Statin Therapy as Potential Treatment for Endocrine Metabolic Disease in Individuals with Chronic Spinal Cord Injury: A Cross-Sectional Study

Miyatani M[1], Alavinia AS[1], Giangregorio L[2], Blencowe L[1], Anderson-Erisman K[3,4], Cheung AM [5,6], Nash MS [7,8], Craven BC [1,6]

[1]Toronto Rehabilitation Institute- University Health Network, Toronto, ON, Canada; [2]Dept. of Kinesiology, University of Waterloo, Waterloo, ON, Canada; [3]Dept. of Physical Medicine and Rehabilitation, Metrohealth Medical Center, Cleveland, OH, USA; [4]Case Western Reserve University School of Medicine, Cleveland, OH, USA; [5]Dept. of Medicine and Joint Department of Medical Imaging, University Health Network, Toronto, ON, Canada; [6]Dept. of Medicine, University of Toronto, Toronto, ON, Canada,[7]The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL, USA; [8]Dept. of Neurological Surgery and Physical Medicine & Rehabilitation, University of Miami Miller School of Medicine, Miami, FL, USA

Background

- Endocrine metabolic disease (EMD) including osteoporosis, fracture, sarcopenic obesity, abdominal obesity, elevated diabetes and heart disease risk and incidence are common established health complications of spinal cord injury (SCI).
- The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) are widely used for treatment of hyperlipidemia. Liu's 2013 meta-analyses concluded statins are osteoprotective in the general population (1).

Objectives

1. To describe the prevalence of EMD including sarcopenia, sarcopenic obesity, and abdominal obesity, low bone mass and prior fracture in adults with chronic motor-complete SCI.
2. To describe differences in lower extremity, hip and knee region bone mineral density (BMD) among individuals with chronic SCI who are statin users vs. non-users.

Methods

Study Design

- Cross-Sectional Study using bbaseline data from a 2-year prospective longitudinal study (2)

Participants

- 41 adults with chronic SCI (C2-T12, AIS A &B ; duration of injury ≥5 years; and, age 18 -70 years)

Dual-Energy X-ray Absorptiometry (DXA) Scans

- Whole body, total hip, distal femur and proximal tibia scans (Hologic Inc. 4500 Discovery W, MA)
- Body composition software was used to measure visceral adipose tissue area (VAT, cm^2), appendicular lean mass index (Appendicular lean mass/height^2: ALMI, kg/m^2)
- Standard hip and spine software was used to measure BMD (g/cm^2) of the total hip, distal femur and proximal tibia (g/cm^2)

Definitions of Obesity, Sarcopenia, Sarcopenic Obesity and Low bone mass

- Abdominal obesity: ≥VAT 100cm^2
- Sarcopenia: ALMI (men, ≤7.26kg/m^2; women, ≤5.5kg/m^2)
- Sarcopenic obesity: Presence of both abdominal obesity and sarcopenia
- Low bone mass : Z-score ≤ -3.0 of the total hip, distal femur and/or proximal tibia, or prior fracture.

Chart Abstraction

- Bisphosphonate and statin exposure
- Demographics (Age, duration of injury, NLI, and sex)

Results

Table 1: Participant Characteristics (Mean ± Standard Deviation)

	Total	Non-Statin User	Statin User	P-value *
# Participants	41	36	5	-
Male, n (%)	36 (87.8)	25 (69.4)	3 (60.0)	0.65
Age (years)	45.9 ± 10.3	44.8 ± 1.6	53.7 ± 6.3	0.09
Duration of Injury (years)	18.8 ± 9.2	18.6 ± 1.5	19.8 ± 4.8	0.73
NLI, n (% Tetraplegia)	20 (53.7)	18 (50.0)	2 (40.0)	1.00
Height (cm)	175.2 ± 9.2	175.0 ± 1.5	176.3 ± 5.1	0.72
Weight (kg)	78.2 ± 19.5	77.0 ± 3.3	86.4 ± 8.7	0.32
Bisphosphonate Users, n (%)	27 (65.9)	23 (64.0)	4 (87.0)	0.65

*Non-Statin User vs statin User. The Mann-Whitney U test and Fisher's exact test were used for continuous variables and categorical variables, respectively.

Objective 1. Prevalence of Abdominal Obesity, Sarcopenia, Sarcopenic Obesity and Low Bone Mass

Table 2: DXA-measured body composition outcomes (Mean ± Standard Deviation)

		Women		Men		Total
	n		n		n	
VAT Area (cm^2)	12	107.7 ± 22.6	28	175.1 ± 15.0	40	154.9 ± 84.1
ALMI (kg/m^2)	12	5.58 ± 0.33	27	6.28 ± 0.26	39	6.07 ± 1.32
Total Hip BMD (g/cm^2)	11	0.624 ± 0.033	27	0.643 ± 0.035	38	0.637 ± 0.161
z-score	11	-2.2 ± 0.28	27	-2.3 ± 0.23	38	-2.3 ± 1.13
Distal Femur BMD (g/cm^2)	11	0.425 ± 0.03	25	0.529 ± 0.03	36	0.497 ± 0.130
z-score	11	-5.3 ± 0.31	25	-4.7 ± 0.18	36	-4.9 ± 0.960
Proximal Tibia BMD (g/cm^2)	13	-0.383 ± 0.02	28	-0.416 ± 0.02	41	0.406 ± 0.099
z-score	13	-3.1 ± 0.11	28	-3.0 ± 0.16	41	-3.1 ± 0.55
History of fracture (n,%)	13	6 (54.5)	28	11 (39.3)	41	17 (41.5)

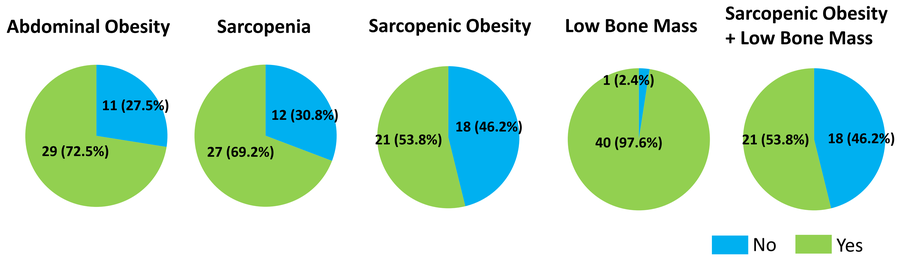
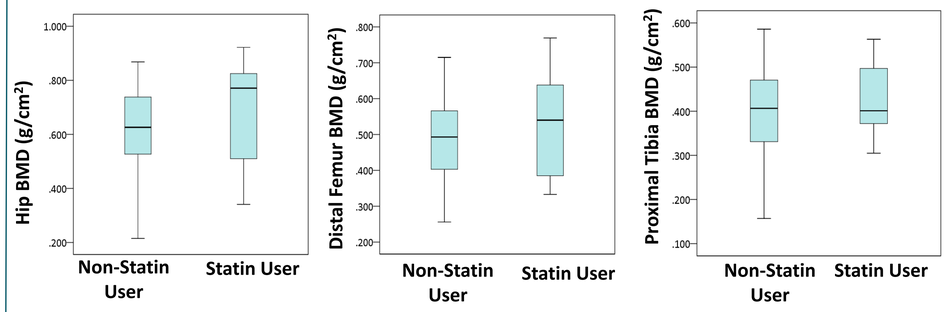


Figure1: Prevalence of Abdominal Obesity, Sarcopenia, Sarcopenic Obesity and Low Bone Mass

Objective 2. Regional BMD in Non-Statin User vs. Statin User groups



Discussion and Conclusion

Objective 1. Prevalence of Abdominal Obesity, Sarcopenia, Sarcopenic Obesity and Low Bone Mass

- A majority of the cohort had sarcopenic obesity and low bone mass indicating individuals with chronic SCI are at high risk of EMD.
- Population-specific threshold values are necessary to identify intervention thresholds based on EMD risk profiles.

Objective 2. Regional BMD in Non-Statin User vs. Statin User groups

- The statin user group tended to have higher mean hip (6.6%), distal femur (8.3%) and proximal tibia (6.2%) BMD compared to non-users, despite their older age.
- The effects of statins on bone anabolism include promotion of osteoblast differentiation, suppression of osteoblast apoptosis, and blocking of osteoclastogenesis. However, the signaling pathways involved in the regulation of bone remodeling by statins are varied and complex (4).
- The individual bone effects of statins likely differ as a result of differences in their polarity and bone absorption. Lipophilic statins are believed to have greater capacity to enter bone cells than hydrophilic statins (i.e. pravastatin, rosuvastatin, and fluvastatin). Therefore, Lipophilic statins may be more effective than hydrophilic statins in protecting bone (4). However, there is insufficient date to identify which are most beneficial. Hydrophilic statins have low drug interaction potential due to their hydrophilic nature (5); an attractive feature for individuals with SCI requiring multiple medications.
- We plan to conduct a prospective RCT (NCT#03113994) to evaluate the safety and efficacy of Rosuvastatin therapy for modifying distal femoral BMD and cardiometabolic disease outcomes among adults with chronic motor-complete SCI in Toronto, Ontario and Miami, Florida. (RoBaCO Trial [NTC03113994]: https://www.robacotrial.com/)

References

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Acknowledgements

This study was funded by the Canadian Institutes of Health Research (Grant #: 86521), SCI Solutions Network (RHI; Grant #: 2010-43), SCI IMPACT (Grant #: 2011-ONF-REPAR-885), Toronto Rehab Foundation and Craig H. Neilsen Foundation (Grant#: # 350642)

Contact: **Masae Miyatani, PhD, Toronto Rehab – UHN**
masae.miyatani@uhn.ca