Cycling with Functional Electrical Stimulation Before and After a Distal Femur Fracture in a Man with Paraplegia

Therese E. Johnston, PT, PhD, MBA,¹ Ralph J. Marino, MD, MS,² Christina V. Oleson, MD,²
Mary Schmidt-Read, PT, DPT, MS,³ and Christopher M. Modlesky, PhD⁴

¹Department of Physical Therapy, Jefferson School of Health Professions, Thomas Jefferson University, Philadelphia, Pennsylvania;

²Department of Rehabilitation Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania; ³Magee Rehabilitation Hospital, Philadelphia, Pennsylvania; ⁴Department of Kinesiology and Applied Physiology, University of Delaware, Newark, Delaware

Case Presentation: A man with chronic paraplegia sustained a distal femur fracture following an unrelated fall while enrolled in a study examining musculoskeletal changes after 6 months of cycling with functional electrical stimulation (FES). After healing, he restarted and completed the study. **Management and Outcome:** Study measures included areal bone mineral density, trabecular bone microarchitecture, cortical bone macroarchitecture, serum bone formation/resorption markers, and muscle volume. The patient made small gains in bone- and muscle-related measures. Bone markers had not returned to baseline prior to restarting cycling, which may have impacted results. **Discussion:** This case shows that cycling with FES may be safely resumed after distal femur fracture. **Key words:** bone, cycling, fracture, functional electrical stimulation, spinal cord injury

Cycling with functional electrical stimulation (FES) is an intervention for people with spinal cord injury (SCI) that is often used to improve overall health by targeting fitness, bone density, muscle volume, and other health indicators that impact risk for metabolic syndrome, diabetes, and cardiovascular disease.¹⁻⁶ Inclusion in FES cycling programs is often impacted by bone status; programs and studies may exclude people with bone density that is a predetermined standard deviation below normal.^{7,8} Other programs base exclusion on lower extremity fracture history.^{9,10}

Even though people are excluded due to concerns about fractures during interventions, there is no evidence to support an increased fracture risk with FES cycling, with or without a fracture history. One study reported greater shear and less compressive forces at the knee with standing versus seated electrical stimulated exercise, suggesting greater risk with the knee flexed to 90°. ¹¹ However, the only fracture reported in the literature occurred during a high force flexed isometric contraction, ¹² not cycling. For people with SCI, lower extremity fractures typically occur during nontraumatic activities such as transfers ^{13,14} and are labeled

fragility fractures,¹⁵ with the majority occurring in the distal femur and proximal tibia.^{13,14} These fractures are thus caused by a different mechanism than what may occur during FES cycling. Furthermore, people with a history of low bone density and fragility fractures may have the greatest benefit from interventions such as FES cycling to decrease fracture risk by improving bone health.

This case report describes the outcomes for a man with chronic paraplegia who sustained an unrelated distal femur fracture while enrolled in an FES cycling study. There are 2 objectives of this case report. The first is to demonstrate that FES cycling can be safely resumed following fracture healing, and the second is to discuss the subject's musculoskeletal outcomes after he restarted the study once medically cleared after fracture healing.

Case Report

Subject

The subject was a 56-year-old male with a T4 American Spinal Injury Association Impairment Scale (AIS) A SCI sustained 4 years prior when he

Corresponding author: Therese E. Johnston, Department of Physical Therapy, Jefferson School of Health Professions, Thomas Jefferson University, 901 Walnut Street, Room 515, Philadelphia, PA 19107; phone: 215-503-6033; fax: 215-895-3151; e-mail: therese.johnston@jefferson.edu

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was hit by a car while he was bicycling. He was 1.8 m tall and weighed 77.1 kg. Other medical conditions included hypercholesterolemia, neurogenic bowel and bladder, benign prostatic hyperplasia (BPH), and a past history of bladder stones. Medications included Lipitor (cholesterol), Flo-Max (BPH), Boniva (to prevent osteoporosis), Zyrtec (seasonal allergies), vitamin D 1,000 IU/day, and calcium 600 mg/day. While he was taking Boniva, he did not have any imaging performed to diagnose osteoporosis prior to study enrollment. He had an FES cycle at home but reported not having used it in at least a year. He enrolled in the study to get back to cycling to improve his health. The subject worked full time from home. He signed an institutional review board–approved informed consent form before starting the study.

Intervention

The subject exercised at an outpatient rehabilitation center for 1 hour, 3 times a week^{2,16,17} using the RT300 FES cycle (Restorative-Therapies, Inc., Baltimore, MD). Cyclical FES of the bilateral quadriceps, hamstrings, and gluteal muscles was delivered via skin surface electrodes (Axelgaard, Inc., Fallbrook, CA) with stimulation parameters of 250 μ s, 33.3 Hz, and up to 140 mA (amplitude increased automatically to maintain a cadence of 20 rpm). A cadence of 20 rpm was used, as research indicates that higher resistances can be obtained at a lower cadence.^{18,19} Each session included 56 minutes of FES cycling and a 2-minute warm-up and 2-minute cool-down of passive cycling. Initial resistance was 0.5 Nm (lowest setting). When 60 minutes of cycling at 20 rpm was achieved, resistance automatically increased in 0.14 Nm increments. The goal was to complete 6 months of training with 80% adherence (at least 63 sessions).

Outcome measures

As the primary goal was to improve bone and muscle, measures included magnetic resonance imaging (MRI) to assess distal femur trabecular bone microarchitecture,²⁰ midfemur cortical bone macroarchitecture,²¹ and thigh muscle volume and dual-energy x-ray absorptiometry (DXA) to assess distal femur areal bone mineral density

(aBMD).²² Cortical and trabecular bone were both measured to obtain a more in-depth analysis of bone properties. All imaging tests were performed for the left lower extremity. Bone formation and resorption were assessed using bone turnover markers: serum bone specific alkaline phosphatase (BALP; formation marker), osteocalcin (formation marker), and urine n-telopeptide (N-Tx; resorption marker). Parathyroid hormone (PTH), 25-hydroxy vitamin D [25-(OH)D], and calcium levels were also monitored during the study.

For the MRI, one set of 80 high-resolution axial images (1 mm thickness/image) was collected beginning at the distal femoral condyles and extending to the femoral metaphysis using an 8-channel knee coil and 3D fast gradient echo sequence with a partial echo acquisition (echo time [TE] = 4.5 ms; repetition time [TR] = 30 ms; field of view [FOV] = 10 cm; 40° flip-angle; 15.6 kHz bandwidth). Measures of trabecular bone microarchitecture including apparent trabecular bone volume to total volume (appBV/TV), trabecular number (appTb.N, number of trabeculae/mm), trabecular thickness (appTb.Th, reflects size of trabeculae), and trabecular separation (appTb.Sp, amount of spacing between trabeculae) were estimated in 12 images beginning where the condyles ended and extending toward the femoral shaft using custom software developed using Interactive Data Language (IDL; Exelis Visual Information Solutions, Boulder, CO).²³ The region was chosen for analysis because it could be matched with aBMD in all participants, which was estimated using a high-resolution distal femur scan from DXA and the forearm scan mode.²⁴ The procedure for assessing trabecular bone microarchitecture is described in **Figure 1**. One set of proton density weighted images (0.8 cm thick; 0.6 cm spacing; FOV = 16 cm; TE = 17 ms; TR = 2,000 ms; phase = 512; frequency = 288) and one set of T1 weighted images (0.8 cm thick; 0.6 cm spacing; FOV = 24 cm; TE = 19 ms; TR = 550 ms; phase = 512; frequency = 288) were collected from the left middle-third of the femur using a torso PA coil.^{23,25} Using custom software developed with IDL, measures of cortical bone macroarchitecture (total bone volume and cortical bone volume) were estimated from the proton density weighted images and muscle volume was estimated using

Figure 1. Visual description of the procedure used to determine measures of trabecular bone microarchitecture in the distal femur using MRI. First, a 3-plane localizer that included coronal (A), sagittal, and axial images was used to set the region of interest. Second, 80 axial images (as indicated by the large white box in A) were collected beginning in the knee joint at the most distal end of the femur. Third, 12 images above the femoral condyles (subregion in A indicated with a white arrow) were then processed using the following procedure: (1) the raw images (B) were filtered and reversed in gray scale (C); (2) their trabecular bone region was manually identified (D); (3) 12 samples were taken from the cortical bone rim (E); (4) the 3 cortical bone samples with the highest signal intensity were used to separate the region of interest into bone and marrow phases (binarized) (F); and (5) measures of trabecular bone microarchitecture were calculated for each of the 12 images, as described by Majumdar et al,³¹ and the averages are reported.

the T1 weighted images. Areal BMD was measured via a high-resolution distal femur scan via DXA using the forearm scan mode.²⁴

Fracture

After completing 35 cycling sessions, the subject fell forward out of his wheelchair when he was exiting from a train and sustained a left nondisplaced distal femur fracture. The fracture was treated with 8 weeks of immobilization; his orthopedist cleared him to restart cycling 6 months after the fracture occurred. Due to the length of time away from cycling, the subject agreed to restart the study from the beginning. Baseline data were recollected and all imaging data were collected for the right lower extremity, the contralateral side, as postfracture bone remodeling could impact the results.

Results

In examining his initial left lower extremity prefracture baseline measures, it was noted that bone and muscle measures (aBMD,

trabecular bone microarchitecture, cortical bone macroarchitecture, muscle volume) were similar to those in the larger study sample enrolled in the randomized controlled trial (RCT) (**Table 1**). Bone formation markers (BALP, osteocalcin) were at the lower end of the range and 25-(OH)D levels were at the higher end.

After the fracture, new baseline measures for the right lower extremity showed a different picture with aBMD, trabecular bone measures, and osteocalcin at the extremes of values for subjects enrolled in the RCT (**Table 1**). Bone formation markers (BALP, osteocalcin) remained at the lower end of the range and 25-(OH)D levels at the higher end compared to the larger study sample. Osteocalcin declined further and N-Tx increased between the 2 baseline measures.

Following fracture healing, the subject successfully completed 65 cycling sessions. He only tolerated 0.5 Nm of resistance upon restarting despite reaching a maximum of 3.7 Nm before the fracture. By the end of the study, he was tolerating 5.3 Nm. Following intervention, small improvements were seen in trabecular bone

Table 1. Study measures

Measures	Baseline 1 (pre fracture)	Baseline 2 (post fracture)	Post intervention	Percent change	Means from RCT ^a
appBV/TV ^b	0.201	0.106	0.118	11.3	0.198 ± 0.069
appTb.N ^b , 1/mm	1.072	0.710	0.791	11.4	1.115 ± 0.289
appTb.Sp ^b , mm	0.756	1.264	1.127	-10.8	0.797 ± 0.319
appTb.Th ^b , mm	0.188	0.150	0.149	-0.7	0.174 ± 0.021
Total bone volume ^b	103.2	104.7	103.7	-1.0	93.1 ± 22.0
Cortical volume ^b , mm ³	42.2	46.6	47.7	2.4	51.3 ± 17.4
aBMD ^b , cm ²	0.703	0.311	0.306	-1.6	0.699 ± 0.330
Muscle volume of the thigh ^b , mm ³	1217	957	1138	18.9	1192 ± 513
BALP (norm 6.5-20.1 µg/L)	8.4	8.2	7.5	-8.5	13.2 ± 4.1
Osteocalcin (norm 11-50 ng/mL)	9	6	10	66.7	17.9 ± 7.2
N-Tx (norm 12-99 mg/dL)	43	59	62	5.1	52.7 ± 31.6
25-(OH)D (norm 30-100 ng/mL)	66.4	87.3	53.5	-38.7	40.4 ± 14.2
Calcium (norm 8.5-10.5 mg/dL)	9.8	9.4	9.8	4.3	9.6 ± 0.5
PTH (norm 11-67 pg/mL)	28	27	26	-3.7	25.5 ± 10.1

Note: appBV/TV = apparent trabecular bone volume to total volume; appTb.N = trabecular number; appTb.Th = trabecular thickness; appTb.Sp = trabecular separation; aBMD = areal bone mineral density; BALP = bone specific alkaline phosphatase; N-Tx = N-telopeptide; 25-(OH)D = vitamin D; PTH = parathyroid hormone.

^aPreintervention means (not published at this time).

^bCollected on left lower extremity before fracture and right lower extremity after fracture.

and muscle volume, specifically an increase in the number of trabeculae, cortical bone, and muscle volume and a decrease in spacing between trabeculae, suggesting positive changes in bone and muscle (**Table 1**). Bone markers did not change significantly before and after intervention, but differences were seen before and after the fracture (comparing the 2 baseline values) for 25-(OH)D and BALP.

Discussion

The subject in this case report safely resumed FES cycling following a distal femur fracture and made gains in trabecular and cortical bone and in muscle volume. This case may differ from that of a person with an SCI who sustains a fracture during a lower force activity such as passive range of motion exercise. This subject had a known trauma that resulted in a fracture. His initial trabecular bone microarchitecture measurements at the distal femur were similar to those of other subjects enrolled in the RCT, although his bone formation markers were lower. Upon restarting the RCT, trabecular bone microarchitecture in his right distal femur was even more compromised than what was initially demonstrated in his left distal femur, and his bone markers showed greater bone resorption with less bone formation compared to other subjects in the study. The combination of these 2 factors suggests a greater fracture risk. It is possible that the patient experienced additional bone loss following his fracture in his right, nonfractured, side. A notable difference between sides is unlikely as the subject had no prior history that would suggest a difference, and differences between sides were not found by Shields et al in their subjects after SCI.²⁶ However, it is not known whether the right lower extremity had greater deficits initially.

The decrease in bone formation markers and the increase in bone resorption markers between the 2 baselines suggest a possible systematic difference before and after the fracture that may have impacted bone. These bone marker values may still have been influenced by fracture healing and remodeling. Studies^{27,28} report that BALP and osteocalcin were elevated after ankle or distal forearm fractures and N-Tx increased only after

forearm fractures. All values remained elevated for up to 52 weeks. This timeframe of 52 weeks may be important, as our subject in this case report resumed cycling 6 months after the fracture and stable values may not have been reached. Another study reported that BALP and osteocalcin normally increase after fracture, but that delayed bone healing may be accompanied by only small changes in BALP and osteocalcin.²⁹ Therefore the subject in the case report may have had slower healing due to the effects of his SCI. It is not known why vitamin D values decreased, as the subject continued to take his daily supplements. His baseline testing was conducted during the winter, when 25-(OH)D concentration is lowest, and his postintervention testing was conducted during the summer, when 25-(OH)D concentration is highest.³⁰ PTH also has been shown to have a seasonal effect with the opposite trends seen,³⁰ and our subject showed no changes in PTH. Therefore, seasonal effects likely did not have a significant impact on 25-(OH)D values.

This case report demonstrates that people with SCI who have sustained a lower extremity fracture may still benefit from FES cycling and be able to cycle safely. It is not known whether the small positive changes in trabecular and cortical bone and in muscle volume that were seen after the subject completed the full cycling protocol will decrease his risk of future fractures. His aBMD, the most common clinical measure of bone, declined slightly. It has been reported that the amount of epiphyseal trabecular bone loss may better differentiate people with SCI with and without prior fractures,¹⁶ and our subject showed small gains in trabecular bone. The percent change in trabecular and cortical bone in this subject is similar to that seen by Frotzler et al,⁶ who reported significant changes in these measures.

Following the FES cycling intervention, N-Tx remained elevated and osteocalcin returned to prefracture levels. It is possible that systemic effects after fracture were still present. Therefore cycling may have helped to prevent further decline in bone; however this possibility cannot be confirmed. Waiting at least 52 weeks after fracture may have allowed bone marker levels to return to prefracture levels, thus allowing better assessment of changes

that can be attributed to the FES cycling protocol. However, starting earlier may have been of greater benefit to the subject. Further research is needed to better understand the effects of a fracture on bone and bone markers in people with SCI.

Future research should also examine ways to further increase resistance tolerated or loading to determine whether further gains in bone

and muscle can be made. Increasing the pulse duration greater than the 250 μ s used in this study and increasing the size and rate of resistance changes are suggested; however it is not known how these changes would impact the amount of time that subjects can cycle, which may also impact outcomes or the potential benefit to the musculoskeletal system.

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