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Influences of nutrition and adiposity on bone mineral density in individuals with chronic spinal cord injury: A cross-sectional, observational study

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ABSTRACT

Background: Dietary inadequacy and adiposity, both prevalent in the chronic spinal cord injury (SCI) population, are known to influence bone turnover and may be potential modifiable risk factors for the development of sublesional osteoporosis following SCI. This pilot study in an SCI cohort aimed to assess measures of nutrition and obesity, to determine if these measures were associated with bone mineral density (BMD), and to compare these measures to a non-SCI control cohort.

Methods: In a cross-sectional observational study, volunteers with chronic SCI (>1 year post-injury, lesions from C1 to T12 and severity category A–D by the American Spinal Injury Association Impairment Scale) were assessed, and 8 non-SCI individuals were recruited as a comparison group. BMD at the femoral neck (FN) and lumbar spine (LS), and an estimate of visceral adipose tissue (VAT) from lumbar vertebrae 1 through 4 were measured using dual energy X-ray absorptiometry (DXA); nutrient intake of calcium, vitamins D & K, and protein were estimated using a food frequency questionnaire; plasma 25-hydroxyvitamin D (25(OH)D) was analyzed using ultra-high performance liquid chromatography/tandem mass spectroscopy; and serum leptin, adiponectin and insulin were analyzed using a multiplex assay.

Results: A total of 34 individuals with SCI ($n = 22$ tetraplegic; $n = 12$ paraplegic; 94% male) who averaged 12.7 (9.0) years post-injury, age 40.0 (10.9) years and % body fat of 28.4 (7.3) were assessed. Multiple linear regression analyses in the SCI cohort showed significant associations between BMD at the FN and LS with leptin (FN: $r = 0.529$, $p = 0.005$; LS: $r = 0.392$, $p = 0.05$), insulin (FN: $r = 0.544$, $p = 0.003$; LS: $r = 0.388$, $p = 0.05$), and VAT percent (FN: $r = 0.444$, $p = 0.02$; LS: $r = 0.381$, $p = 0.05$). Adiponectin was only correlated with LS BMD ($r = 0.429$, $p = 0.03$). No significant relationships were found between BMD and serum 25(OH)D, or intakes of calcium, vitamins D & K, and protein. Intake of vitamin D was adequate in 69% of participants with SCI, where 91% of those persons consumed either vitamin D and/or multivitamin supplements. Vitamin D status was similar between SCI and non-SCI groups as was sub-optimal status (25(OH)D < 75 nmol/L) (60% of SCI compared to 50% of non-SCI). Participants with SCI had significantly lower FN BMD in comparison to non-SCI controls ($p = 0.001$).

Conclusions: Compromised BMD among individuals with SCI was not associated with a deficiency of vitamin D or other bone nutrients. The observed positive associations between BMD and leptin, insulin, adiponectin and VAT provide a framework to evaluate links between adiposity and bone health in a larger SCI cohort.

1. Introduction

Sublesional osteoporosis (SLOP) is a disease specific to the spinal cord injury (SCI) population associated with excess bone resorption paired with reduced bone formation below the level of lesion (Craven et al., 2009). The dramatic loss of bone mineral density (BMD) increases the risk of acquiring fragility fractures at the distal femur, proximal tibia, and hip regions (Craven et al., 2009). There is a preservation of BMD at the lumbar spine (LS) during the chronic phase of SCI, which may be due to the maintenance of load on the spine while sitting in a

Abbreviations: AIS, American Spinal Injury Association Impairment Scale; DRI, dietary reference intakes; EAR, estimated average requirement; FFQ, food frequency questionnaire; IOM, Institute of Medicine; SCI, spinal cord injury; SLOP, sublesional osteoporosis; UPLC/MS–MS, ultra high performance liquid chromatography tandem mass spectrometry; VAT, visceral adipose tissue; WC, waist circumference.

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wheelchair (Biering-Sorensen et al., 1988). However the trabecular composition of the LS with high bone turnover can cause changes in BMD prior to fracture (Craven et al., 2009) and many vertebral compression fractures at this site go undetected in other clinical disorders such as steroid drug-induced bone loss (Rodd et al., 2012a). The occurrence of SLOP is estimated to be up to 82% in individuals with SCI (Craven et al., 2009). Although nutrition and adiposity have known roles in the regulation of bone metabolism, the importance of these factors compared to loss of weight bearing in those with SCI is not well defined.

Sub-optimal vitamin D status is common in the SCI population (Hummel et al., 2012; Bauman et al., 1995, 2005; Oleson et al., 2010; Nemunaitis et al., 2010). It is attributed to limited exposure to sunlight due to reduced mobility, use of medications that accelerate vitamin D metabolism, and/or low vitamin D intake due to calcium-restricted diets during acute care to avoid hypercalciuria (Bauman et al., 1995). Intake of calcium may thus also be compromised. Whether persons with greater fracture risk, such as the SCI population, require nutrient intakes higher than the dietary reference intakes suggested for the average population is unknown (Hanley et al., 2010; WHO Scientific Group, 2003).

Other factors that may influence bone formation and resorption in persons with SCI include pro-inflammatory cytokines released from excess adipose tissue (Cao, 2011). Leptin has been suggested to regulate bone metabolism primarily through the peripheral pathway promoting bone formation (Turner et al., 2013; Khosla, 2002). Leptin receptors on osteoblasts increase osteoblast differentiation while decreasing adipocyte differentiation, as they are both derived from a common multipotential mesenchymal stem cell lineage (Thomas, 2003). Excess adiposity also increases exogenous insulin, which binds to insulin receptors on osteoblast cells and directly induces osteoblast activity (Karsenty and Ferron, 2012). Similarly, adiponectin may be a biomarker for bone loss and fracture risk as it is inversely related to BMD and central adiposity (Liu et al., 2013). Alternative theories regarding the fat–bone relationship suggest that mechanical loading by fat and muscle mass on bone tissue is associated with increased osteoblast activity, strengthening bones in regions of high stress (Jiang et al., 2006). In persons with SCI, body weight percentage as adipose tissue mass can be 8–18% higher than in age-, height-, and/or weight-matched non-SCI controls (Buchholz and Bugaresti, 2005). Following SCI, adipose tissue accumulation in parallel with loss of muscle and bone tissue indicates a disruption in adipose-associated bone metabolism (Jiang et al., 2006).

The presence of SLOP (Craven et al., 2009), nutrient inadequacy (Walters et al., 2009), and obesity (Rajan et al., 2008) in the SCI population suggests that a unique cross-regulation may exist. Characterizing relationships between markers of these physiologic states will further our understanding of bone health in the SCI population and may help in the detection and treatment of SLOP. This pilot study sought to assess bone-related measures of nutrition and obesity in a SCI cohort and determine if these measures are associated with BMD at the femoral neck (FN) and LS. Secondary goals were to identify correlates of suboptimal vitamin D status (e.g. winter assessment, vitamin D intake), and compare measurement outcomes to a small representative sample of non-SCI individuals.

2. Methods

2.1. Study setting and population

The study was conducted at McMaster University in Hamilton, Ontario, Canada; data were collected between March 2011 and April 2013. The Hamilton Integrated Health Sciences Research Ethics Board approved the study protocol and consent was obtained from each volunteer. Individuals enrolled in the study were at least 12 months post-SCI (traumatic or non-traumatic) ranging in impairment from C1 to T12, and ranging in severity from A to D as categorized by the American Spinal Injury Association Impairment Scale (AIS) (Kirshblum et al., 2011). The non-SCI individuals serving as a comparison group were matched for sex, age, waist circumference (WC), and body mass index (BMI).

2.2. Outcome measures

2.2.1. Medical history and demographics

Demographics, injury characteristics, and medical history were obtained by interview. Body mass was measured using a digital wheelchair scale (Detecto BRW-1000 Digital Bariatric Wheelchair Scale, DETECTO, Webb City, MO, USA) to the nearest 0.1 kg and body length was measured on the right side of the body while lying supine to the nearest 0.1 cm. WC was taken in the supine position after normal expiration immediately below the lowest rib with the same tape measure as used for participant length (Gulick II) (Edwards et al., 2008). For each WC measurement, the tape measure was placed directly on the skin with the participants' arms by their sides. Each measurement was taken to the nearest 0.1 cm.

2.2.2. Body composition

Dual energy X-ray absorptiometry (DXA) scans were performed using Hologic QDR-4500A (Hologic Inc., Waltham, MA, USA). Scan acquisition and analyses were completed following the manufacturers' guidelines for assessing areal BMD (aBMD) at the LS (lumbar vertebrae 1–4 or a minimum of two consecutive vertebrae) and FN of the left hip (Rajan et al., 2008); body fat and visceral adipose tissue (VAT) were analyzed from a whole body scan, where a demarcated region of interest from lumbar vertebrae 1 through 4 quantified VAT (Glickman et al., 2004). Quality control tests were performed daily using a phantom, and measurements were maintained within the manufacturer's standards of <1%. Both T and Z-scores were calculated using a reference database for non-SCI individuals provided by the Hologic software; T-scores were used for participants over 50 years and Z-scores were used for participants under 50 years (Schousboe et al., 2013).

2.2.3. Food and supplemental nutrient intake

Average daily dietary intakes of calcium, vitamins D and K, and protein were assessed using a previously validated food frequency questionnaire (FFQ) (Pritchard et al., 2010). Supplement use of multivitamins, calcium, and vitamin D were documented regarding amount(s) and duration of use. Dietary nutrient intake refers to the consumption of the nutrient from food, whereas absolute nutrient intake refers to the consumption of food plus supplements. To assess the adequacy of nutrient intake, reported intakes were compared to the estimated average requirement (EAR) for vitamin D (400 IU/day), calcium (800 mg/day) and protein (0.66 g/kg/day) and the adequate intake of vitamin K (120 μg/day) for adults aged over 18 years as recommended by Health Canada (Institute of Medicine, 2001, 2011, 2002).

2.2.4. Blood collection and analyses

Blood samples collected following a 12-hour fast were spun and frozen at −80 °C. Plasma 25(OH)D was quantified in triplicate using ultra high performance liquid chromatography tandem mass spectrometry (UPLC/MS–MS). The protocol for sample preparation was based on the Waters Alliance and Hymoller and Jensen protocol for HPLC LC/MS–MS with minor modifications (Hymoller and Jensen, 2011; Calton et al., 2008). The coefficient of variation (CV) for low and high 25(OH)D quality control measurements run five times was <10%. Although there is no universal definition for optimal 25(OH)D status for bone health, the Institute of Medicine (IOM) defines adequacy as >50 nmol/L (Institute of Medicine, 2011). We defined sub-optimal vitamin D status as <75 nmol/L as recommended by the International Symposium on the Nutrition Aspects of Osteoporosis for persons with increased risk of fracture (Dawson-Hughes et al., 2005). Serum samples were analyzed for leptin, insulin, and adiponectin using the Milliplex® Map Kit for Human Adipokine Magnetic Bead Panel 2 (Millipore Corporation, Billerica, CA) in duplicate.