions. Weights for the resistive exercises described below were increased to maintain a 10-repetition maximum intensity level such that participants felt maximally fatigued after each set. If participants could complete 11 consecutive repetitions, therapists were instructed to increase resistance with the exercise. Resistive exercises consisted of seated knee extensions, straight leg raises, side-lying hip abduction, and standing hamstring muscle curls. Body-weight exercises consisted of step-ups, lateral step-ups, step-downs (5- to 15-cm step), terminal knee extensions, single-limb stance, and wall slides.

All participants were given a home exercise program to be performed twice daily during the acute phase of recovery (first 30 days) and then daily until discharge from therapy. The home exercise program included ROM exercises and weight-bearing and non–weight-bearing strengthening exercises for the quadriceps, hamstring, hip abductor, hip extensor, and plantar-flexor muscles. The intensity and type of exercises for the home program were similar to those performed during the supervised home and outpatient physical therapy sessions.

Physical therapists reported treatment session details via a detailed flow sheet that was reviewed by the study team to monitor consistency of treatment. Participants also were given home exercise logs and were asked to track their progress with home exercises.

A portable Empi 300PV stimulator (Empi Inc, a DJO Global company, St Paul, Minnesota) was used for the NMES intervention because this device has been found to produce levels of average peak torque comparable to those produced by the VersaStim 380 clinical stimulator (Electro-Med Health Industries, Miami, Florida) at comparable levels of discomfort in previous NMES investigations,[21,28–30] but the latter stimulator is not practical for home use.

During treatment, the lower limb was secured by Velcro straps (Velcro USA Inc, Manchester, New Hampshire) to a stable chair to allow for approximately 85 degrees of hip flexion and 60 degrees of knee flexion. Self-adherent, flexible rectangular electrodes (7.6 × 12.7 cm, Supertrodes, SME Inc, Wilmington, North Carolina) were placed on the distal

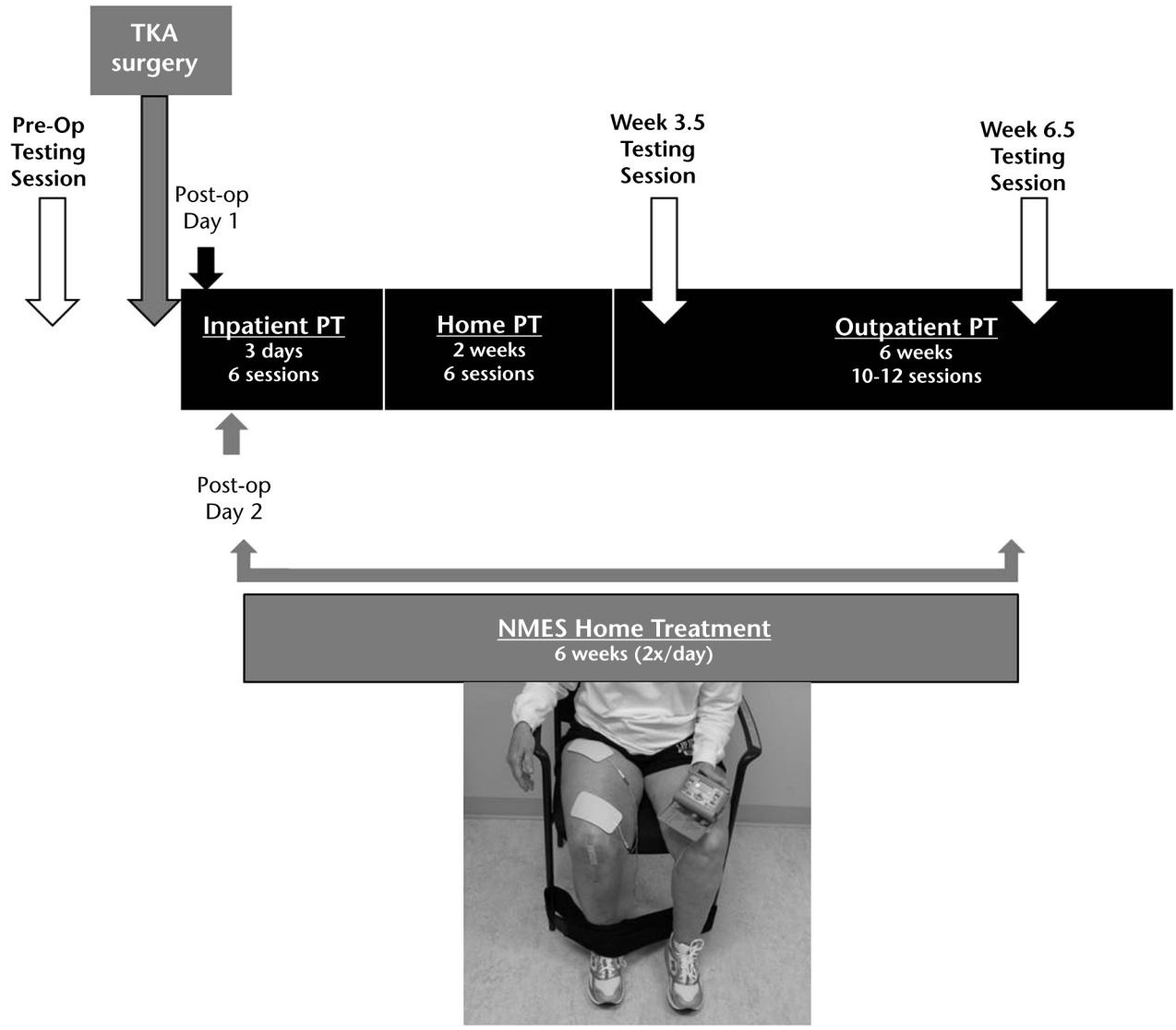

Figure 1.
Study treatment and testing session timeline. All participants received a similar inpatient, home, and outpatient physical therapy (PT) regimen. The neuromuscular electrical stimulation (NMES) intervention group also received 6 weeks of NMES treatment at home, which started 2 days after total knee arthroplasty (TKA) surgery (NMES setup pictured). Participants completed 6 testing sessions (preoperatively [pre-op] and 3.5, 6.5, 13, 26, and 52 weeks postoperatively [post-op]). The week 3.5 and week 6.5 time points represent the midpoint and completion of the NMES intervention, respectively, for the NMES group.

medial and proximal lateral portions of the anterior thigh and marked to ensure consistent reapplication by the participant (Fig. 1). Electrode size for NMES is important because it has a direct effect on the density of the current. Small electrodes result in a high current density and can cause painful stimulation before reaching a sufficient muscle contraction to allow for muscle strengthening.[31] Selection of appropriate electrode size, therefore, is essential for comfortable stimulation, and application of the electrode over the motor point of the muscle reduces the current threshold required. In the present study, we used large, rectangular electrodes to maximize tolerance to treatment.

Neuromuscular electrical stimulation from the portable electrical stimulator was applied to the resting muscle, and the participant was instructed to relax during the induced muscle contraction. The intensity was set to the maximal intensity tolerated during each session, and participants were repeatedly encouraged to increase the intensity as tolerated. The stimulator

was set to deliver a biphasic current, using a symmetrical waveform, at 50 pps for 15 seconds (including a 3-second ramp-up time) and a 45-second off time (250-microsecond pulse duration).

This intervention began 48 hours after surgery in patients assigned to the NMES group. A total of 15 NMES repetitions were performed during each session, twice a day for 6 weeks after TKA (Fig. 1). Initial familiarization with the NMES device (EMPI 300PV stimulator) occurred during preoperative testing to facilitate application of NMES early after surgery. Participants used the NMES unit a few times at home prior to surgery to become familiar with the device. An emphasis was placed on the importance of using the stimulator at an intensity that was tolerable, but slightly uncomfortable, although there was no minimum intensity required for the study protocol. In addition, participants were repeatedly instructed to continue to increase the intensity as much as tolerated within and between sessions. Most participants demonstrated safe and proper use of the stimulator in the hospital. When there were concerns about patient implementation or tolerance to NMES, a study physical therapist paid a home visit within the first week of discharge to monitor a home treatment session. The EMPI 300PV stimulator has an adherence meter to verify the accuracy of patient reporting. Participants also were given paper logs to track adherence.

Outcome Measures and Follow-up

Isometric quadriceps muscle torque and activation testing. Isometric quadriceps muscle torque (primary outcome) and activation testing was performed using a doublet interpolation test, as described previously.[27,32,33] A HUMAC NORM electromechanical dynamometer (CSMi, Stoughton, Massachusetts) was utilized to measure torque. Data were collected using a Biopac Data Acquisition System at a sampling frequency of 2,000 samples per second (Biodex Medical Systems Inc, Shirley, New York) and analyzed using AcqKnowledge software, version 3.8.2 (Biodex Medical Systems Inc).

Participants were positioned in an electromechanical dynamometer stabilized with 60 degrees of knee flexion. They were asked to perform a maximal voluntary isometric contraction (MVIC) of the quadriceps muscles using visual and verbal feedback. Testing was repeated up to 3 times, with 1 minute of rest between trials, until 2 attempts were within 5% of each other. The trial with the largest maximal volitional isometric force output then was normalized to each participant's body weight (in kilograms) and used for data analysis. A Grass S48 stimulator with a Grass model SIU8T stimulus isolation unit (Grass Instrument Co, West Warwick, Rhode Island) was utilized for testing voluntary muscle activation via self-adherent, flexible electrodes (7.6 × 12.7 cm, Supertrodes). With the participant seated and the muscle relaxed, the intensity of stimulation was set using a 2-pulse, 600-microsecond pulse duration, 100-pps electrical train by increasing the output in 10-V increments until the electrically induced torque reached a plateau (supramaximal doublet in resting muscle). Voluntary activation of the quadriceps muscle was assessed using the doublet interpolation technique, where a supramaximal stimulus was applied during an MVIC and again, immediately afterward, while the quadriceps muscle was at rest.[27,32,33] A value of 100% represents full voluntary muscle activation, and anything less than 100% represents incomplete motor unit recruitment or decreased motor unit discharge rates.[32–34] Normalization of the torque from the superimposed doublet to the resting doublet allows for comparisons of quadriceps muscle activation across individuals and lower extremities.

Isometric hamstring muscle torque. Isometric hamstring muscle torque was measured using the same positioning described above, although no hamstring muscle activation testing was performed. The trial with the largest maximal volitional isometric force output was used and was normalized to the participant's body weight (in kilograms) for analysis.

NMES dose assessment. The NMES training intensity (dose) was assessed at week 3.5 and week 6.5 testing sessions for participants in the NMES group. While seated in the electromechanical dynamometer, participants were asked to use their NMES stimulator at the same intensity used at home. The average electrically elicited (rather than voluntary) torque while the stimulator was on was recorded across 15 contractions. This average torque then was expressed as a percentage of the quadriceps muscles' MVIC during the preoperative session to minimize the potential for activation deficits to confound torque measurements.

Functional performance measures. Measures of functional performance included the Timed "Up & Go" Test (TUG), the Stair-Climbing Test (SCT), and the Six-Minute Walk Test (6MWT). The TUG measures the time to rise from an armchair, walk 3 m, turn around, and return to sitting in the same chair without physical assistance.[35] The minimal detectable change associated with the 90% confidence interval (MDC_{90}) for the TUG in patients 1.5 months after TKA is 2.49 seconds.[36] The SCT measures the total time to ascend a flight of stairs, turn around, and descend. Participants were tested on

Table 1.
Baseline Characteristics of the Intervention and Control Groups[a]

Variable	NMES Group		Control Group		p[b]
	n	%	n	%	
Women	20	57.1	16	51.6	.65
Men	15	42.9	15	48.4	
	n	$\bar{X}$ (SD)	n	$\bar{X}$ (SD)	p[b]
Age (y)	35	66.2 (9.1)	31	64.8 (7.7)	.49
Height (cm)	35	168.9 (9.3)	31	169.6 (9.6)	.77
Weight (kg)	35	78.0 (17.4)	31	90.0 (17.0)	.01
BMI (kg/m^2)	35	27.1 (4.9)	31	31.2 (4.2)	<.001
Pedometer (steps/day)	25	5,133 (3,109)	18	4,842 (3,757)	.79

[a] NMES=neuromuscular electrical stimulation, BMI=body mass index.
[b] *P* values are based on chi-square test for independent proportions or a 2-sided, 2-group *t* test for difference in group means. Baseline data include all patients who were randomized preoperatively.

1 of 2 staircases during the study due to a change in facilities. Nine participants in the control group and 8 participants in the NMES group were consistently tested on a 10-step staircase with 17.14-cm (6.75-in) step height. All other participants were tested on a 12-step staircase with 17.14-cm step height. This difference did not affect analysis because within-subject changes were measured over time. The MDC_{90} for this measure has been estimated at between 2.6 and 5.5 seconds in patients recovering from TKA, depending on the time point assessed and number of stairs.[36,37] The 6MWT measures the total distance walked (in meters) over 6 minutes. This test has been used extensively to measure endurance and has been validated as a measure of functional mobility following knee arthroplasty.[38] The 6MWT has excellent test-retest reliability, with intraclass correlation coefficients ranging from .95 to .97, and a low coefficient of variation (10.4%).[39] The MDC_{90} for the 6MWT is 61.34 m in patients 1.5 months after TKA.[36] Participants also were asked to wear a pedometer (Accusplit AE120XL Pedometer, Steps Only, Accusplit, Livermore, California) prior to TKA surgery to evaluate baseline levels of physical activity (Tab. 1).[40] The pedometer was secured to the waist and worn for 3 consecutive days, from which the average number of steps per day was calculated.

Pain. Pain was measured utilizing an 11-point verbal numeric pain rating scale. Participants were asked to rate their pain on a scale of 0 to 10, with 0 representing "no pain" and 10 representing "worst pain imaginable."

ROM. Active range of motion (AROM) of the knee was measured in the supine position using a long-arm goniometer as previously described.[41] For active knee extension, the heel was placed on a 10.16-cm (4-in) block, and the participant was instructed to actively extend the knee. For active knee flexion, the participant was instructed to actively flex the knee as far as possible while keeping the heel on the supporting surface. Throughout this report, negative values of extension represent hyperextension.

Health status questionnaires. Health status was assessed using the Physical Component Score (PCS) and Mental Component Score (MCS) of the 36-Item Short-Form Health Survey questionnaire (SF-36). The SF-36 has been shown to capture improvements in 7 of its 8 domains in patients after TKA in the first 3 months after surgery[42] and continues to indicate improvements in health-related quality of life over the next 6 to 12 months.[43] The SF-36 is reliable and internally consistent.[43–45]

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to evaluate self-report of knee-specific impairment.[46] It assesses the pain, joint stiffness, and physical, social, and emotional function of a person with OA to determine the overall level of disability. The WOMAC is a valid, reliable, and responsive self-administered instrument that can be used for short-term and long-term follow-up of knee injury, including OA.[46]

Participants were asked to rate their perception of knee functional ability on a global rating scale (GRS) of 0 to 100. A score of 0 represented complete disability, and a score of 100 represented a level of knee function before the individual had any OA symptoms.[47,48]

Data Analysis

The study was designed to achieve 90% power to detect the effects of

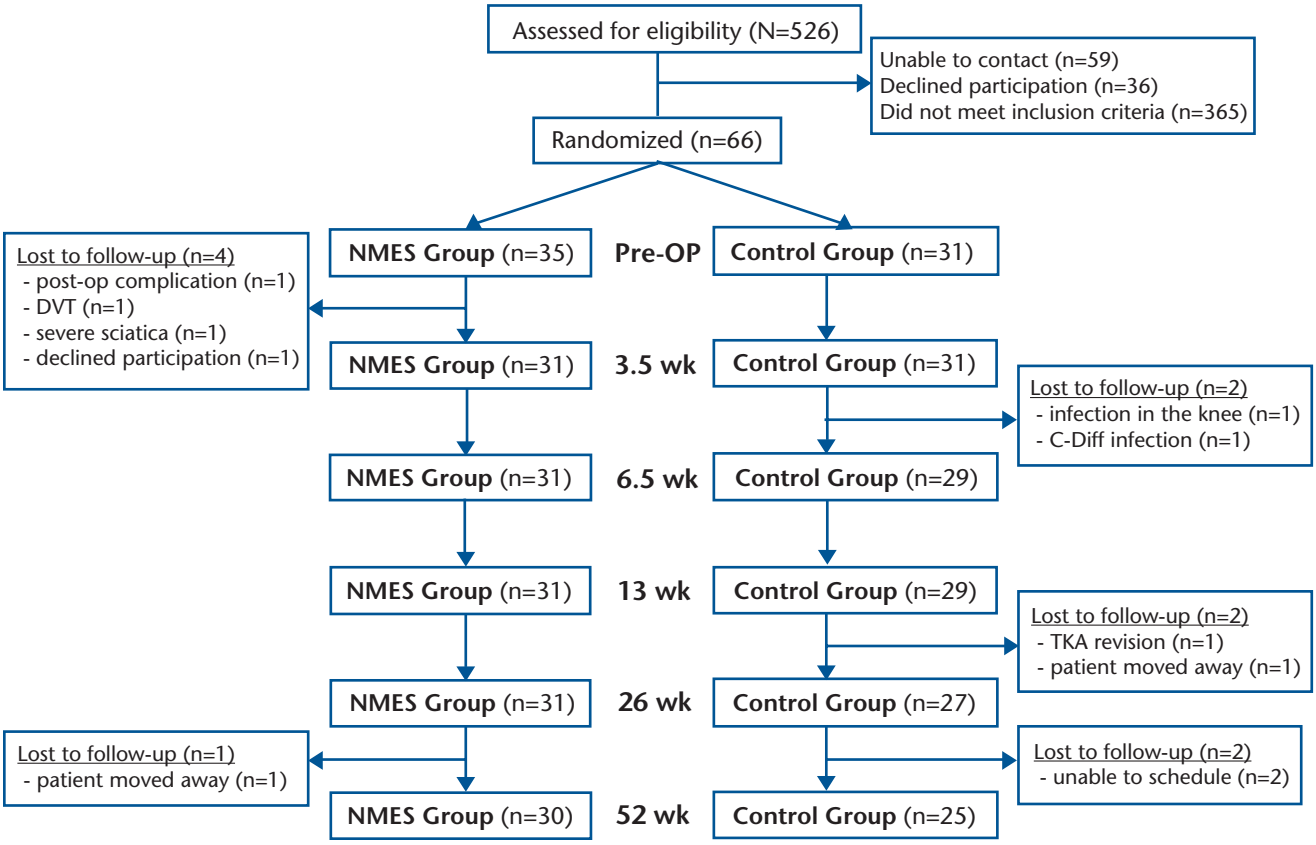

Figure 2.
Recruitment, enrollment, and adherence of study participants. Enrollment numbers and withdrawals or those lost to follow-up are indicated in the boxes between time points. Overall, the total number of participants lost to follow-up through 52 weeks were 5 in the neuromuscular electrical stimulation (NMES) group and 6 in the control group. DVT=deep venous thrombosis, TKA=total knee arthroplasty, C-Diff=clostridium difficile, pre-op=preoperatively, post-op=postoperatively.

the intervention 3.5 weeks after TKA with 25 participants per group. The primary outcome measure, difference in quadriceps muscle torque between intervention (NMES) and usual care (control) at 3.5 weeks, was tested using an analysis of covariance model; the 3.5-week change from baseline was regressed on sex, age, and baseline quadriceps muscle torque with 59 complete cases (28 in the NMES group, 31 in the control group). Confirmatory measures were evaluated at 3.5 weeks after surgery in the same way. Baseline characteristics of the treatment groups were compared using 2-sample *t* tests for continuous measures or a chi-square test for independent proportions for categorical measures.

A secondary aim of the study was to evaluate the long-term sustainability of the effects of NMES. Differences in all outcomes at 3.5, 6.5, 13, 26, and 52 weeks after TKA were evaluated using maximum likelihood estimation of a multivariate, repeated-measures, mixed-effects model using all available data. This approach is conceptually identical to repeated-measures analysis of variance, but avoids the case-wise deletion of participants with missing assessments. The maximum likelihood method provides unbiased estimates under the assumption that missing data are missing at random.[49]

SAS version 9.2 (SAS Institute Inc, Cary, North Carolina) was used for all statistical analyses. All analyses were intention-to-treat and did not adjust for nonadherence or intolerance to NMES. A 2-sided alpha level of .05 was designated for statistical significance.

Role of the Funding Source

This study was supported by the National Institute of Aging (K23AG029978), an American College of Rheumatology New Investigator Award, the Foundation for Physical Therapy Marquette Challenge Grant, and Clinical and Translational Science Award Grant (UL1 RR025780). A peer-reviewed research grant from Empi Inc, a DJO Global company, was used for the purchase of 300PV electrical stimulators and

Table 2.
Mean Changes and 95% Confidence Intervals for the Primary and Secondary Outcome Measures at 3.5 Weeks (Primary Endpoint)[a]

Variable	Change From Baseline to 3.5 Weeks $\bar{X}$ (SE)[b]		Between-Group Difference in the Change From Baseline	
	NMES Group	Control Group	Mean (95% CI)	P[c]
Normalized quadriceps muscle strength[d] (N-m/kg)	−0.40 (0.05)	−0.67 (0.06)	0.27 (0.12, 0.41)	≤.001
Normalized hamstring muscle strength[d] (N-m/kg)	−0.25 (0.03)	−0.35 (0.04)	0.10 (0.01, 0.19)	.04
Six-Minute Walk Test (m)	−34.7 (15.5)	−137 (18.3)	102.4 (58.1, 146.8)	≤.001
Stair-Climbing Test (s)	−8.9 (2.8)	−22.2 (3.0)	13.3 (5.7, 21.0)	.001
Timed "Up & Go" Test (s)	−1.5 (0.6)	−4.2 (0.7)	2.7 (1.0, 4.5)	.003
Quadriceps muscle activation (%)	5.2 (3.3)	−2.9 (3.7)	8.1 (−1.2, 17.4)	.09
Extension active range of motion (°)	−2.2 (0.8)	−5.2 (0.9)	3.0 (0.8, 5.2)	.01
Flexion active range of motion (°)	−26.4 (2.1)	−25.5 (2.2)	−0.9 (4.9, 6.8)	.75
Global rating scale (points)	3.9 (3.3)	−7.9 (3.8)	11.8 (2.0, 21.5)	.02
SF-36 PCS (points)	0.0 (1.6)	1.1 (1.8)	−1.1 (−5.8, 3.6)	.65
SF-36 MCS (points)	−0.3 (1.6)	−3.9 (1.8)	3.6 (−0.9, 8.1)	.12
WOMAC (points)	−11.9 (2.7)	−6.9 (2.9)	−5.0 (−12.4, 2.4)	.18
Resting pain (points)	−1.0 (0.4)	−0.6 (0.4)	−0.4 (−1.4, 0.7)	.50

[a] NMES=neuromuscular electrical stimulation, CI=confidence interval, SF-36=36-Item Short-Form Health Survey questionnaire, PCS=Physical Component Score, MCS=Mental Component Score, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.
[b] Values are means ± standard error of the estimate. Negative values reflect a deficit from baseline; positive values reflect an improvement from baseline.
[c] *P* values are from the estimated between-group difference in change from baseline, conditioned on baseline. The model is change from baseline regressed on baseline and treatment assignment.
[d] Normalized to weight.

recruitment/transportation costs for patient visits. None of the sponsors had any influence on the study design, implementation, or data analysis and interpretation.

Results

Five hundred twenty-six patients scheduled for TKA at the University of Colorado Hospital were assessed for eligibility. Fifty-nine patients were unable to be contacted, 365 did not meet the inclusion criteria, and 36 declined to participate. Of those who were ineligible, 11% were not between the ages of 50 to 85 years, 13% had a BMI of greater than 35 kg/m^2, 31% had moderate to severe contralateral pain or staged TKAs within 6 months of each other, 7% had other orthopedic conditions that limited their function, 8% were smokers, 7% had uncontrolled diabetes or neuropathy, and 23% had other health conditions (eg, neurological, cardiovascular). Therefore, 66 patients (30 male, 36 female) were enrolled in the study (Fig. 2). There were no differences between groups in sex, age, or height, but differences in weight and BMI were present (Tab. 1). There were no group differences in baseline self-reported and performance measures with the exception of SF-36 PCS (Tab. 2). There were no adverse events resulting from participation in the study in either group.

Raw data for strength and functional performance outcome measures at all time points are presented in Table 3. At the 3.5-week visit, the NMES group had significantly greater improvements than the control group in quadriceps and hamstring muscle strength; TUG, SCT, 6MWT, and GRS scores; and extension AROM (Tab. 2, Fig. 3). Quadriceps muscle activation tended to be greater with NMES (*P*=.09). No differences between groups were noted for changes in the SF-36 (MCS and PCS) and WOMAC scores.

At 52 weeks after TKA, between-group differences were attenuated, but remained significant (ie, favoring NMES) for quadriceps and hamstring muscle strength and TUG, SCT, 6MWT, GRS, SF-36 MCS, and WOMAC scores; improvement in active extension ROM tended to be better in NMES (*P*=.08). There were no differences in SF-36 PCS scores between groups.

The NMES dose ranged from 1.6% to 76.7% of the preoperative MVIC (mean [SD]: 16.1% [14.8%] at 3.5 weeks; 17.7% [11.3%] at 6.5 weeks). Adherence to NMES treatment is rep-

Table 3.
Mean (SD) Values for Strength and Functional Performance Outcome Measures[a]

Variable	Preoperatively		3.5 Weeks Postoperatively		6.5 Weeks Postoperatively		13 Weeks Postoperatively		26 Weeks Postoperatively		52 Weeks Postoperatively	
	NMES Group	Control Group	NMES Group	Control Group	NMES Group	Control Group	NMES Group	Control Group	NMES Group	Control Group	NMES Group	Control Group
Quadriceps femoris muscle strength[b] (N-m/kg)	1.33 (0.57), n=35	1.32 (0.49), n=31	0.93 (0.41), n=31	0.66 (0.24), n=28	1.20 (0.47), n=31	1.04 (0.35), n=28	1.42 (0.52), n=30	1.20 (0.42), n=29	1.51 (0.48), n=31	1.39 (0.44), n=27	1.66 (0.52), n=30	1.50 (0.43), n=25
Hamstring muscle strength[b] (N-m/kg)	0.76 (0.28), n=35	0.72 (0.26), n=31	0.49 (0.18), n=30	0.39 (0.19), n=28	0.65 (0.23), n=31	0.55 (0.20), n=28	0.73 (0.21), n=29	0.65 (0.24), n=30	0.79 (0.25), n=31	0.72 (0.25), n=27	0.83 (0.25), n=30	0.72 (0.29), n=25
Quadriceps muscle activation (%)	76.4 (14.8), n=34	75.5 (19.0), n=29	82.3 (17.2), n=30	73.6 (17.9), n=26	84.9 (13.7), n=31	86.3 (10.6), n=24	86.5 (12.9), n=30	85.4 (11.5), n=29	88.4 (10.1), n=31	84.2 (10.0), n=26	87.6 (9.2), n=30	85.9 (11.9), n=23
Stair-Climbing Test (s)	18.1 (10.9), n=35	20.2 (12.3), n=31	25.2 (10.4), n=30	39.3 (21.1), n=28	16.5 (7.2), n=31	23.5 (17.1), n=26	13.6 (7.1), n=30	16.3 (7.5), n=30	12.1 (5.1), n=31	14.8 (7.8), n=26	11.5 (4.3), n=29	14.8 (9.3), n=25
Timed "Up & Go" Test (s)	9.0 (4.2), n=35	10.1 (3.6), n=31	10.4 (3.8), n=31	13.9 (4.5), n=28	8.0 (2.1), n=31	11.3 (6.8), n=26	7.5 (2.2), n=30	9.5 (2.8), n=30	7.1 (2.0), n=31	8.6 (2.1), n=26	6.7 (1.7), n=29	8.3 (2.8), n=25
Six-Minute Walk Test (m)	404.2 (128.2), n=35	433.6 (99.2), n=31	390.1 (92.4), n=31	295.3 (103.4), n=24	466.6 (93.0), n=31	388.0 (94.9), n=24	495.7 (95.6), n=30	433.1 (88.9), n=29	496.2 (104.3), n=31	465.8 (83.9), n=26	524.6 (81.6), n=29	477.8 (94.0), n=25
Flexion AROM (°)	123.3 (13.7), n=35	119.4 (13.1), n=31	96.4 (12.3), n=31	95.2 (11.9), n=28	107.3 (10.6), n=31	103.8 (12.1), n=26	113.9 (8.9), n=30	111.0 (10.0), n=30	116.5 (8.8), n=31	113.0 (10.7), n=25	119.4 (6.3), n=30	117.0 (9.1), n=25
Extension AROM (°)	0.6 (3.2), n=35	1.5 (4.0), n=31	2.6 (3.6), n=31	6.4 (5.2), n=28	1.2 (4.0), n=31	2.9 (4.3), n=26	−0.8 (2.8), n=30	1.6 (3.8), n=30	−0.5 (3.7), n=31	−0.1 (2.9), n=25	−2.0 (3.5) n=30	−1.4 (3.4), n=25
Global rating scale (points)	60.2 (24.8), n=29	54.2 (21.5), n=26	60.5 (17.5), n=28	50.2 (17.2), n=23	75.5 (11.3), n=28	73.0 (18.8), n=22	85.9 (10.9), n=28	80.8 (19.4), n=26	89.8 (9.9), n=30	85.2 (14.9), n=26	95.6 (5.7), n=30	87.3 (15.0), n=25
Resting pain (points)	2.5 (1.9), n=30	2.7 (2.4), n=28	1.8 (1.7), n=30	2.1 (1.8), n=26	0.6 (0.9), n=29	1.2 (1.3), n=24	0.6 (1.2), n=30	1.5 (2.1), n=26	0.6 (1.3), n=30	0.7 (1.5), n=25	0.6 (1.4), n=29	0.4 (1.5), n=23
WOMAC total (points)	36.9 (12.3), n=34	42.0 (13.7), n=30	26.6 (12.0), n=28	31.4 (14.1), n=21	18.1 (8.9), n=29	23.7 (14.2), n=24	11.2 (8.7), n=26	18.0 (17.6), n=21	7.5 (6.6), n=28	13.6 (11.6), n=21	5.7 (5.9), n=26	10.0 (12.2), n=21
SF-36 PCS (points)	38.3 (9.2), n=34	33.4 (7.4), n=29	36.3 (9.4), n=28	35.8 (7.3), n=22	43.0 (7.9), n=28	42.9 (6.4), n=23	49.0 (7.6), n=25	45.8 (8.5), n=21	52.2 (5.2), n=28	48.3 (7.6), n=21	52.6 (5.9), n=27	50.7 (7.4), n=21
SF-36 MCS (points)	54.6 (9.9), n=34	52.2 (12.0), n=29	55.0 (9.6), n=28	51.0 (11.5), n=22	56.8 (9.4), n=28	53.7 (7.5), n=23	57.9 (8.2), n=25	54.2 (9.7), n=21	57.2 (4.4), n=28	55.2 (7.6), n=21	57.8 (4.4), n=27	54.8 (6.9), n=21

[a] NMES=neuromuscular electrical stimulation, AROM=active range of motion, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, SF-36=36-Item Short-Form Health Survey questionnaire.
[b] Normalized to body weight.

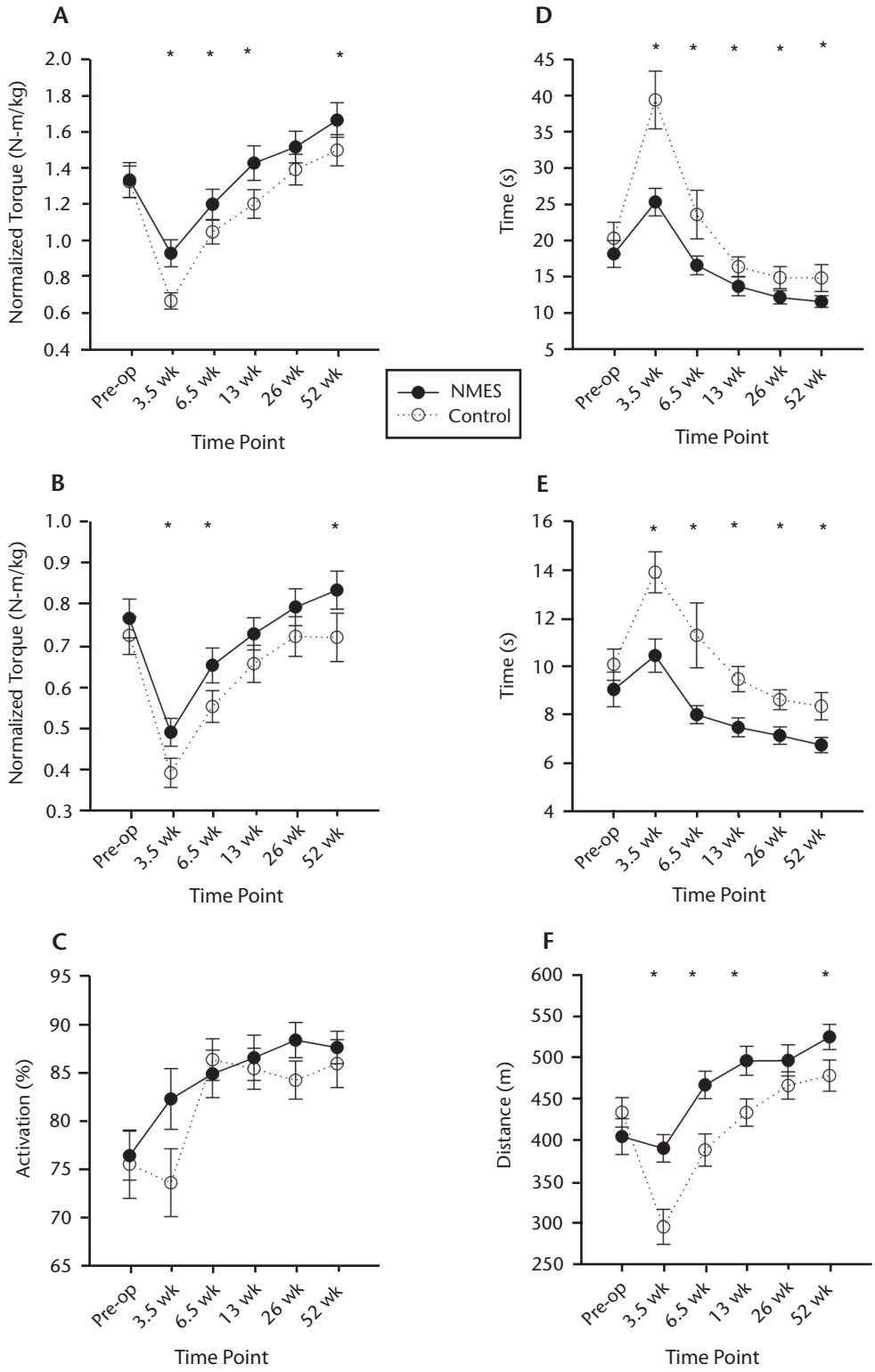

Figure 3.
Changes in strength and functional performance over time (mean ± standard error of the mean) in the neuromuscular electrical stimulation (NMES) group (black circles) and the control group (white circles): (A) quadriceps femoris muscle maximum voluntary isometric contraction (MVIC) normalized to body weight, (B) hamstring muscle MVIC normalized to body weight, (C) quadriceps muscle central activation, (D) Stair-Climbing Test, (E) Timed "Up & Go" Test, (F) Six-Minute Walk Test. Significant differences between groups are indicated by asterisks ($P<.05$). Pre-op=preoperatively.

Table 4.
Treatment Adherence During the 6-Week Intervention[a]

Treatment Adherence	No. of NMES Group Participants (% of Total Participants)						
	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Overall
Adherent (>80%)	26 (83.9%)	26 (83.9%)	24 (77.4%)	19 (61.3%)	20 (64.5%)	18 (58.1%)	24 (77.4%)
Partially adherent (50%–80%)	4 (12.9%)	3 (9.7%)	6 (19.4%)	7 (23%)	6 (19.4%)	6 (19.4%)	6 (19.4%)
Not adherent (<50%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	2 (6.5%)	0 (0.0%)
No records	1 (3.2%)	1 (3.2%)	1 (3.2%)	4 (12.9%)	4 (12.9%)	5 (16.1%)	1 (3.2%)

[a] Treatment adherence is reported as the number of participants, and the percentage of the total number of participants who received neuromuscular electrical stimulation (NMES) is noted in parentheses. Treatment adherence was based on the percentage of expected home NMES treatment. The expectation was 15 contractions per session, 2 sessions per day, 6–7 days per week.

resented in Table 4. The average (SD) intensity of stimulation was 83.7 (3.1) mA at 3.5 weeks and 82.1 (3.3) mA at 6.5 weeks). These findings generally corresponded to a muscle contraction that was *at least* equivalent to that achieved during a straight leg raise. Ten participants (32.3%) reached the limiting voltage of the stimulator (100 mA) during at least 1 week of treatment; 3 participants set the stimulator at 100 mA for all 6 weeks of treatment.

Discussion

The addition of NMES treatment to the quadriceps muscles effectively attenuated loss of quadriceps muscle strength and improved functional performance following TKA. Although the effects were most pronounced and clinically meaningful within the first month after surgery,[36,33] benefits persisted through 1 year after surgery. Notably, 3.5 weeks after TKA, NMES application substantially attenuated loss of quadriceps muscle strength (67% loss in control group and 40% loss in NMES group). This finding translated into even greater attenuation of functional performance deficits, with changes in the 6MWT distance at 3.5 weeks being the most notable (loss of 137 m in the control group and loss of 34.7 m in the NMES group). Self-report measures of physical function (SF-36, WOMAC) did not demonstrate early improvements with NMES treatment, whereas performance-based measures of physical function (TUG, SCT, 6MWT) did show improvements. These findings were expected because patient perception fails to capture the acute functional declines after TKA and may overstate the long-term functional improvement with surgery, largely because patient-reported outcomes typically parallel pain relief after surgery.[48,50]

In 2003, a National Institutes of Health consensus statement on total knee replacement stated that "the use of rehabilitation services is perhaps the most understudied aspect of the perioperative management of TKA patients."[51(p15)] Yet, since 2003, few studies have provided additional guidelines for evidence-based rehabilitation following TKA.[52] One large-scale clinical trial with a progressive exercise program involving 6 weeks of outpatient physical therapy 2 to 3 times per week demonstrated a 38% faster SCT time, a 17% increase in 6MWT distance, and a 24% increase in quadriceps muscle strength 1 year after TKA compared with standard care.[24] These findings were despite the fact that the progressive component of the intervention was initiated 3 to 4 weeks after TKA, when large strength and functional losses had already occurred. Using rehabilitation strategies such as NMES immediately after surgery may be more effective because preventing the decline of muscle function early after surgery is likely to be more effective than working to reverse losses after they occur. Importantly, the aforementioned investigation[24] also used NMES for one treatment arm 2 times per week (10 contractions per session) and showed no added benefits in quadriceps muscle strength or functional performance. Although the average dose of NMES was greater than that of the present study, it is possible that the frequency of NMES application (2 times per week) may not have been sufficient to induce changes or that the initiation of NMES was too late to capitalize on the early marked deficits in quadriceps muscle activation.

Other studies indicate that NMES holds promise for restoring muscle function after TKA.[23,53,54] Avramidis et al[23] found a significant increase in walking speed in response to 6 weeks of daily NMES treatment (4 hours per day) to the quadriceps muscle compared with controls at 6 weeks after TKA. There was a carryover in faster walking speed with NMES at 12 weeks postoperatively, which is likely secondary to an initially faster recovery of quadriceps muscle strength and subsequent ability to participate more fully in the voluntary exercise program. Although that investigation demonstrated benefits of NMES application, the length of daily NMES treatment (4 hours per day) may be problem-

atic in ensuring patient adherence to the treatment. The present study suggests that decreasing treatment time while encouraging a maximally tolerable intensity was even more effective in attenuating loss of quadriceps muscle strength and improving functional performance than the aforementioned study. Gotlin et al[55] studied the effects of NMES applied within the first week after TKA and found that NMES reduced knee extensor lag from 7.5 to 5.7 degrees compared with controls, who had an increase in extensor lag from 5.3 to 8.3 degrees in the same time frame. In addition, NMES decreased the length of hospital stay from 7.4 to 6.4 days. Finally, when unilateral NMES was initiated 3 to 4 weeks after bilateral TKA and continued for 6 weeks, quadriceps muscle activation and strength increased 431% in the limb that received NMES plus voluntary exercise and only 182% in the contralateral limb with voluntary exercise alone.[21] There is additional support for the use of NMES in other patient populations with activation deficits, such as anterior cruciate ligament reconstruction, stroke, and cerebral palsy.[20,56–59]

Although it has been difficult to determine the underlying muscular and neural mechanisms responsible for improved muscle performance with NMES, some theories have emerged. The first is related to the intensity of the muscle contraction produced during stimulation. Training programs for people with minimal activation deficits require training intensities of at least 50% to 60% of maximal voluntary effort to overload the muscle sufficiently to induce hypertrophy, with higher intensities producing greater hypertrophy.[60,61] Similar to higher-intensity voluntary muscle contractions, electrically elicited muscle contractions at high intensities produce muscle hypertrophy and corresponding increases in strength.[29,59,62,63] In the present study, the training intensities were lower than those expected to produce muscle hypertrophy. As such, altered motor unit recruitment may explain some of the improvements in muscle function. Electrically elicited muscle contractions allow for activation of a greater proportion of type II muscle fibers than volitional exercise at comparable intensity.[64–66] Type II muscle fibers are larger than type I fibers, so greater activation of these fibers amplifies force production.[67] Evidence also suggests that NMES influences functional measures of motor performance via peripheral afferent inputs that alter motor cortex excitability.[68–71] Stimulation of peripheral afferent nerves can induce prolonged changes in the excitability of the human motor cortex, which may help explain the improvements in muscle function with NMES.[70,71]

There are some methodological issues to consider when using NMES, including the length of treatment, safety considerations, and patient tolerance. The length of NMES treatment (ie, 6 weeks) in this study was chosen to maximize the potential for physiological changes in the quadriceps muscle to translate into improvements in functional performance, but it remains uncertain whether the full 6 weeks is necessary because of the robust early response to NMES treatment. After 3 weeks, the trajectory of improvement was similar for both treatment groups. Early application of NMES attenuated the magnitude of decline seen with controls, but whether 3 additional weeks of application was needed to sustain improvements is less clear.

Safety is an important consideration with the use of NMES in a home setting. All participants demonstrated independence with the NMES unit within the first week at home, although some required an additional training session at home to ensure safety and encourage tolerance. Marking the electrode locations on the thigh was important to ensure proper electrode placement. Additionally, familiarization with the NMES unit before surgery increased patient comfort with its application after surgery. Although preoperative familiarization may not always be possible, oversight by physical therapists in any setting (inpatient, home health, or outpatient) and encouragement to tolerate as much stimulation as possible may be important for similar outcomes and safe implementation of this treatment. Another safety consideration is the use of NMES in patients with pacemakers. Although none of the patients in the present study had pacemakers, the use of NMES with a pacemaker is controversial because potential electromagnetic interference may result in pacemaker malfunction. Some evidence suggests that electrical stimulation of the quadriceps muscle poses no risk to pacemakers,[72] whereas other evidence suggests potential electromagnetic interference with pacemaker function.[73]

Finally, tolerance to NMES treatment may be an important determinant of effectiveness, as suggested by the dose-response relationship between the amount NMES applied and the strength gains following anterior cruciate ligament reconstruction.[29] Therefore, a major emphasis of NMES treatment for the present study was to encourage patients to apply NMES to their maximum tolerance. The study team provided substantial verbal encouragement to patients to regularly turn up the intensity of stimulation both within and between treatment sessions. Our clinical observations of NMES application in some clinical settings have shown that therapists often are reluctant to push patients to tolerate uncomfortable doses of stimulation. Patients likely sense this hesitation,

which limits the potential to see benefits of NMES treatment. Therefore, we repeatedly educated patients at each testing session regarding the importance of tolerating the maximal dose possible. Nevertheless, for a handful of patients, the NMES dose was very low despite substantial efforts to encourage greater tolerance, suggesting that some patients may be better candidates than others for NMES treatment. Further investigation of the present study will evaluate whether there is a dose-response relationship in this population to further guide clinical decision making regarding which patients are the best candidates for this treatment.

There were several limitations to the present study that should be considered. The lack of matching treatment volume in the control and NMES groups could have contributed to differences in the responses to treatment. We considered adding isometric contractions of the quadriceps muscle for controls in the same seated position used for NMES, but we felt that this approach was not used clinically. Rather, we chose to compare 2 accepted clinical approaches to treatment. Another limitation of this investigation was the lack of blinding, although standardized scripts and testing methods were used. Neuromuscular electrical stimulation treatment application during testing was important for assessing safety and adherence, pushing patient tolerance, and measuring dose of NMES application. Baseline differences in BMI were present, but BMI does not affect normalized quadriceps muscle strength or functional performance capabilities if it is less than 40 kg/m^2.[74] In the present study, lower BMI in the NMES group may have facilitated treatment success because NMES treatment may be more effective for individuals who have less impedance from adipose tissue in their thighs. Finally, 10 patients reached the maximum output of the stimulator, suggesting that the benefits of NMES might have been even greater with stimulation at higher intensities.

Conclusion

The addition of quadriceps muscle NMES initiated within 48 hours after TKA attenuated loss of quadriceps muscle strength 3.5 weeks after TKA and improved functional performance; benefits of NMES treatment persisted through 1 year. Functional performance for the NMES group at 1 year began to approach outcomes for older adults who were healthy, tested using identical methods,[9] yet they still lagged behind in clinically meaningful differences in TUG, SCT, and 6MWT performance.[36] Even the control group in this study exceeded outcomes previously reported in the literature,[52] yet they lagged even further behind adults who were healthy compared with the NMES group. Therefore, further research focused on early intervention after TKA is warranted to continue to optimize patient outcomes.

Dr Stevens-Lapsley, Ms Balter, Dr Eckhoff, and Dr Kohrt provided concept/idea/research design. Dr Stevens-Lapsley, Ms Balter, and Ms Wolfe provided writing and data analysis. Dr Stevens-Lapsley and Ms Balter provided data collection and project management. Dr Stevens-Lapsley and Dr Kohrt provided fund procurement. Dr Eckhoff provided participants. Dr Stevens-Lapsley provided facilities/equipment. Dr Eckhoff and Dr Kohrt provided consultation (including review of manuscript before submission).

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The study was approved by the Colorado Multiple Institutional Review Board.

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Appendix.

Standardized Rehabilitation Protocol for Inpatient (Early), Home Health (Middle), and Outpatient (Late) Physical Therapy in Addition to Home Neuromuscular Electrical Stimulation Treatment[a]

Early	**Inpatient Rehabilitation Exercise Program** **Postoperative day 1** • Bedside exercises: ankle pumps, quadriceps sets, gluteal sets, hip abduction (supine), short-arc quads, straight leg raise (if able) • Knee ROM: heel slides • Bed mobility and transfer training (bed to and from chair) **Postoperative day 2** • Exercises for AROM, active-assisted ROM, and terminal knee extension • Strengthening exercises (eg, ankle pumps, quadriceps sets, gluteal sets, heel slides, short-arc quads, straight leg raises, supine hip abduction) 1–3 sets of 10 repetitions for all strengthening exercises, twice/day • Gait training with assistive device on level surfaces and functional transfer training (eg, sit to and from stand, toilet transfers, bed mobility) **Postoperative days 3–5 (or on discharge to rehabilitation unit)** • Progression of ROM with active-assisted exercises and manual stretching, as necessary • Progression of strengthening exercises to the patient's tolerance, 1–3 sets of 10 repetitions for all strengthening exercises, twice/day • Progression of ambulation distance and stair training (if applicable) with the least restrictive device • Progression of activities-of-daily-living training for discharge to home
	NMES Treatment (Weeks 1–6) **Begin on postoperative day 2** • **For NMES group:** 15 electrically elicited contractions 2×/day • **NMES parameters:** biphasic current, symmetrical waveform, 250-microsecond pulse duration, 50 pps for 15 seconds (including a 3-second ramp-up time) and a 45-second off time
Middle	**Home Health Rehabilitation Exercise Program (Weeks 2–3)** **ROM** • Active-assistive ROM for knee flexion, sitting or supine, using other leg to assist • Passive knee extension stretch with manual pressure by physical therapist or weights • Patellar and knee mobilizations **Strength** • Quad sets • Short-arc quads* • Straight leg raises (without quad lag)* • Hip abduction (side lying)* • Hamstring curls (standing)* • Sitting knee extension (long-arc quad)* • 1–3 sets of 10 repetitions for all strengthening exercises; *maximal fatigue should occur after each set • **Progression:** *weights can be added if patient can complete the exercise and maintain control through 3 sets of 10 repetitions without increased pain or swelling **Functional activities** • Gait training with assistive device, as appropriate, with emphasis on heel-strike, proper toe-off, and normal knee joint excursions • Emphasis on heel-strike, proper toe-off, and normal knee joint excursions when able to walk without assistive device • Step-ups (5.8-cm [2-in] block) • Mini squats (30° of knee flexion) • **Progression**: step-ups (10.16-cm [4-in] block), mini squats to 45° of knee flexion **Pain and swelling** • Ice and compression as needed **Incision mobility** • Soft tissue mobilization until incision moves freely over subcutaneous tissue
	NMES Treatment • **For NMES treatment:** continue NMES 2×/day

(*Continued*)

Appendix.

Continued

Late	**Outpatient Rehabilitation Exercise Program (Weeks 4–8)** **ROM** • Exercise bike (10–15 min), initiate with forward and backward pedaling and no resistance until enough ROM for full revolution; **progression**: lower seat height to produce a stretch with each revolution • Knee flexion stretch: sitting (planting foot and scooting to edge of chair); standing (surgical extremity on a stair with stretch into knee flexion) • Knee extension stretch with manual pressure (in clinic) or weights (at home) **Strength** • Straight leg raises (without quad lag)* • Hip abduction (side lying)* • Hamstring curls (standing)* • Sitting knee extension* • 1–3 sets of 10 repetitions for all strengthening exercises; maximal fatigue should occur after each set • **Progression:** *weights are to be progressed only once the patient can complete the exercise and maintain control through 3 sets of 10 repetitions without increased pain or swelling **Functional activities** • Terminal knee extensions from 45° to 0° • Gait training with emphasis on heel-strike, proper toe-off, and normal knee joint excursions without assistive device • Step-ups and step-downs (5.8- to 10.16-cm) with good concentric and eccentric control • Wall slides to 45° of knee flexion • Stair ascending and descending, step over step, when patient has sufficient concentric and eccentric strength • Sit-to-stand repetitions with emphasis on eccentric control • **Progression**: increase step height for step-ups and step-downs to 15.24 cm (6 in) if demonstrating good concentric and eccentric control, increase wall slides to 60° and 90° knee flexion, lower chair height for sit-to-stand **Pain and swelling** • Ice and compression as needed
	NMES Treatment • **For NMES treatment:** continue NMES 2×/day until week 6

[a] ROM=range of motion, AROM=active range of motion, NMES=neuromuscular electrical stimulation.