

Original Article

Body weight supported treadmill training in acute spinal cord injury: impact on muscle and bone

LM Giangregorio^{*,1,2}, AL Hicks², CE Webber³, SM Phillips², BC Craven^{1,4}, JM Bugaresti⁵ and N McCartney²

¹Spinal Cord Rehabilitation Program, Toronto Rehabilitation Institute, Ontario, Canada; ²Department of Kinesiology, McMaster University, Ontario, Canada; ³Department of Nuclear Medicine, Hamilton Health Sciences, Ontario, Canada; ⁴Department of Medicine, University of Toronto, Ontario, Canada; ⁵Department of Medicine, McMaster University, Ontario, Canada

Design: Longitudinal prospective case series.

Objective: To evaluate the impact of early introduction postspinal cord injury (SCI) of twice-weekly body-weight supported treadmill training (BWSTT) on muscle and bone.

Setting: Centre for Health Promotion and Rehabilitation, McMaster University, Canada.

Methods: Five individuals who had sustained traumatic SCI within 2–6 months participated in the study. Bone mineral densities (BMD) of proximal femur, distal femur, proximal tibia and lumbar spine were measured before and after training, as well as muscle cross-sectional area (CSA), BMD and bone geometry at mid-femur and proximal tibia. Serum osteocalcin and urinary deoxypyridinoline were measured at baseline, and after 24 and 48 sessions of training.

Results: All participants experienced increased muscle CSAs, ranging from 3.8 to 56.9%. Reductions in BMD were evident in all participants at almost all lower limb sites after training, ranging in magnitude from –1.2 to –26.7%. Lumbar spine BMD changes ranged from 0.2 to –7.4%. No consistent changes were observed in bone geometry. BWSTT did not alter the expected pattern of change in bone biochemical markers over time. The individual with the greatest improvement in ambulatory ability demonstrated the smallest reduction in lower limb BMD. Conversely, the individual who completed the fewest BWSTT sessions demonstrated the greatest reductions in BMD.

Conclusions: Twice-weekly BWSTT appeared to partially reverse muscle atrophy after SCI, but did not prevent bone loss. Larger, controlled trials should evaluate whether relative preservation of bone loss occurs with regular BWSTT following acute SCI.

Sponsorship: Ontario Neurotrauma Foundation.

Spinal Cord (2005) **43**, 649–657. doi:10.1038/sj.sc.3101774; published online 21 June 2005

Keywords: treadmill; walking; bone density; muscle; body weight support; osteoporosis

Introduction

Osteoporosis and muscle atrophy are frequently cited complications after spinal cord injury (SCI). Changes in muscle commence soon after injury and include both reductions in fiber size as well as fiber type changes.^{1,2} For example, Castro *et al*³ noted that, when compared to controls without SCI, average muscle cross-sectional areas (CSAs) were 18–46% lower in individuals who had sustained SCI only 6 weeks earlier. A further decline in average thigh and lower limb muscle CSA of 12–24% was observed at 6 months postinjury.³ Bone loss after SCI has been reported to be rapid and

linear in the acute stages, establishing a new, lower steady-state bone mass level 1–2 years after the event.⁴ Other studies have suggested that bone loss may not plateau as previously reported.^{5–7} A recent study demonstrated that losses in both trabecular bone and cortical bone at the tibia persisted for more than 3 years after SCI, and that there was a large inter-individual variability in the pattern of bone loss.⁵ Bone loss after SCI may increase fracture risk; the fracture rate in the SCI population has been reported to be from 1 to 6% of patients.^{8–11} Common fracture sites appear to be those around the knee, such as the distal femur or proximal tibia.^{8,10} Fractures during transfers from bed to chair, or while being turned in bed, have been reported in SCI.^{10–12}

*Correspondence: L Giangregorio, Lyndhurst Centre, Toronto Rehabilitation Institute, 520 Sutherland Drive, Toronto, ON, Canada M4G 3V9

Interventions have been implemented in the acute stages following SCI as a potential strategy to ameliorate the musculoskeletal changes that occur. Functional electrical stimulation (FES) has been demonstrated to have a positive impact on muscle CSA when employed in both the acute and chronic stages after SCI.^{13–17} The effects of FES on the skeleton in the acute stages after SCI are less well established, and conflicting studies point to the need for further study before any conclusions can be made.^{18,19} Body weight supported treadmill training (BWSTT) is an intervention that allows individuals with SCI to walk on a treadmill with some of their body weight externally supported. Therapists aid in the movement of the lower limbs during ambulation on the treadmill, if necessary, to mimic normal gait. Individuals with SCI who train with BWSTT have demonstrated improvements in their treadmill speed and exercise duration, and some have shown functional improvements in their ambulatory abilities.^{20–22} Since BWSTT involves mechanical loading of the lower limbs, it was hypothesized that it might prevent bone loss and prevent muscle atrophy in individuals with acute SCI. Previous work incorporating either standing or treadmill walking exercise five times per week for 25 weeks in individuals who were 1–4 weeks post-SCI resulted in no loss or only moderate losses in trabecular bone, compared to subjects immobilized because of medical complications, who lost 7–9% of trabecular bone at the tibia.²³ No studies have evaluated the effects of treadmill walking on muscle and bone together in acute SCI. The current study reports the impact of twice-weekly BWSTT for 48 sessions on bone and muscle in individuals with acute SCI.

Methods

Participants

The study was approved by the local Research Ethics Board of Hamilton Health Sciences. Participants were recruited via contact with medical staff at The Central West Regional SCI Rehabilitation Program at Hamilton Health Sciences. Five individuals who had sustained a traumatic SCI from 66 to 170 days prior to starting the intervention agreed to participate and provided informed written consent (Table 1). Exclusion criteria were as follows: cardiac pacemaker or documented heart disease; uncontrolled cardiac dysrhythmia; chronic

obstructive lung disease; uncontrolled autonomic dysreflexia; recent fracture; tracheostomy; bilateral hip and knee flexion contractures greater than 20°; drug addiction; age > 60 years; persons > 40 years who failed the first stage of a progressive incremental exercise tolerance test; severe muscle shortening or severe skin ulcerations. None of the participants were known to have diseases that would affect bone metabolism. All participants continued conventional in-patient rehabilitation until they were discharged, and continued outpatient rehabilitation for the duration of the study. None of the participants were taking bisphosphonates during the study.

Intervention: BWSTT

The Woodway Loco-system (Woodway USA Inc., Waukesha, WI, USA) is a treadmill with an accompanying suspension system. Weight stacks attached to cables can be used to provide graded vertical support for an individual to stand on the treadmill. Participants are fitted into a specialized harness that is secured to overhead cables. During the first training session, a level of body weight support (BWS) was chosen for each participant so that they could maintain an upright trunk and their knees did not buckle in quiet standing. The treadmill training strategy focused on proper weight shifting and weight bearing during the loading phase, and on maintenance of an upright torso. The initial sessions comprised of walking bouts of 5–15 min in duration. Walking duration during each bout was increased gradually, according to tolerance (a duration that was acceptable to the patient and did not cause dizziness or excessive fatigue). Most participants began training with 60% or greater of their body weight externally supported, walking at treadmill speeds of 0.6 km/h or less. Over the course of training, both percentage of BWS and treadmill speed were modified on an individual basis to increase training intensity, following the strategy of first unloading a portion of the BWS, then increasing treadmill speed at each level of BWS. The maximum number of walking bouts per training session was three. Trained assistants aided in BWSTT; one stood behind the participant to provide trunk support and help initiate weight shifting, and the other two were positioned beside the lower limbs to assist with stepping and limb control.

Table 1 BWSTT participants with acute SCI

ID	Sex	Age (years)	Height (cm)	Pre-injury weight (kg)	Lesion level ^a	ASIA classification	Days postinjury at intervention start
1	M	26	173	90.7	C6	B	66
2	M	26	188	81.6	C3	B	82
3	F	40	152	52.2	C8	B	94
4	F	37	169	90.7	C5	B	159
5	F	19	180	72.6	C6	C	170

^aC (lesion level) = cervical spine

Outcome measures

Walking duration, walking speed and amount of BWS provided were recorded after each training session. A modified version of a scale developed by Wernig *et al.*^{22,24} described previously²⁰ was used to evaluate over-ground walking abilities at each 3-month time point.

Bone biochemical markers First morning urine samples and venous blood samples were taken at baseline, and after 24 and 48 training sessions. Serum and urine aliquots were stored at -80°C for later analysis. Urinary deoxypyridinoline (DPD) and serum osteocalcin (OC) were analyzed using competitive enzyme immunoassays (Quidel Corporation, San Diego, CA, USA) and compared to reference ranges. Samples were processed in duplicate. Urinary DPD data were corrected for urinary creatinine concentration, determined by a modified Jaffe method.²⁵

Bone mineral density, muscle mass, muscle CSA Dual-energy X-ray absorptiometry (DXA, Hologic 4500A densitometer Bedford, MA, USA) scans were performed at baseline and after training cessation to obtain bone mineral density (BMD) (g/cm^2) measurements of the lumbar spine, right and left proximal femora, right distal femur and right proximal tibia. A whole body scan was performed to measure whole body BMD as well as muscle and fat masses. The coefficient of variation for the lumbar spine quality control phantom during the period of the study was 0.52%. The proximal femur, lumbar and whole body scans were analyzed using commercially available software from Hologic. Distal femur and proximal tibia scans were analyzed using a modified lumbar spine protocol, as described previously.²⁶

A General Electric CTI Scanner (GE, Milwaukee, WI, USA) was used to perform computed tomography (CT) scans at baseline and after cessation of training. A scout scan was taken of the lower limbs to determine the femur and tibia lengths, and 5 mm slices were taken at two sites: 60% of femur length, starting from the distal end and measuring proximally, and at the point of maximal lower limb muscle CSA, defined to be 66% of the tibia length, starting from the distal end and measuring proximally (from here called thigh and lower leg sites, respectively). The system parameters used were as follows: slice thickness 5 mm, pixel matrix 512×512 , and exposure factors of 120 kV, 200 mA and standard reconstruction algorithm.

CT scans were analyzed using a validated software program (BonAlyse 1.3, BonAlyse Oy, Jyväskylä, Finland), according to the manufacturer's instructions. Thresholds -270 to -101 Hounsfield Units (HU) were used to identify fat, and thresholds -101 to 270 HU were used to identify muscle. BonAlyse was used to calculate muscle CSA (mm^2), bone CSA (mm^2) and volumetric bone mineral density (vBMD, mg/cm^3) at thigh and

lower leg sites. Thresholds for outer and inner borders of bone were 280 and $70 \text{ mg}/\text{cm}^3$, respectively. Maximum (I_{max}) and minimum (I_{min}) cross-sectional moments of inertia and polar cross-sectional moment of inertia (I_{polar}) were also calculated for thigh and lower leg slices. We have determined that muscle and bone variables obtained from CT scans using our scanner can be measured with reproducibility, as assessed via the root mean squared coefficient of variation,²⁷ of less than 2% for area and density variables and less than 2.6% for moment of inertia variables. For both sites, values obtained for right and left legs were averaged for each variable in each participant.

Design and statistical analyses A longitudinal, prospective cases series was used in which participants completed 48 sessions of twice-weekly BWSTT over a period of 6–8 months. DXA scan results were normalized to T scores using age- and sex-specific normative values provided with the Hologic QDR 4500A software. Since changes in muscle CSA occur quite rapidly after SCI, we recruited non-SCI control subjects to provide estimates of pre-injury muscle CSAs for comparison. Controls were matched to participants as follows: same gender, same age within 4 years, same height ± 6 cm and same weight ± 9.1 kg. The significance of changes in muscle CSA, fat CSA and bone geometry variables was evaluated by comparing the observed change to the method error. If the observed change for a given variable was greater than the RMSSD for that variable multiplied by three, it can be stated with 99% confidence that the change that occurred was greater than that expected resulting from measurement error.

Results

Adherence and adverse events

Participants were considered adherent with the intervention if they were able to complete the required 48 sessions in a maximum of 8 months. One individual, participant 4, was not able to fulfill this requirement. Therefore, for all of her outcome measures, the last time point did not represent values after 48 training sessions, rather they were taken approximately 8 months after she entered the study. Average (\pm SD) adherence (the number of sessions completed divided by the total possible sessions $\times 100$) for all five subjects during the BWSTT study was $78.0 (\pm 18.4)$ percent. The average number of sessions completed per week was $1.6 (\pm 0.4)$. Excluding subject 4, the average (\pm SD) adherence was $85.4 (\pm 8.4)\%$, and the average number of sessions completed per week was $1.7 (\pm 0.2)$. No adverse events were reported.

Treadmill and over-ground walking abilities

At the beginning of training, all participants required some assistance with both legs while walking on the treadmill (Table 2). Of the five participants, only

Table 2 Changes in % BWS, treadmill speed and walking duration with BWSTT

ID	% Body weight support			Treadmill speed (km/h)			Walking duration per bout (min)		
	B	24	48	B	24	48	B	24	48
1	94	55	45	0.5	1.6	2	5	10	10
2	87	52	57	0.5	1.7	1.7	5	10	10
3	91	77	66	0.7	1.7	1.8	5	12	15
4	97	55	N/A	0.5	1.7	N/A	5	7	N/A
5	54	0	0	0.6	1.0	0.7	5	10	10

B = baseline, 24 = 24 sessions, 48 = 48 sessions

N/A = not applicable

participant 5 improved her over ground walking; she progressed from no walking initially to being able to walk greater than five steps with a rolling frame, or going from a score of 0 on the Modified Wernig Scale to a score of 7. The amount of BWS required during treadmill walking decreased with training for all participants, although only participant 5 was able to reduce BWS to zero. All participants were able to increase the speed at which they walked on the treadmill during training, and most were also able to increase walking duration.

Bone biochemical markers

Levels of osteocalcin were at the high end of the normal range (where normal is 3.7–10.0 ng/ml for females and 3.4–9.1 ng/ml for males) at baseline and throughout the study (Figure 1). When compared to the mid-point of the normal range, deoxypyridinoline levels were approximately 6.5–21 times higher than the normal range at baseline (where normal is 3.0–7.4 nmol DPD/mmol Cr for females and 2.3–5.4 nmol DPD/mmol Cr for males). After 24 and 48 sessions of training, DPD levels were reduced compared to baseline, but on average were still 2.4 to 10 times higher than the normal ranges (Figure 2).

BMD and body composition

Applying the World Health Organization criteria for osteoporosis to the proximal femur BMD data, one participant would have been considered osteopenic at baseline, and at the end of the study two more people became osteopenic and one had progressed to osteoporosis. All participants experienced reductions in total proximal femur BMD, ranging from 4.3 to 22.6% (Table 3). Similar reductions in proximal tibia and distal femur BMD were noted in almost all participants after BWSTT. Of note, the individual experiencing the smallest reductions in BMD at almost all lower limb sites was the same person who made the greatest improvements in ambulatory abilities. Also, the largest decreases in BMD at all lower limb sites occurred in subject 4, who did not complete 48 sessions of training. Lumbar spine BMD was reduced by more than 2% in three of the five participants.

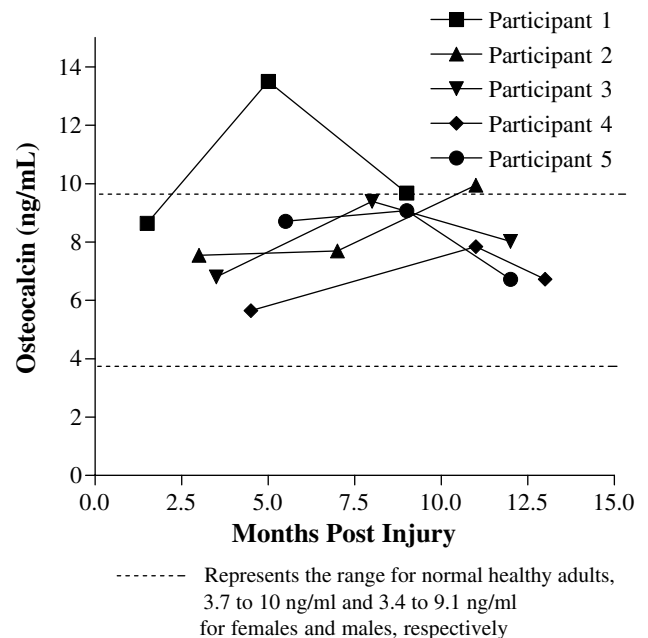
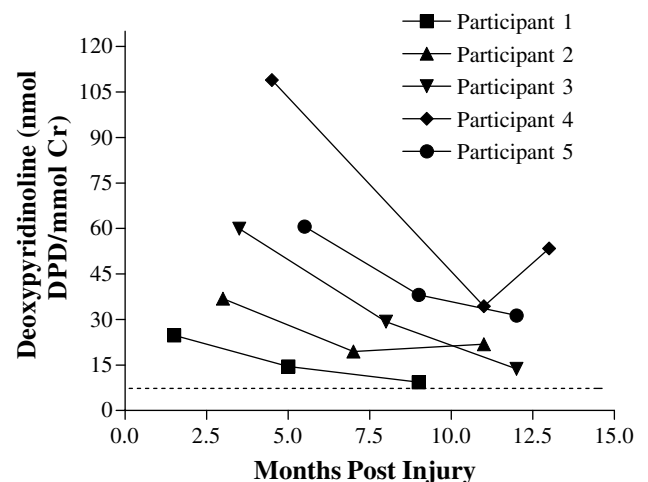
**Figure 1** Osteocalcin levels at baseline, and after 24 and 48 sessions of BWSTT, relative to time postinjury**Figure 2** Deoxypyridinoline levels at baseline, and after 24 and 48 sessions of BWSTT, relative to time postinjury

Table 3 BMD at lower limb sites, lumbar spine and whole body pre- and post-BWSTT for each participant

Variable	Participant				
	1	2	3	4	5
<i>Lumbar spine BMD (g/cm²)</i>					
Baseline	1.020	1.063	0.972	1.225	1.186
After BWSTT	1.022	1.023	0.936	1.134	1.174
% change	0.2	-3.8	-3.7	-7.4	-1.0
<i>Proximal femur BMD (g/cm²)</i>					
Baseline	1.245	0.935	0.929	0.980	1.036
After BWSTT	1.154	0.747	0.835	0.758	0.991
% change	-7.3	-20.1	-10.1	-22.6	-4.3
<i>Proximal tibia BMD (g/cm²)</i>					
Baseline	0.829	0.933	0.952	1.105	0.985
After BWSTT	0.950	0.879	0.855	0.894	0.973
% change	14.6	-5.8	-10.2	-19.1	-1.2
<i>Distal femur BMD (g/cm²)</i>					
Baseline	1.209	1.032	0.901	1.141	1.211
After BWSTT	1.093	0.944	0.844	0.836	1.056
% change	-9.6	-8.5	-6.3	-26.7	-12.8
<i>Whole body BMD (g/cm²)</i>					
Baseline	1.215	1.204	1.137	1.223	1.193
After BWSTT	1.191	1.138	—	1.14	1.202
% change	-2.0	-5.5	—	-6.8	0.8
<i>60% femur BMD (mg/cm³)</i>					
Baseline	816.8	775.7	821.5	782.0	777.0
After BWSTT	747.1	776.0	793.0	667.0	770.2
% change	-8.5	0	-3.5	-14.7	-0.9
<i>66% tibia BMD (mg/cm³)</i>					
Baseline	776.3	783.9	870.5	794.0	754.5
After BWSTT	686.1	784	829.5	691.3	739.4
% change	-11.6	0	-4.7	-12.9	-2.0

On average, total body lean mass and fat mass were increased after 48 sessions of BWSTT compared to baseline; however, participant 5 experienced a reduction in whole body lean mass. The average increase in lean mass was of 3.8%, whereas the average increase in fat mass was 31%.

Muscle CSA

All participants experienced an increase in thigh and calf muscle and fat CSA after BWSTT (Table 4). The increase in thigh muscle CSA was greater than three times the measurement error for two of the five individuals (participants 3 and 4), and greater than the measurement error multiplied by two in participant 5. For calf CSA, the increase in muscle CSA was greater than three times the measurement error in four of five participants. Increases in thigh and calf fat CSA were greater than the measurement error in almost all cases. At baseline, the participants with SCI had thigh and calf

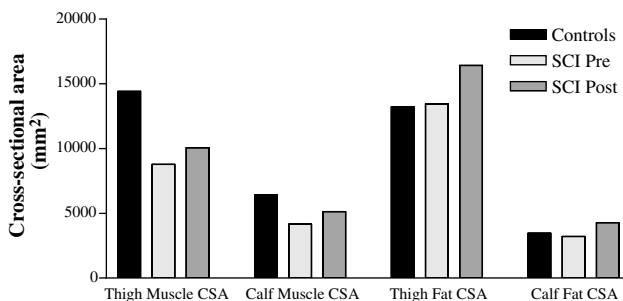
muscle CSAs that were on average 60 and 65% of control values, respectively (Figure 3). Fat CSAs for the thigh and calf in the SCI participants were 113 and 100% of controls, respectively, at baseline. After 48 sessions of BWSTT, the participants with SCI had increases in muscle CSA so that their values were on average 72 and 79% of controls at the thigh and calf, respectively (Figure 3). The corresponding fat CSAs were 142 and 133% of control values.

Bone density and geometry measured with computed tomography

There were definite reductions in volumetric BMD at both the femur and tibia sites in several subjects (Table 3). With respect to all other variables the only changes that were greater than three times the measurement error were reductions of 3.6 and 2.5% in bone area at femur and tibia sites, respectively, for participant 4,

Table 4 Lean and fat mass before and after BWSTT in each participant

Variable	Participant				
	1	2	3	4	5
<i>Lean mass (kg)</i>					
Baseline	52.7	46.8	29.4	34.9	46.9
After BWSTT	55.9	47.9	—	36.8	43.8
% change	5.9	2.3	—	5.3	−6.7
<i>Fat mass (kg)</i>					
Baseline	26.6	11.7	20.6	33.8	25.2
After BWSTT	27.1	17.3	—	47.2	38.3
% change	1.9	47.2	—	39.6	52.0
<i>Mid-thigh muscle CSA (mm²)</i>					
Baseline	13979	9478	5438	5402	9567
After BWSTT	14553	9891	8531	6970	10328
% change	4.1	4.4	56.9	29.0	7.9
<i>Lower leg muscle CSA (mm²)</i>					
Baseline	7001	3396	3922	2587	3884
After BWSTT	9007	3524	4295	3974	4772
% change	29.7	3.8	9.5	53.6	22.9
<i>Mid thigh fat CSA (mm²)</i>					
Baseline	13794	7033	13707	18573	14098
After BWSTT	16209	10859	15124	21482	18353
% change	17.5	54.4	10.3	15.7	30.2
<i>Lower leg fat CSA (mm²)</i>					
Baseline	2944	1452	3422	5269	2930
After BWSTT	3693	1989	4625	7419	3618
% change	25.4	37.0	35.1	40.8	23.5

**Figure 3** Muscle CSAs at the thigh and calf in individuals with acute SCI before and after BWSTT, compared to non-SCI individuals

and a 3% increase in the polar moment of inertia at the 60% femur site in participant 5.

Discussion

Previous studies of shorter duration demonstrated that BWSTT could improve walking abilities in both chronic and acute incomplete SCI.^{22,28–30} The current study represents the first prospective, longitudinal study

evaluating the effects of BWSTT on bone and muscle in individuals with acute SCI.

Effects of BWSTT on walking abilities

BWSTT allows participants to strengthen the lower limb musculature and focus on improving motor skills without having to bear their full body weight. As locomotion improves the amount of support can be reduced. It has been suggested that BWSTT is more effective than conventional rehabilitation in the acute stages after SCI for retraining locomotion.²² With locomotor training, the spinal cord can elicit electromyographic activity in muscles resembling that observed during locomotion.^{28,29,31–33} However, most studies in SCI concur that functional improvements in walking with locomotor training can only be achieved in individuals with incomplete lesions, suggesting that other factors are important for the attainment of over-ground walking abilities.^{22,28–30}

One participant made a striking improvement in treadmill walking abilities and progressed to over-ground walking with a rolling frame. Given that this participant was the only one with a motor incomplete lesion (ASIA C), it was expected that she would have the

greatest potential for improvement. However, this participant entered the BWSTT study later than the other participants (5.5 months postinjury) and had completed conventional in-patient rehabilitation. The likelihood of spontaneous recovery decreases substantially 6 months after injury,³⁴ so her improvements in ambulation were, at least in part, attributable to training. Based on the ASIA impairment classifications of the other participants, it would be less likely that they would be able to achieve any degree of independent ambulation.

Effects of BWSTT on the skeleton

BWSTT did not prevent bone loss from occurring after acute SCI. The small fluctuations in the bone formation marker osteocalcin and the larger changes in the bone resorption marker deoxypyridinoline both demonstrated patterns similar to those normally occurring after acute SCI in the absence of any intervention.³⁵ Similarly, the DXA-measured reduction in BMD was evident at all lower limb sites in the participants. A unique observation is that four of the five participants experienced reductions of lumbar spine BMD and three experienced reductions greater than 2%, indicating that bone loss after SCI is not limited to the lower limbs. Lumbar spine BMD has been documented to be increased, decreased or unchanged after SCI.^{6,36–40} However, the changes in lumbar spine BMD were much smaller compared to the decrement in BMD that occurred at the lower limb sites, reflecting the importance of mechanical loading for the maintenance of bone mass in the lower limbs.

The participant who made the largest gains in ambulatory capacity (participant 5) experienced the smallest changes in bone mineral density at almost all sites, whereas the participant whose attendance did not fulfill the adherence criteria (participant 4) lost the most bone, had the highest levels of the bone resorption marker deoxypyridinoline and had the lowest levels of osteocalcin throughout the study. Similarly, reductions in bone area measured using computed tomography were only evident in participant 4. Clearly, we would require more participants to fully test the relationships among ambulatory capacity, training compliance and attenuation of bone loss; however, these preliminary data are suggestive that such a relationship exists. It is also important to note that participant 5 was the only individual with an ASIA C classification, and may have lost less bone than the others in the absence of intervention. Our results are not consistent with a previous study, where walking on a treadmill with weight support or passive standing resulted in attenuated bone loss in individuals with acute SCI compared to the loss experienced in a control group.²³ However, in that study the control group consisted of 4 individuals excluded from the weight-bearing intervention based on predetermined criteria, such as lower motor neuron involvement, other lesions or infirmity, and these criteria might have made them more likely to experience bone

loss than the weight-bearing group.²³ In that study, bone loss experienced by the group that performed treadmill walking was not significantly different than that of the group that did passive standing.²³ Given the other potential advantages of BWSTT over conventional rehabilitation (ie improved cardiac performance,⁴¹ muscle atrophy reversal⁴²) more controlled studies are necessary to ascertain whether BWSTT is more effective than conventional rehabilitation for attenuating the physiological changes that can occur after SCI.

It is possible that the level of mechanical strain on the bone imposed by the BWSTT was not sufficient to prevent bone loss, especially since most participants still required some BWS by the end of the study, and most walking speeds were below what would be considered a normal walking speed. Also, the intervention lasted a total of less than 1 h twice weekly, meaning that even if the level of strain on bone was at a sufficient level to be osteogenic, the participants' bones experienced that level of strain only infrequently. Recent research has suggested that shorter, more frequent exercise bouts may be the best means for preventing bone loss or increasing bone mass.⁴³ Finally, a component of the strain on bone comes from the strain imposed by muscle contraction pulling on the bone. Even at baseline, participants had already experienced substantial muscle atrophy when compared to matched control subjects, so the strain associated with muscle contraction would have been reduced.

Effects of BWSTT on muscle and fat

There is a tendency for individuals with SCI to have increased fat mass relative to non-SCI individuals.^{44,45} BWSTT did not prevent an increase in fat deposition in our participants with acute SCI. This may be related to reductions in overall activity level and/or metabolic rate that occurred with immobilization and muscle atrophy and/or impairment in catecholamine release associated with lesions above T6 and subsequent lack of inhibition of hormones involved in fat metabolism.

The observation that BWSTT results in increases in thigh and calf muscle CSA in individuals with acute SCI is exciting. Although we hypothesized that BWSTT would have a positive impact on muscle, we anticipated only a prevention of muscle atrophy, not an increase in muscle. Treadmill walking would not normally be considered a method for inducing muscle hypertrophy, but in individuals who have experienced a dramatic reduction in muscle activity, the walking stimulus may represent a considerable challenge to the atrophied muscle. It is difficult to elucidate why some participants experienced changes in muscle of a greater magnitude than others, but it may be related to residual motor function, injury level and exercise intensity achieved. These results indicate that the potential to increase muscle CSA with BWSTT exists even in individuals with motor complete lesions. Since the highest rate of atrophy occurs in the first few weeks of immobilization,

strategies to prevent atrophy should be implemented as soon as possible after SCI.

Clinical relevance

Individuals with SCI have a reduced metabolic rate and are predisposed to carbohydrate and lipid abnormalities, in direct relation to their level of inactivity.^{45–47} A benefit of more muscle mass may be improved glucose tolerance and increased metabolic rate, leading to less fat deposition. A recent study by our research group demonstrated improved glucose regulation after BWSTT in individuals with chronic incomplete SCI.⁴⁸ BWSTT has been demonstrated to have a beneficial effect on blood lipid profiles in individuals with chronic SCI, with significant reductions in total and low-density lipoprotein cholesterol, as well as decreases in total cholesterol/high-density lipoprotein cholesterol ratios.⁴² Increased lower limb muscle mass may also reduce seating pressures, and along with improved peripheral blood flow, may reduce the prevalence of decubitus ulcers.¹³

Limitations and future directions

Unless a large number of participants are recruited, it is difficult to establish adequate matching between control and intervention groups in the SCI population due to inter-individual variability in characteristics such as age, gender, level of lesion, ASIA score and time postinjury. Indeed, adequate matching may never be possible in this heterogeneous group. Future studies of BWSTT should aim to incorporate multiple centers in order to include a greater number of participants. The inclusion criteria that are chosen for future BWSTT studies should be appropriate to the outcomes of interest. Outcome measures that may be relevant to the participants, such as lower limb edema or objective measures of spasticity, should also be considered.

Conclusions

In summary, twice-weekly BWSTT for approximately 6 months prevented and/or partially reversed lower limb muscle atrophy in individuals with acute SCI. Individuals participating in regular BWSTT demonstrated improved ambulation on the treadmill, and an individual with a motor incomplete lesion was able to achieve over-ground ambulation after BWSTT. BWSTT did not prevent bone loss in the lower limbs. Multicenter trials are required to further clarify the effects of BWSTT on important health outcomes.

Acknowledgements

We gratefully acknowledge the support of the Ontario Neurotrauma Foundation (ONF) for providing the operating funds for this study awarded to A Hicks. L Giangregorio was a recipient of a CIHR Bone Scholar Award. We also express sincere thanks to Becky Smith, Howard Hollingham, all the volunteer trainers and the study participants for their dedication to this research.

References

- 1 Burnham R, Martin T, Stein R, Bell G, MacLean I, Steadward R. Skeletal muscle fibre type transformation following spinal cord injury. *Spinal Cord* 1997; **35**: 86–91.
- 2 Castro MJ, Apple Jr DF, Staron RS, Campos GE, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* 1999; **86**: 350–358.
- 3 Castro MJ, Apple Jr DF, Hillegass EA, Dudley GA. Influence of complete spinal cord injury on skeletal muscle cross-sectional area within the first 6 months of injury. *Eur J Appl Physiol Occup Physiol* 1999; **80**: 373–378.
- 4 Garland DE et al. Osteoporosis after spinal cord injury. *J Orthopaed Res* 1992; **10**: 371–378.
- 5 de Bruin ED, Vanwanseele B, Dambacher MA, Dietz V, Stussi E. Long-term changes in the tibia and radius bone mineral density following spinal cord injury. *Spinal Cord* 2005; **43**: 96–101.
- 6 Sabo D, Blaich S, Wenz W, Hohmann M, Loew M, Gerner HJ. Osteoporosis in patients with paralysis after spinal cord injury. A cross sectional study in 46 male patients with dual-energy X-ray absorptiometry. *Arch Orthop Trauma Surg* 2001; **121**: 75–78.
- 7 Szollar SM, Martin EM, Parthemore JG, Sartoris DJ, Deftos LJ. Densitometric patterns of spinal cord injury associated bone loss. *Spinal Cord* 1997; **35**: 374–382.
- 8 Comarr AE, Hutchinson RH, Bors E. Extremity fractures of patients with spinal cord injuries. *Am J Surg* 1962; **103**: 732–739.
- 9 Nottage WM. A review of long-bone fractures in patients with spinal cord injuries. *Clin Orthop* 1981; **(155)**: 65–70.
- 10 Ragnarsson KT, Sell GH. Lower extremity fractures after spinal cord injury: a retrospective study. *Arch Phys Med Rehabil* 1981; **62**: 418–423.
- 11 Vestergaard P, Krogh K, Rejnmark L, Mosekilde L. Fracture rates and risk factors for fractures in patients with spinal cord injury. *Spinal Cord* 1998; **36**: 790–796.
- 12 Freehafer AA, Hazel CM, Becker CL. Lower extremity fractures in patients with spinal cord injury. *Paraplegia* 1981; **19**: 367–372.
- 13 Baldi JC, Jackson RD, Moraille R, Mysiw WJ. Muscle atrophy is prevented in patients with acute spinal cord injury using functional electrical stimulation. *Spinal Cord* 1998; **36**: 463–469.
- 14 Belanger M, Stein RB, Wheeler GD, Gordon T, Leduc B. Electrical stimulation: can it increase muscle strength and reverse osteopenia in spinal cord injured individuals? *Arch Phys Med Rehabil* 2000; **81**: 1090–1098.
- 15 Dudley GA, Castro MJ, Rogers S, Apple Jr DF. A simple means of increasing muscle size after spinal cord injury: a pilot study. *Eur J Appl Physiol Occup Physiol* 1999; **80**: 394–396.
- 16 Pacy PJ, Hesp R, Halliday DA, Katz D, Cameron G, Reeve J. Muscle and bone in paraplegic patients, and the effect of functional electrical stimulation. *Clin Sci (London)* 1988; **75**: 481–487.
- 17 Scremin AM, Kurta L, Gentili A, Wiseman B, Perell K, Kunkel C et al. Increasing muscle mass in spinal cord injured persons with a functional electrical stimulation exercise program. *Arch Phys Med Rehabil* 1999; **80**: 1531–1536.
- 18 Eser P, de Bruin ED, Telley I, Lechner HE, Knecht H, Stussi E. Effect of electrical stimulation-induced cycling on bone mineral density in spinal cord-injured patients. *Eur J Clin Invest* 2003; **33**: 412–419.

- 19 Hangartner TN, Rodgers MM, Glaser RM, Barre PS. Tibial bone density loss in spinal cord injured patients: effects of FES exercise. *J Rehabil Res Dev* 1994; **31**: 50–61.
- 20 Hicks AL et al. Long-term body-weight-supported treadmill training and subsequent follow-up in persons with chronic SCI: effects on functional walking ability and measures of subjective well-being. *Spinal Cord* 2005; **43**: 291–298.
- 21 Hicks AL, McCartney N, Phillips S, Smith M, Radforth L. The effects of long-term body-weight supported treadmill training on walking ability in persons with incomplete spinal cord injury. *Can J Appl Physiol* 2002; **27**: S21.
- 22 Wernig A, Muller S, Nanassy A, Cagol E. Laufband therapy based on 'rules of spinal locomotion' is effective in spinal cord injured persons [published erratum appears in *Eur J Neurosci* 1995 Jun 1; 7(6): 1429]. *Eur J Neurosci* 1995; **7**: 823–829.
- 23 de Bruin ED, Frey-Rindova P, Herzog RE, Dietz V, Dambacher MA, Stussi E. Changes of tibia bone properties after spinal cord injury: effects of early intervention. *Arch Phys Med Rehabil* 1999; **80**: 214–220.
- 24 Wernig A, Nanassy A, Muller S. Maintenance of locomotor abilities following Laufband (treadmill) therapy in para- and tetraplegic persons: follow-ups studies. *Spinal Cord* 1998; **36**: 744–749.
- 25 Bowers LD, Wong ET. Kinetic serum creatinine assays. II. A critical evaluation and review. *Clin Chem* 1980; **26**: 555–561.
- 26 Moreno JC. *Protocol for using dual photon absorptiometry software to measure BMD of distal femur and proximal tibia*. (Dissertation) McMaster University, 2001.
- 27 Gluer CC, Blake G, Lu Y, Blunt BA, Jergas M, Genant HK. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. *Osteoporos Int* 1995; **5**: 262–270.
- 28 Dietz V, Colombo G, Jensen L. Locomotor activity in spinal man. *Lancet* 1994; **344**: 1260–1263.
- 29 Dietz V, Colombo G, Jensen L, Baumgartner L. Locomotor capacity of spinal cord in paraplegic patients [see comments]. *Ann Neurol* 1995; **37**: 574–582.
- 30 Wernig A, Muller S. Laufband locomotion with body weight support improved walking in persons with severe spinal cord injuries. *Paraplegia* 1992; **30**: 229–238.
- 31 Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR. Human lumbosacral spinal cord interprets loading during stepping. *J Neurophysiol* 1997; **77**: 797–811.
- 32 Pinter MM, Dimitrijevic MR. Gait after spinal cord injury and the central pattern generator for locomotion. *Spinal Cord* 1999; **37**: 531–537.
- 33 Wirz M, Colombo G, Dietz V. Long term effects of locomotor training in spinal humans. *J Neurol Neurosurg Psychiatry* 2001; **71**: 93–96.
- 34 Behrman AL, Harkema SJ. Locomotor training after human spinal cord injury: a series of case studies. *Phys Ther* 2000; **80**: 688–700.
- 35 Roberts D et al. Longitudinal study of bone turnover after acute spinal cord injury. *J Clin Endocrinol* 1998; **83**: 415–422.
- 36 Biering-Sorensen F, Bohr HH, Schaadt OP. Longitudinal study of bone mineral content in the lumbar spine, the forearm and the lower extremities after spinal cord injury. *Eur J Clin Investigat* 1990; **20**: 330–335.
- 37 Dauty M, Perrouin VB, Maugars Y, Dubois C, Mathe JF. Supralesional and sublesional bone mineral density in spinal cord-injured patients. *Bone* 2000; **27**: 305–309.
- 38 Garland DE, Adkins RH. Bone loss at the knee in spinal cord injury. *Topics Spinal Cord Injury Rehabil* 2001; **6**: 37–46, Winter (27 ref) 2001;(3):37–46.
- 39 Leslie WD, Nance PW. Dissociated hip and spine demineralization: a specific finding in spinal cord injury. *Arch Phys Med Rehabil* 1993; **74**: 960–964.
- 40 Szollar SM, Martin EME, Parthemore JG, Sartoris DJ, Deftos LJ. Demineralization in tetraplegic and paraplegic man over time. *Spinal Cord* 1997; **35**: 223–228.
- 41 Ditor DS, Kamath MV, MacDonald MJ, Bugaresti J, McCartney N, Hicks AL. Effects of body weight-supported treadmill training on heart rate variability and blood pressure variability in individuals with spinal cord injury. *J Appl Physiol* 2005; **98**: 1519–1525.
- 42 Stewart BG et al. Treadmill training-induced adaptations in muscle phenotype in persons with incomplete spinal cord injury. *Muscle Nerve* 2004; **30**: 61–68.
- 43 Robling AG, Hinant FM, Burr DB, Turner CH. Shorter, more frequent mechanical loading sessions enhance bone mass. *Med Sci Sports Exerc* 2002; **34**: 196–202.
- 44 Kocina P. Body composition of spinal cord injured adults. *Sports Med* 1997; **23**: 48–60.
- 45 Sedlock DA, Lavature SJ. Body composition and resting energy expenditure in long-term spinal cord injury. *Paraplegia* 1990; **28**: 448–454.
- 46 Bauman WA, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. *Metabolism* 1994; **43**: 749–756.
- 47 Karlsson AK. Insulin resistance and sympathetic function in high spinal cord injury. *Spinal Cord* 1999; **37**: 494–500.
- 48 Phillips SM et al. Body-weight-support treadmill training improves blood glucose regulation in persons with incomplete spinal cord injury. *J Appl Physiol* 2004; **97**: 716–724.