Case-Based Learning Module: BONE HEALTH

INTRODUCTION

Patients with spinal cord injury (SCI) are at an increased risk of low bone mineral density (BMD) and subsequent fragility fractures. As such, it is important for primary care providers to know how to appropriately screen for and manage bone health for patients with SCI.
This module will help clinicians to:

- Identify risk factors associated with low BMD
- Perform screening for low BMD appropriately for patients with SCI
- Prescribe pharmacologic and non-pharmacologic therapies to prevent and treat low BMD

CASE

Susan, age 53

Susan is a relatively new patient who presents to your office with concerns regarding her bone health as her mother recently fell and had a hip fracture. She is paraplegic; at 42 she sustained a complete T7 SCI. She is currently taking Vitamin D 1000 IU/day and Calcium 500 mg/day. She thinks she had a bone mineral density (BMD) performed a couple of years after her injury. Her last menstrual period was two years ago. She is taking levothyroxine for hypothyroidism and oxybutynin for neurogenic bladder. She has not had a fracture. She rarely drinks alcohol and is a non-smoker.

Is there anything else she could be doing to prevent fractures?

- *It would be important to thoroughly review secondary causes for osteoporosis as well as the risk factor checklist for patients with SCI. In terms of secondary causes, Susan is post-menopausal and has hypothyroidism. She has three risk factors for fracture: she has >10 year history of SCI, a positive family history of fracture, and is female. This places her at a moderate fracture risk.*

Are there further investigations you would like to order?

- *Bloodwork should be ordered including a CBC, Cr, TSH (ensure appropriate supplementation), Ca, Albumin, ALP, and SPEP (if vertebral fracture), plus 25-hydroxy vitamin D (3-4 months after supplementation). A screening BMD should be ordered. It is important to write on the requisition that the patient has a spinal cord injury, and a BMD of the hip and spine (and knee, if possible), should be completed.*

Susan's bloodwork is normal, and the results of her BMD are consistent with a diagnosis of sublesional osteoporosis (SLOP; T score less than or equal to -2.5 at the hip or knee for post-menopausal women). How would you manage this patient?

- *It is important to discuss pharmacologic and non-pharmacologic measures to maintain or improve bone health. Susan is already a non-smoker and low drinker. More information regarding her dietary calcium intake and activity level would be helpful. Activity based therapy or functional electrical stimulation could also be considered, depending on local resources. She should continue taking her Vitamin D supplementation. Discuss the option of starting an oral bisphosphonate. Alendronate has evidence for the treatment of SLOP and would be a good starting point. It should be noted that even if her BMD results did not meet the criteria for SLOP, she could still be considered a candidate for bisphosphonate therapy has she has 3 risk factors on the fracture risk profile checklist*

INFORMATION SECTION

Introduction:

Patients with spinal cord injury (SCI) are at a greater risk of low bone mineral density (BMD) and subsequent fragility fractures compared to their non-SCI counterparts. This change is most prominent in bones below the level of injury, and is termed sublesional osteoporosis (SLOP).[1]

Pathophysiology:

Initially, following the acute SCI, patients undergo excessive bone resorption, manifested as hypercalciuria which continues for the first four to six months post injury, then slows over the course of the first year.[2] This is thought to be due to decreased muscle function and decreased weight bearing, as well as potential autoimmune, hormonal, neural, vascular and nutritional changes.[2] There is conflicting evidence regarding whether homeostasis of bone resorption and bone formation is reached, with older studies suggesting that BMD stabilizes 1-2 years following the initial injury, and more recent studies suggesting a continual 3% per year decrease in BMD.[1] The distal femur and proximal tibia are at greatest risk for fracture.[2]

Assessment of SLOP:

Identification and management of bone health pathology/issues should occur soon after the initial SCI as there is a significant decline in bone density in the first year and pharmacologic therapy has shown the greatest efficacy when initiated early.[2] A screening BMD is often completed while patients are in rehabilitation. For patients who are followed by physiatry, the decision to initiate pharmacologic therapy will generally be done by the specialist. However, not all patients have regular follow-up with physiatrists, therefore it is important for primary care providers to be familiar with the assessment and management of low BMD.

Clinical Pearl: Identification and prevention of SLOP is important for the health of patients with SCI, as it can result in high rates of fragility fractures and subsequent complications, such as infection, deep venous thrombosis, decreased function and rarely amputation.[1,3]

Assessment of bone health should include a review of secondary causes of osteoporosis, SCI-specific risk factors for fracture, as well as a physical exam including the patient's height and weight. It should also involve laboratory investigations as well as a bone mineral density.[1]

Step 1: Review common secondary causes of osteoporosis

Comorbid health conditions
Thyroid, parathyroid disease
Hypogonadism
Malabsorption (e.g., Crohn's, colitis)
Chronic malnutrition (e.g., anorexia)
Chronic liver disease
Renal failure, renal stones
Hypercalciuria
Multiple myeloma
Rheumatoid arthritis
Osteogenesis imperfecta
Marfan's syndrome
Prostate cancer
Cancer managed with chemotherapy, radiation therapy
Menopause, amenorrhea
Lifestyle (excessive ETOH, caffeine, smoking)
Medications
Prolonged use of glucocorticoids (>7.5 mg for >3 months)
Anticonvulsants (carbamazepine, phenytoin)
Lithium
Inadequate or excessive thyroid replacement
Loop diuretics
Heparin
Aromatase inhibitors
Androgen deprivation therapy

Table 1: Common secondary causes of osteoporosis[1,4]

Clinical Pearl: Do NOT assume that a decrease in bone mass in a patient with SCI is due to SLOP; up to one third of SCI patients have an additional secondary cause of osteoporosis.[5]

Step 2: Review SCI specific risk factors for fracture

Below is a risk factor profile checklist that can be used when screening patients with SCI for risk of fragility fractures. The presence of three or more risk factors indicates a moderate fracture risk, and the presence of 5 or more indicates a high fracture risk.[1,5]

Yes	Risk Factors
☐	Age at Injury < 16 years
☐	Alcohol Intake > 5 servings/day
☐	BMI < 19
☐	Duration of SCI ≥ 10 years
☐	Female
☐	Motor Complete (AIS A-B)
☐	Paraplegia
☐	Prior fragility fracture
☐	Family history of fracture
☐	Anticonvulsant use
☐	Heparin use
☐	Opioid analgesia use

Table 2: Fracture Risk Factors[1,5]

AIS – ASIA (American Spinal Injury) Impairment Scale
AIS A – complete injury. No sensory or motor function in S4-S5 segments
AIS B – incomplete injury. Sensory sensation is preserved, but no motor function below the neurologic level and to the S4-S5 segments

Clinical Pearl: <u>Does my patient have a fragility fracture?</u>
Fragility fracture can be defined as a fracture that occurs spontaneously or following a minor trauma that would not be sufficient to cause a fracture in normal bone (e.g., fall from standing height).[4,6] Among patients with SCI, fragility fractures can occur during a transfer or fall from a seated position.[1] If a patient presents with pain (note sensation is often lacking), deformity, or skin change following an injury, transfer or fall, it is critical to have a **high index of suspicion for fracture** and investigate appropriately.

The common tools for predicting fracture risks such as the CAROC or Canadian FRAX tools are not optimal for individuals with SCI, as these tools underestimate fracture risk.[15] Clinicians should combine the SCI-specific risk factors with the scores from BMD (hip- or knee-region BMD T-scores or Z-scores in accordance with recommendations by the International Society for Clinical Densitometry) to stratify risk of fractures. Patients who fall into moderate to high fracture risk categories will require therapy and risk factor modifications. These include abstaining from smoking, cutting down caffeine and alcohol consumption and addressing medication history. Benefits from opioids, benzodiazepines and heparin therapy need to outweigh fracture risk.[15]

Step 3: Laboratory Investigations

It is important to screen for secondary causes of osteoporosis not evident on history and physical with bloodwork and urinalysis.[1,4]

☐ CBC	☐ Serum protein electrophoresis (if vertebral fracture)
☐ Calcium, corrected for albumin	☐ 25 – hydroxyl vitamin D (after 3-4 months supplementation)
☐ Creatinine, CrCl	☐ TSH
☐ ALP	☐ 25-OH Vitamin D

Table 3: Laboratory Investigations[1,4,14]

Step 4: Screening Bone Mineral Density

It is critical to do screening bone mineral densities (BMD) using dual energy X-ray absorptiometry (DXA) for patients. As per the International Society for Clinical Densitometry (2013),[7] a follow-up BMD can be done one year after starting or changing therapy for a patient. Although there are no clear guidelines regarding the frequency of screening BMD for patients with SCI, experts generally recommend completing the first BMD while in rehabilitation, and repeating every 1-2 years thereafter.

Age	Definition
Men ≥ 60 yo, and post-menopausal women	Hip or knee region **T score** ≤ **-2.5**
Men < 59 yo or pre-menopausal women	Hip or knee region **Z score** ≤ **-2.0** plus ≥ **3 or more** fracture **risk factors**
Men or women age 16-90	**Prior fragility fracture** and **no other identifiable cause** for osteoporosis other than SCI

Table 3: DXA Results indicative of Osteoporosis[7]

Prevention and Treatment of Low Bone Mineral Density:

Management of bone health should occur soon after a SCI is sustained as there is a significant loss of bone mass in the first year after injury. Management is comprised of lifestyle, pharmacologic and non-pharmacologic options.

Lifestyle

Patients should be counselled on lifestyle measures to help prevent and/or treat decreased bone mineral density, including[1,2]:

- decreased alcohol intake
- decreased caffeine intake (< 3 servings/day)
- smoking cessation
- review any changes in mobility, e.g., safety of transfers, need for mobility aids
- activity based training (involving active assisted exercise, resistance training, cycle ergometry, gait training, and load bearing for at least 2-3 hours/day at least 2 days per week for 6 months)[12]
- some individuals may be able to participate in weight bearing using wheelchair with sit-stand

functionality or body weight supported treadmill

Calcium and Vitamin D

The majority of patients with SCI should have a **calcium intake of 1000 mg/day**, primarily through diet. If this target is not met through diet alone, patients can supplement with calcium at a dose of no more than 400-500 mg at a time. There are two exceptions to this:

- In patients who have recurrent calcium oxalate or citrate renal stones or significant renal impairment, target calcium intake to 500 – 666 mg/day and a low oxalate diet should be initiated.
- In males and females who have not reached peak bone mass at time of SCI, pregnant or breast feeding women, and elderly patients with inadequate dietary intake, a target of 1500 mg/day of calcium should be recommended.[1]

In terms of vitamin D intake, all patients with SCI should follow the Osteoporosis Canada guidelines which recommend a **vitamin D intake of 800 – 2000 IU/day** for all adults year round.

Pharmacologic Options:

Treatment should be offered to patients who have:

- Low BMD at hip or knee (Z score less than or equal to -2.0)
- Three or more risk factors as identified by the risk factor profile checklist[1]

Medications

Medication	Dose	Comments
Calcium	1000mg/d	
Vitamin D	800-2000 IU/d	
Bisphosphonates **Alendronate**	- 5 mg/day (prevention) or 10 mg/day (treatment) or 70 mg once weekly	- Alendronate can be taken safely for 10 – 13 years, at which point a drug holiday and/or discontinuation can be considered Note: bisphosphonates are teratogenic and should be used with caution in premenopausal women[2]
Risedronate	- 5 mg/day or 35 mg once weekly (prevention and treatment)	

Zoledronic Acid	- 5 mg once yearly iv, infuse over 15-30 minutes	
RANK Ligand Inhibitors - Denosumab	- 60 mg sc once every 6 months	Evidence regarding efficacy in patients with SCI are limited, however, there is promising research suggesting it may be a beneficial option[13]

Table 4: Pharmacological Options[1,14]

Currently, there is a lack of clear cut evidence for the duration of treatment or possible side effects of long-term treatment with anti-resorptive medication.

SUMMARY

- Individuals with SCI are at a greater risk of developing osteoporosis
- This is most prevalent in bones below the level of injury
- Review secondary causes of osteoporosis with history, physical, bloodwork & urinalysis
- Assess Risk Factors for fracture
- Asses BMD with DXA (usually done in rehabilitation first, then q1-2 years)
- Begin bone health treatment soon after SCI with lifestyle, pharmacologic and non-pharmacologic interventions

REFERENCES

1. Craven, BC, Robertson, LA, McGillivary CF, & Adachi JD. (2009). Detection and treatment of sublesional osteoporosis among patients with spinal cord injury: Proposed paradigms. Top spinal cord inj rehabil, 14(4) 1-22.
2. Craven C, Lynch CL, Eng JJ. (2014). Bone Health Following Spinal Cord Injury. In Eng JJ, Teasell RW, Miller WC, Wolfe DL, Townson AF, Hsieh JTC, Connolly SJ, Noonan VK, Loh E, McIntyre A, editors. Spinal Cord Injury Rehabilitation Evidence. Version 5.0. Vancouver: p 1- 37.
3. Sobel M, & Lyden J. (1991). Long bone fracture in a spinal-cord injured patient: Complication of treatment – a care report and review of the literature. Journal of Trauma and Acute Care Surgery 21 (1): 1440-1444.
4. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al; Scientific Advisory Council of Osteoporosis Canada. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. *Canadian Medical Association Journal* 182(17): 1864-1873.
5. Craven B C, Hawker GA, Bugaresti & JM. (2008). Importance of screening of secondary causes of osteoporosis among patients with spinal cord injury. *Journal of Spinal Cord Medicine*31(3): 335.
6. Guidelines for preclinical evaluation and clinical trials in osteoporosis. World Health Organization Geneva. 1998.
7. The International Society For Clinical Densitometry (2013). Official Positions – Adult, from http://www.iscd.org/official-positions/2013-iscd-official-positions-adult/
8. Garland DE, Adkins RH, & Stewart CA. (2005). Fracture threshold and risk for osteoporosis and pathologic fractures in individuals with spinal cord injury. *Topics in Spinal Cord Injury and Rehabilitation* 11 (1): 70-78.
9. Gaspar AP, Lazaretti-Castro M, & Brandão. (2012). Bone mineral density in spinal cord injury: an evaluation of the distal femur. *Journal of Osteoporosis*: 519754
10. Comarr A., Hutchinson RH, & Bors E. (1962). Extremity fractures of patients with spinal cord injuries. *American Journal of Surgery* 103: 732-739.
11. Ragnarsson KT, & Sell GH. (1981). Lower extremity fractures after spinal cord injury: a retroscpective study. *Archives of Physical Medicine and Rehabilitations* 62: 418-423.
12. Atorino TA, Harness ET, & Witzke LA. (2013). Effect of chronic activity-based therapy on bone mineral density and bone turnover in persons with spinal cord injury. *European Journal of Applied Physiology*, 113: 3027-3037.
13. Gifre L, Vidal J, Carrasco JL, Muxi A, Portell E, Monegal A, et al. (2016). Denosumab increases sublesional bone mass in osteoporotic individuals with spinal cord injury. *Osteoporosis International* 1: 405-410.
14. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al; Scientific Advisory Council of Osteoporosis Canada. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. CMAJ. 2010;182:1864 [PMID: 20940232]
15. *Cervinka T, Lynch CL, Giangregorio L, Adachi JD, Papaioannou A, Thabane L, et al. Agreement between fragility fracture risk assessment algorithms as applied to adults with chronic spinal cord injury. Spinal Cord. 2017;*