Plum Diet Mitigates Osteopenia Following Spinal Cord Injury

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Disclosures: XL (None), LL (None), ML (None), AD (None), RN (None), HK (None), BH (None).

INTRODUCTION: Severe osteopenia is a known consequence of spinal cord injury (SCI) and bone loss occurs in all SCI patients. SCI patients lose up to 40 % of sublesional bone mineral density (BMD) by 2 years post-injury with peak reduction rates of 1% per week. Bone loss after SCI leads to increased risk of spontaneous low impact fractures and significantly increases the morbidity and mortality of SCI patients. Pharmacological and non-pharmacological treatment approaches are limited. Recent studies have shown that dietary supplementation with dried plum (DP) can prevent and reverse the bone loss accompanying aging, estrogen deficiency, radiation and disuse. Importantly, DP has both anabolic and antiresorptive effects making it preferable to bisphosphonate therapies. In this study, we examined the efficacy of DP to prevent and restore bone loss in a mouse model of SCI.

METHODS: Twelve weeks of age male C57B/L6 mice underwent midthoracic spinal cord impaction injury as described previously [1]. In brief, under isoflurane anesthesia a 2-cm incision in the skin over the midthoracic spinal cord (between T8 and T10) was made on mice. The lamina was removed to expose the spinal cord. A 35-g stainless steel rod was dropped from a height of 50 mm onto the exposed spinal cord with a penetrating depth of 1.8 mm using a custom made spinal cord impactor. This impaction injury generates permanent paralysis of both hindlimbs. Mice were then randomly divided into DP-enriched diet (25%) fed treated group and control diet fed control group (N=6 in each group). Mice were scanned with a Scanco VivaCT40 microCT scanner before SCI and at 2 and 4 weeks after SCI at the distal femoral metaphysis. Total volume (TV), bone volume (BV), relative bone volume (BV/TV), and volumetric density of distal femoral trabecular bone were quantified. To test if DP can reverse the osteopenia induced by SCI, another set of male C57B/L6 mice underwent SCI and were fed control diet for 4 weeks and then switched to 25% DP-enriched diet for another 4 weeks (N=6). CT scans were performed before SCI and at 4 and 8 weeks after SCI at the distal femoral metaphysis in those mice.

RESULTS: MicroCT scanning showed that in the control diet fed group, relative bone volume (BV/TV) dropped 63% and 81% at 2 weeks and 4 weeks respectively after SCI. In the DP-enriched diet group, BV/TV decreased by only 24% and 34% at 2 weeks and 4 weeks respectively. DP diet significantly reduced bone loss after SCI (Figure 1) ($P<0.05$). In the reversal experiment, microCT scanning showed that a short course of 4 weeks of DP-enriched diet doubled the relative bone volume (BV/TV) in the distal femur of mice after SCI (from 0.03 at 4 weeks after SCI to 0.06 at 8 weeks after SCI). (Figure 2) ($P<0.05$).

DISCUSSION: There are no standardized treatment guidelines for management of osteopenia in patients with SCI at this time. Vitamin D supplementation is generally considered for SCI patients to restore vitamin D levels in individuals with vitamin D deficiency. However, the role of Vitamin D supplementation for preventing osteopenia and fracture remains undefined. Various pharmacologic approaches have been applied to reduce sublesional bone loss after spinal cord injury (SCI), but the results are inconsistent. Among all of the agents tested in SCI patients in clinical trials, the bisphosphonates are the most common. A recent meta-analysis containing a total of 19 studies involving 364 patients showed that acute SCI participants treated with bisphosphonate therapy demonstrated a trend toward less bone loss than participants who received placebos or usual care [2]. However, a long-term study showed that a 2-year course of treatment with alendronate (bisphosphonate) did not increase bone mineral density (BMD) at any skeletal site tested. In another study, Bauman et al. found that zolendronic acid, another bisphosphonate, did not prevent BMD loss at the knee in SCI patients [3]. These results were significantly different from those reported in able-bodied post-menopausal women in which bisphosphonate treatment results in increased BMD. A recent study showed that Denosamab, a human monoclonal antibody to RANKL decreases bone turnover markers in patients with recent SCI [4]. However, its long term effect in preventing bone and restoring bone after SCI remain unknown. Thus, development of new rehabilitative approaches to prevent and restore bone loss in patients with SCI is highly demanded. Our results from this study suggests that plum diet supplements may serve as a novel, economic and effective treatment option for limiting and for treating SCI-induced osteopenia.

SIGNIFICANCE: Musculoskeletal complications, especially osteopenia after SCI are among the major catastrophic complications of SCI patients. Thus, the development of effective treatment options to prevent and treat osteopenia has high impact on the rehabilitation of SCI patients.

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ACKNOWLEDGEMENTS: Funding for this study was provided by UCSF Core Center for Musculoskeletal Biology and Medicine (NIH 1P30AR066262-01) and California Plum Board.

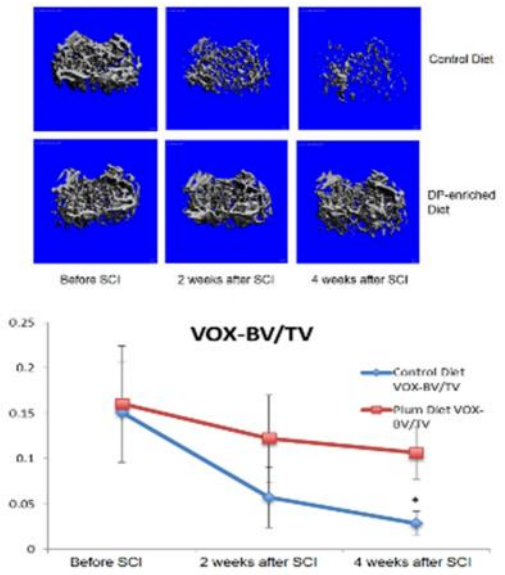

Figure 1. Typical microCT of distal femur trabecular bone and quantification of relative bone volume (Bv/Tv) of SCI mice fed with DP-enriched and control diet.

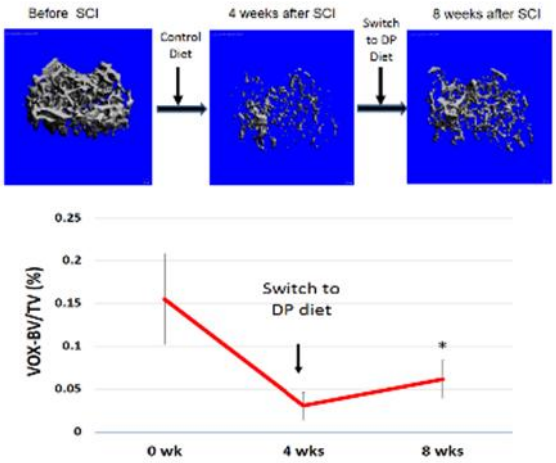

Figure 2. Typical microCT of distal femur trabecular bone and quantification of relative bone volume (Bv/Tv) of SCI mice with delayed onset of DP-enriched diet.