Research Article

Spinal cord injury providers' perspectives on managing sublesional osteoporosis

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Objective: Persons with spinal cord injuries (SCI) experience rapid sublesional bone loss following injury (1, 3). Evidence on preventing/managing osteoporosis in SCI is lacking. This project examined how providers manage bone loss in SCI.
Design: Telephone interviews with SCI providers.
Setting: VA SCI centers and clinics.
Participants: Veterans Administration SCI centers and clinics were categorized on their average number of dual-energy X-ray absorptiometry (DXA) scans (FY2014-2016). Twelve SCI providers from high and low DXA-ordering sites were interviewed. Questions included osteoporosis screening/diagnosis, prevention/treatment strategies, secondary causes of osteoporosis, and osteoporotic fracture complications. Interviews were audio-recorded, transcribed, and analyzed.
Results: Providers described a lack of standardized guidelines for managing osteoporosis in SCI. They most often screened for osteoporosis using DXA when: (1) considering use of a new device or activity, (2) for patients with a history of fracture. Some providers assumed that non-ambulatory SCI patients already have osteoporosis so infrequently ordered DXAs. Assessment of secondary causes of osteoporosis was uncommon. Fracture prevention strategies identified included weight-bearing and engaging in activities like adaptive sports. Vitamin D and calcium were frequently prescribed as a result of deficiencies identified during lab testing. Providers seldom prescribed FDA-approved medications for osteoporosis. Post-fracture complications encountered included nonunion/malunion and compartment syndrome. Providers indicated that patients often experienced psychological stress, anxiety and depression following fractures.
Conclusion: Providers described a lack of evidence for screening and management of patients with SCI and osteoporosis. Future efforts should include developing evidence-informed guidelines to aid providers in osteoporosis management.

Keywords: Spinal cord injury, Osteoporosis, DXA

Introduction

Persons with spinal cord injuries (SCI) experience rapid loss of bone density after injury, often leading to osteopenia or osteoporosis.[1] The prevalence of lower extremity osteoporotic fractures in SCI was estimated to be 2.14 per 100 patient-years in one recent report.[2]

The National Osteoporosis Foundation (NOF) has published guidelines for the prevention, risk assessment, diagnosis and treatment of osteoporosis in postmenopausal women and men age 50 and older.[3] These guidelines include advising patients on calcium and Vitamin D intake, need for regular weight-bearing and muscle-strengthening exercises, assessment of risk factors related to falls, and avoiding tobacco use and excessive alcohol intake. Screening for osteoporosis includes

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measurement of bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA). Pharmacological treatment is recommended in those with hip or vertebral fractures, those with DXA T-scores ≤ -2.5 at the femoral neck or spine after exclusion of secondary causes, and for those with low bone mass (T scores between < -1.0 and -2.5) and increased probably of osteoporosis-related fracture based on the Fracture Risk Algorithm (FRAX®).[4] Current FDA-approved treatments for osteoporosis include bisphosphonates, calcitonin, raloxifene, teriparatide, abaloparatide, romozosumab and denosumab.

These guidelines are based on strong research evidence.[4,5] However, there are no specific guidelines for preventing/managing osteoporosis in persons with SCI whose dramatic loss in BMD is secondary to the mechanical unloading and neurogenic complications from the injury itself. Regular weight-bearing is often not possible in these patients, and in patients with a SCI and osteoporosis, there may be a concern for fracture with exercise programs.[5] Further, the majority of people with SCI are male and are often injured in young to middle adulthood.[6] It is not known whether treatment recommendations for osteoporosis in the able-bodied population from the NOF and other organizations are appropriate and effective in the SCI population.

The 2019 Internal Society for Clinical Densitometry position statement for BMD testing in spinal cord injury recommends obtaining a DXA scan of the total hip, proximal tibia, and distal femur to diagnose osteoporosis, predict lower extremity fracture risk and monitor response to therapy where normative data are available.[7] Peripheral quantitative computed tomography (pQCT) provides another imaging technique to determine bone loss. Current information suggests that persons with SCI with BMDt (measured at 4% site of tibia) above 120 mg/cm^3 are unlikely to experience a fragility fracture.[8] However, there is a need for acquisition and analysis protocols at sites including the tibia and femur to develop normative data and inform fracture risk before pQCT becomes an accepted imaging method for assessing bone loss in SCI.[9]

A recent scoping review examined drug, exercise and other therapies to prevent bone loss in SCI.[10] Medications to prevent bone loss were not successful for the most part in persons with SCI, although use of zoledronic acid, a bisphosphonate, administered during the acute phase of SCI did decrease bone loss at the hip in one study.[11] Strategies that increase mobility and weight-bearing in persons with SCI were not sufficient to maintain BMD in the lower extremities,[12,13] although there were variations in responses to some activity-based interventions. Mixed results have also been found for BMD and use of functional electrical stimulation (FES).[10]

The purpose of this study was to examine SCI provider perceptions and practices regarding management of bone health in their patients in the absence of condition-specific guidelines.

Methods

The sampling frame consisted of prescribing providers from VA SCI centers and SCI clinics. Using data obtained from the Veterans Administration's national clinical data warehouse (CDW), we calculated average rates of DXA scans conducted per year at 25 VA SCI comprehensive care centers and 103 SCI outpatient clinics between fiscal years 2014 and 2106. Sites needed to have at least 100 patients/year and to have ordered at least one DXA to be considered for study selection. We selected 5 high and 5 low DXA ordering SCI centers and 4 high and 4 low DXA ordering SCI clinics to contact, with the goal of interviewing 12 providers representing 6 high and 6 low DXA ordering sites. The names of potential interviewees were obtained from email listservs of VHA SCI providers and by contacting these sites by telephone to identify an SCI provider(s) knowledgeable about bone health in SCI. These providers were invited to participate in an estimated 30-minute telephone interview on their bone health practices in SCI. At four of the originally selected sites we were unable to identify an experienced provider to interview either due to staff turn-over, provider time constraints, or lack of a response from the provider(s). In those cases, the original site was replaced with another site with a similar DXA rate and geographic location, to the extent possible. We repeated this process as necessary until we were able to interview a total of 3 providers from each category of site for a total of 12 completed interviews.

Interviews were conducted by telephone. Providers gave verbal consent for their participation. The interviews were audio-recorded and uploaded to a secure server location for transcription and coding.

A set of semi-structured questions were posed including questions about how these providers screened for and diagnosed osteoporosis in their patients with SCI, prevention and treatment strategies used, frequency with which they tested for and/or identified secondary causes of osteoporosis, and post-fracture complications reported by their patients. The audio-recordings were transcribed verbatim. Coding was completed using a data-driven thematic approach and constant comparison.[14,15] A team of 3 experienced coders first developed

an initial coding scheme based on a review of 2 interview transcripts. All 3 coders reviewed these initial transcripts, identified prominent themes within them independently, and then met to discuss themes and their operational definitions. This list of themes comprised the initial codebook. The remaining 10 transcripts were divided among the 3 coders so that each transcript was independently coded by 2 coders. The coders met and compared their codes for each interview, resolved any disagreements until 100% agreement was reached, and when appropriate added additional codes to the code book. A goal of qualitative research is to conduct enough interviews to have saturation in responses (no new ideas or topics).

The study was approved by the institutional review boards of the investigators' institutions . Waiver of written informed consent and HIPAA was obtained for conduct of the provider interviews.

Results

The 12 SCI providers who participated represented 6 VA SCI comprehensive care centers, 3 of which averaged 40.4 DXAs per year across 3 years (high DXA users with an average of 604 patients), and 3 that averaged 5.3 DXAs/year, representing low DXA user sites (average of 693 patients). Similarly, 6 providers from 3 high (mean = 14.1) and 3 low (mean = 2.3) DXA ordering SCI outpatient clinic sites (197 and 204 patients on average, respectively) completed interviews.

Participants included 4 physicians with combined spinal cord medicine (SCM) and physical medicine and rehabilitation (PM&R) board-certification, 3 SCM, 2 PM&R, and 2 internal medicine board-certified providers, and 1 nurse practitioner. The internal medicine physicians were both from low DXA ordering sites and the nurse practitioner was from a high DXA ordering clinic. Years of experience working with SCI ranged from 1 to 16 years, with an average of 8.2 years. Providers were evenly divided between males and females (6 each).

Screening for osteoporosis

Participants were first asked about routine screening for osteoporosis in their patients with SCI. One provider, who was at a SCI clinic, routinely screened patients by performed DXA scans on everyone, as well as obtaining lab tests for Vitamin D levels. Routine screening, however, was not done at other sites. One provider commented that osteoporosis was known to be very prevalent in the SCI population, while another said that doing routine screening was meaningless as treatments for osteoporosis were ineffective in this population.

Several respondents indicated that they would order DXA scans for patients who wanted to use a new device or participate in a wheelchair sport, especially if they had been using a wheelchair (non-ambulatory) most of the time. Some providers commented that a change in patient function would trigger a screening. Participants also described ordering DXA scans for individuals asking to use exoskeleton devices.

One provider specifically commented about screening:

> We do it [DXA] more for safety and also to educate the individual regarding potential risk. Obviously, if the bone density is weaker, then they could potentially have a higher risk of fractures. So, we just need to be on the same page with the individual so that they understand that they are at high risk of a fracture. If anything happens, at least they can make an informed decision.

A few providers commented that there were no specific guidelines for osteoporosis screening in SCI. Providers discussed risk factors related to osteoporosis in SCI including absence of weight-bearing, falling, history of fractures, vitamin D deficiency, and level and duration of injury. The participants consistently noted that the longer individuals were inactive and not weight-bearing, the greater the likelihood of osteoporosis and increased fracture risk. In most cases, a DXA was more likely to occur after an individual with SCI experienced a fracture.

Next, providers were asked about preferred skeletal sites for DXA imaging when ordering these tests to screen for osteoporosis in SCI. Anatomic locations mentioned for DXA included the hip, spine/lumbar region and knee. For some, the anatomic location was limited by the availability of protocols for DXA scanning at their facilities (e.g. lack of a protocol to do DXA scanning around the knee). A few providers mentioned that obtaining imaging around the knee (distal femur/proximal tibia) would be the best location for DXA in SCI. Others said that although they get the DXA for the lumbar spine, it is not helpful in diagnosing osteoporosis in SCI.

Participants were asked whether they routinely screened their patients for secondary causes of osteoporosis using laboratory tests. Providers commented that Vitamin D screening is already part of the VA SCI annual evaluation. Other tests for testosterone, thyroid, and calcium were sometimes used to rule out secondary causes of osteoporosis. One provider

indicated that he would test if the Veteran showed symptoms suggesting deficiencies in hormones or supplements.

One participant specifically elaborated on secondary causes of osteoporosis in SCI:

> The biggest secondary causes [of osteoporosis are] testosterone deficiency and vitamin D deficiency. Vitamin D is … screened [for] every year as part of their annual, and testosterone, we haven't seen any consensus guidelines. … we only screen if they have symptoms, [we're] not universally screening on everybody. But we know most of our spinal cord patients would come back as testosterone deficient and then have a secondary indication to treat for osteoporosis.

Prevention of osteoporosis

With respect to prevention, providers typically mentioned weight-bearing activities and involvement in adaptive sports (when possible and feasible) as ways to try to prevent osteoporosis. Several providers mentioned using standing frames, gait training, and an exoskeleton device. They were less inclined to support other types of interventions such as functional electrical stimulation (FES) due to their perceived lack of evidence to support its value for bone loss prevention in SCI.

Comments about FES included:

> I'm not aware of a lot of data, like as far as just systematically using FES to try to mitigate osteoporosis.

> I know they've looked at whole body vibration and FES and they've sort of had mixed results on those, so we're not routinely using them.

There was also discussion about emphasizing safety and awareness with their patients, particularly with regard to transfers and use of appropriate medical equipment. It was commonly acknowledged that falls often lead to fractures in individuals with SCI.

Treatment of osteoporosis

According to providers, many patients with SCI already receive Vitamin D supplements, often in combination with calcium supplementation. When screened, most patients are found to be deficient in Vitamin D. Providers will treat with Vitamin D to address bone health and fatigue, which is a common symptom when Vitamin D is low. One provider talked about prescribing higher doses of Vitamin D for patients:

> So we usually check their Vitamin D levels … .as part of the annual evaluation. And if their vitamin D levels are marginal and most of them are low, we do supplement them. And this will be [at] higher doses [then general population] and it always get flagged by pharmacy asking me, 'Are you sure you want to give that much?' and I'll say, 'Yes, that's intentional.'

Side effects or complications from Vitamin D were not routinely seen. Some providers, however, mentioned that they are more cautious with the use of calcium supplements especially for patients with a history of renal stones.

Most providers indicated that their patients were not receiving testosterone supplements. Another provider estimated that 10%–15% of his patients with SCI were currently receiving testosterone supplements. Testosterone is a controlled substance in VA. One provider specifically mentioned that testing and treating patients for testosterone deficiency at his facility was very challenging due to pharmacy practices limiting testing and use.

Osteoporosis medication

Treatment with an FDA-approved medication for osteoporosis was uncommon for all of the providers interviewed. They described specific situations in which a patient was already being treated with an osteoporosis medication, such as a young patient who had experienced multiple fractures, a female veteran with an upper extremity fracture, or someone who was weight-bearing and ambulatory. Although bisphosphonate medications for osteoporosis were seldom used, providers noted the following concerns if/when they were used:

> Well, I think the research is not entirely clear and then also like [there are] different side effects, interactions with medication, and a lot of my patients are quite elderly. Once they take the medications, they have to sit up. There's a high risk of having … acid reflux, GERD, and everything. … I have a feeling [that] a lot of the patients wouldn't really tolerate all that so well.

> Most of the stuff I've seen says that once the osteoporosis has occurred, we can't rebuild bone mass and it's a matter of trying to prevent, but I haven't seen anything strong out for putting people [with SCI] on bisphosphonates.

> There's relatively few female Veterans, especially those with cord injuries … and then, the fact that most of them are already being seen by women's health and hopefully they've addressed [osteoporosis] if there is a need.

Fracture complications

Despite fracture prevention efforts in persons with SCI, many patients do experience fractures. Providers described their experiences in managing patients with fracture-related complications including non-union, non-healing fractures, and pressure ulcers. In some cases, amputation was required.

Further, many patients were described as experiencing psychological distress with loss of mobility and greater restrictions during or after fracture treatment. Providers commented that their patients were frustrated with how long it takes for their fractures to heal. Fractures sometimes led to greater dependence on caregivers or inability to transfer as they had before the fracture.

One provider described the treatment process for fractures:

> [the fracture] … that'd be evaluated by an orthopedic surgeon and if it were feasible, if it were needed, they might get some hardware. I mean, if they're not ever, ever, going to walk, anyway … and it's not [as if they use their leg] for transfers … There might be some patients where they say, 'Well, the risk [of surgery] is kind of high given their medical history and it won't change things functionally very much because this person lays in bed 24 h a day anyway. So, we're going to treat it non-surgically,' … . a lot of that decision-making would come from the orthopod.

Overall, providers described being limited in their ability to prevent osteoporosis and/or subsequent fractures in their patients with SCI. Most of the patients seen in VA SCI centers and clinics are chronic injuries (>2 years post injury). One provider specifically commented that:

> So, in terms of treating osteoporosis, I would like to see more medication on the chronic [SCI] side.

Discussion

Based on interviews with 11 physicians and 1 nurse practitioner that care for Veterans with SCI in either a comprehensive center or an SCI outpatient clinic, there is a sense of frustration that there is little they can do to address osteoporosis in SCI given the lack of guidelines or effective treatment strategies to manage osteoporosis in SCI. Screening for osteoporosis using DXA is not routinely done for SCI in VA regardless of whether a site was a high or low DXA-ordering site. Laboratory testing, including Vitamin D and calcium levels often occur as part of an annual evaluation. If the patient has low vitamin D levels, they are usually provided with a supplement to address general health care, more so than specifically for osteoporosis.

Providers were most likely to order a DXA scan if a patient wanted to use some type of weight-bearing equipment like an exoskeleton, or become active in wheelchair sports. The DXA results also were used to assess safety with respect to fracture risk. Providers used the findings in their decision making as to whether a patient should be participating in these activities. The other time that DXAs were ordered was when a patient had experienced a fracture. This was done to determine if the fracture was related to having osteoporosis. VA has issued guidance for providing powered exoskeleton devices to veterans with SCI.[16] In the guidance, a bone mineral density test is required of the hip (and knee, if available), but no criteria are provided as to a cut-off level for BMD that is appropriate for whether a person with SCI can use the exoskeleton. However, an ongoing clinical trial of exoskeleton in VA SCI patients uses a cut-off level of −3.5 or worse for total hip BMD for exclusion in the trial.[17]

A set of guidelines for use of DXA in persons with spinal cord injuries recently published in the Journal of Clinical Densitometry[7] recommends that all persons with SCI receive a baseline DXA of the total hip, proximal tibia and distal femur as soon after injury as possible. The rationale behind this recommendation is that it is important to know where patients are starting from with respect to their bone health. For example, it is possible that some patients may already have osteoporosis due to other conditions. Recent evidence suggests that secondary causes of osteoporosis are common in SCI. We found that when laboratory testing was performed, over half of the SCI patients tested had at least one abnormality, with the most frequent causes of secondary osteoporosis being hypogonadism and hypovitaminosis D.[18] Treating these secondary causes may improve overall bone health in these individuals. The authors suggest that in clinical practice, DXA scans should be used to assess fracture risk in SCI as other imaging strategies to assess bone loss, such as pQCT do not have normative data for SCI, are less commonly available in the clinic, and most of the available reports fail to meet quality reporting criteria for image acquisition.[9] The WHO criteria for defining osteoporosis using DXA based on T-score (−1.1 and −2.4 for osteopenia, ≥−2.5 for osteoporosis) are also used to determine osteoporosis in the SCI population.[19]

The providers we interviewed had few recommendations for prevention of osteoporosis other than encouraging their patients to get some type of regular

physical activity, weight-bear when possible, and to provide supplements such as Vitamin D. Deficiency in Vitamin D is common in persons with SCI, ranging from 32% to 93%.[20] While there are no guidelines for how best to manage Vitamin D insufficiency in SCI, Lamarche & Mailhot[21] recommend that providers routinely monitor Vitamin D levels and treat patients with SCI who have low levels. Most studies of SCI used 50 nmol/L (20 ng/ml) as the threshold for serum 25 (OH) D level to define vitamin D deficiency and 75 nmol/ L (30 ng/ml) to define suboptimal or insufficient vitamin D status.[21] Bauman *et al*. reported that oral administration of 2000 IU vitamin D_s (i.e. Cholecalciferol) daily combined with 3.25 g. calcium carbonate safely raised Vitamin D levels to the normal range with calcium supplementation.[22] Moreover, while there are currently no evidence-based nutritional guidelines specific for patients with SCI, calcium intakes are often below recommended USDA guidelines (2015–2020 USDA guidelines).[23] This is of potential concern, as a number of observational studies in the able-bodied population have reported that low dietary intakes of calcium are associated with nephrolithiasis,[24,25] and nephrolithiasis is a substantial problem for persons with a SCI.[26]

Prescriptions for FDA-approved osteoporosis medications such as bisphosphonates were uncommon as providers indicated that the available research literature did not support that these medications are effective for sublesional osteoporosis. Most of the patients seen in VA facilities are chronic SCI patients; injured for more than 2 years.[27,28] The literature on bone loss in SCI has shown that in the first months after injury, patients lose almost 1% of their BMD per week, slowing down but continuing after the first 12 months.[1] Thus, for the majority of the VA SCI population, in which the magnitude of bone loss would likely exceed that of postmenopausal or senile osteoporosis in the able-bodied population, it is not known whether any current FDA-approved medications for osteoporosis would be helpful in preventing bone loss. The literature on use of bisphosphonates, particularly zoledronic acid, during the acute injury phase is somewhat encouraging regarding prevention of BMD loss[11,29,30] but findings are hindered by small sample sizes and limited follow-up. Further, while zoledronic acid in acute SCI had a positive effect on BMD in the hip area, it did not improve knee BMD where the majority of lower extremity fractures occur in SCI.[31] These studies did not include any type of mechanical loading (e.g. standing, FES), however in combination with zoledronic acid. Morse *et al*. conducted a study with chronic SCI patients that included a combination of 12 months of FES rowing and a single injection of zoledronic acid.[32] Combination therapy allayed a 2.5% to 8% loss in bone geometric properties of the knee compared to zoledronic acid alone. The feasibility of maintaining combination therapy over the long term, however, is likely to be low.

A new FDA-approved medication, romosozumab may hold promise for persons with a SCI. Romosozumab is a monoclonal antibody to sclerostin that prevents fractures in the general population.[33,34] It has not been tested in the SCI population yet, but due to mechanisms of action that differ from bisphosphonates or denosumab and the potential role of sclerostin in SCI-related bone loss,[35,36] further studies of this medication in sublesional bone may be upcoming.

Reducing fracture risk in SCI should be a priority. Currently, there are no guidelines for how to treat bone disease in persons with SCI. To date, no drug or mechanical intervention has been shown to decrease incident fractures in in persons with a chronic SCI.[10,37] Nonetheless, the Consortium for Spinal Cord Medicine has identified bone health as the next area for which guidelines should be developed and expects this guideline to be available by late 2020. Despite limited evidence, development of guidelines will offer providers the best available evidence and standard guidance for how to manage bone health in their patients. As new evidence becomes available, the guideline can be updated to reflect this information.

Conclusion

Providers who care for persons with SCI at VA facilities feel that they are limited in what they can do to address osteoporosis in their patients. The evidence for pharmacological treatment is not strong, so they tend to support physical activity and use of supplements, particularly Vitamin D. Continuing efforts to identify pharmacological and activity interventions to address sublesional osteoporosis are needed.

Acknowledgements

This study was funded by the Department of Defense. The views expressed in this article are those of the authors and do not necessarily represent the views of the Departments of Defense or Veterans Affairs or the US government.

Disclaimer statements

Contributors None.

Funding This work was supported by the Department of Defense CMDRP program [SCI50092] and the

Department of Veterans Affairs, Health Research & Development program [IIR15-294].

Conflicts of interest Authors have no conflict of interests to declare.

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