After a spinal cord injury, the effects of exercise and activity-based physical therapy on bone

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Abstract

Paralysis and a distinct form of neurogenic disuse osteoporosis result after spinal cord injury (SCI), which greatly raises the risk of fractures in the distal femur and proximal tibia. This bone loss is caused by increased bone resorption and almost non-existent bone formation during the acute post-SCI recovery phase, as well as a more traditional high-turnover osteopenia that develops over time, which is likely influenced by the ongoing neural impairment and musculoskeletal unloading. These findings have sparked interest in specialised exercise or activity-based physical therapy (ABPT) modalities that reload paralysed limbs and promote muscle recovery and use-dependent neuroplasticity (e.g., neuromuscular or functional electrical stimulation cycling, rowing, or resistance training, as well as other standing, walking, or partial weight-bearing interventions). However, evidence supporting the capacity of these physical rehabilitation regimens to impact bone metabolism or enhance bone mineral density (BMD) at the most fracture-prone areas in people with severe SCI is limited and inconsistent. This review discusses the pathophysiology and cellular/molecular mechanisms that influence bone loss after SCI, describes studies evaluating bone turnover and BMD responses to ABPTs during acute versus chronic SCI, identifies factors that may influence ABPT responses, and offers recommendations for optimising ABPTs for bone recovery.

Keywords: spine surgery, spinal cord, physical therapy

INTRODUCTION

Each year, an estimated 250,000 to 500,000 new spinal cord injuries (SCI) are reported worldwide, with males accounting for 80% of the population. A third of these SCIs are motor-complete, resulting in persistent sublesional paralysis, whereas the rest are incomplete, retaining voluntary contractility in some muscles innervated below the lesion. The most well-known sign of SCI is locomotor impairment, which is often accompanied by other medical complications, such as severe osteoporosis and a high fracture risk, both of which deteriorate with increasing SCI severity and injury length [1]. The most fast and widespread bone losses occur at the distal femur and proximal tibia regions. Bone loss after SCI is referred to as neurogenic or disuse osteoporosis and is confined to the sublesional skeleton. Individuals with SCI acquire 50–100% decreased trabecular bone mineral density (BMD) within the first two to three years, and 40–80 percent lower cortical bone mass exists several years after damage [2]. Some research also suggests that following a SCI, cortical bone becomes more porous. These bone impairments add up to a severe deterioration of skeletal integrity, which may explain why people with SCI have a 20- to 100-fold higher fracture risk than the general population. Due to the mobility constraints of people with SCI, fractures are frequently non-traumatic and arise from low-velocity compressive forces or torsional stresses that develop when seated or during transfers to or falls from a wheelchair. The epiphysis or metaphysis of the distal femur or the proximal tibia are the most common sites for these fractures, where bone loss is the most severe and may necessitate protracted inpatient hospitalisation. Furthermore, a single fracture more than doubles the likelihood of secondary medical comorbidities such as venous thromboembolic events, respiratory diseases, and pressure ulcers after SCI [3]. These comorbidities play a role in the 30% greater five-year mortality risk for people of any age who fracture after SCI, as well as the more than three-fold higher five-year mortality risk for people with SCI who fracture after age 50. The severe bone loss, high fracture rate, and associated morbidity and mortality in the SCI community point to the need for better osteoporosis screening and the development of evidence-based guidelines to prevent and treat osteoporosis.

AFTER A SPINAL CORD INJURY, DETERMINING BMD AND FRACTURE RISK

The standard for assessing osteoporosis and fracture risk at typical osteoporosis sites (e.g., lumbar spine and hip) is dual-energy X-ray absorptiometry (DXA), which quantifies areal (a)BMD and T-scores. Although not all DXA systems are capable of imaging these regions, and T-scores have not been established at these sites, specialised DXA procedures have been developed to detect distal femur and/or proximal tibia aBMD following SCI [4]. As a result, some researchers have proposed that established osteoporosis sites be used as surrogates for the distal femur and proximal tibia. After SCI, however, BMD alterations at the knee occur more quickly than at other bone sites. Furthermore, after SCI, changes in aBMD at the knee are only moderately correlated with total hip and femoral neck aBMD and T-scores, and may not correspond to the degree of bone loss at the hip or femoral neck, with significant predictive inaccuracy between the sites that surround the knee and hip. Alternatively, volumetric (v)BMD of the trabecular and cortical bone compartments can be obtained using peripheral quantitative computerised tomography (pQCT), which has been used to estimate vBMD fracture thresholds at the distal femur epiphysis (114 mg/cm3) and distal tibia epiphysis (71 mg/cm3) in people with SCI. High-resolution (HR)-pQCT with finite element analysis (FEA) can assess vBMD as well as bone microstructural parameters and model bone tensile properties at the same time, revealing bone microarchitecture and mechanical changes that lead to higher fracture risk following SCI. For example, over the first few months after SCI, the reduction in proximal femur bone strength estimated by FEA was three times greater than the aBMD loss determined by DXA, likely because DXA cannot distinguish trabecular vs. cortical BMD or quantify other bone parameters that influence fracture risk [5-7]. Regardless, the restricted availability of pQCT devices limits their utility, emphasising the need of DXA

examinations in identifying fracture risk in people with SCI.

SCI-INDUCED BONE LOSS PATHOPHYSIOLOGY

Persons with total paralysis had the most significant bone loss and the highest fracture risk, which is likely due to the residual voluntary muscle function, which reduces bone loss. As evidenced by the fact that people with partial SCI had reduced bone loss in the less affected limb. Furthermore, in a rat severe SCI model, cast immobilisation (a treatment that reduces muscle contraction and inhibits voluntary joint motions) has been demonstrated to increase bone loss, suggesting that even a little amount of residual muscle contractility helps to preserve BMD [8]. These findings back up the hypothesis that disuse is a factor in SCI-induced bone loss. For example, in adults with total SCI, trabecular and cortical bone loss occurs at a rate of 4–10 times quicker than in other types of disuse (e.g., prolonged bed rest or microgravity exposure) during the first several months after SCI. Similarly, bone loss is two to three times faster in rodent SCI models than in cast immobilisation or sciatic neurectomy. Other factors that occur as a result of SCI, such as systemic hormonal changes, altered bone innervation, and/or reduced bone perfusion, may exacerbate bone loss, according to these studies. Readers are recommended to the following review for further discussion.

AFTER A SPINAL CORD INJURY, BONE TURNOVER OCCURS.

During homeostasis, bone undergoes constant remodelling, which is balanced by integrated resorption and creation processes that maintain skeletal integrity. However, after a severe SCI, bone loss is caused by a particular type of unopposed bone resorption. Minaire et al. looked at people with SCI and found indicators of enhanced osteoclastic resorption, as well as a near-absence of surface-level bone production at the iliac crest, which suggests uncoupled bone turnover. Throughout the acute (four months) to subacute (4–12 months) post-injury periods when bone loss is most rapid, circulating bone resorption markers are several-fold greater than upper reference levels in people with SCI, whereas circulating bone formation indicators remain around reference ranges. Similarly, in rodent models of severe SCI, dynamic histomorphometry revealed that trabecular bone resorption persists in the absence of bone formation at the distal femur and proximal tibia during the first one to three weeks after SCI, when nearly all trabecular bone loss occurs. Trabecular bone growth returns to normal after that, and bone loss slows. RANKL is an osteocyte-derived protein that is required for the development of monocyte-macrophage lineage hematopoietic progenitors into osteoclasts. By binding RANK receptors on the cell surfaces of osteoclast precursors and osteoclasts, RANKL induces osteoclastogenesis and bone resorption. The response of RANKL-mediated osteoclastic resorption to released amounts of RANKL and OPG, an endogenous RANKL decoy receptor generated by osteoblast-lineage cells that blocks RANK binding, is primarily altered. The ratio of RANKL to OPG is a critical determinant in RANKL signalling, with more RANKL and/or lower OPG driving bone resorption and osteoclastogenesis, respectively. The following review provides an overview of RANKL signalling in bone biology to readers. In rodent SCI models, signs of altered RANKL signalling coexist with bone loss. For example, compared to controls, cultured bone marrow mesenchymal or stromal cells from spinalized mice have higher RANKL and lower OPG, which could explain the two- to three-fold increase in tartrate-resistant acid phosphatase (TRAP)+ osteoclast-like cells that develop in bone marrow culture from spinalized mice. When compared to controls, RANKL mRNA and protein expression in the distal femur and proximal tibia were 75–300% higher and OPG mRNA and protein expression were 30–75% lower in rodent SCI models.

BMD PARAMETERS TO IMPROVE AFTER A SPINAL CORD INJURY

Several common criteria were found in studies that indicated higher BMD at other sites or improved BMD at the proximal tibia or distal femur. First, studies that reported reduced BMD loss at the knee all enrolled people with acute/subacute SCI and used FES-based

modalities that were performed 3–5 days/week, 20–60 minutes/day, for 3 months, and studies that reported increased BMD at the knee all enrolled people with chronic SCI and used FES-based regimens that were performed 3–5 days/week, 30+ minutes/day, for 6 months. Second, no study that included standing without FES found improvements in BMD in the distal femur or proximal tibia, however several that used these regimens 3–7 days per week, 60+ minutes per day, for >3 months indicated reduced BMD loss or enhanced BMD at other sites [9]. These findings emphasise the importance of tailoring ABPTs to the precise region(s) where BMD development is most needed, as well as using a training intensity, frequency, and duration that is sufficient to improve BMD. Regardless, it's worth noting that not all FES modalities or passive/active standing regimens that satisfied these requirements improved BMD. Clark et al. and Arija-Blazquez et al. found that FES-based RT regimens lasting 14 weeks to 5 months (performed 5-days/week for 30+ min/day) did not reduce sublesional aBMD loss in people with acute/subacute SCI, and other FES studies that met the chronic criteria found no BMD improvement at the distal femur or proximal tibia [10].

CONCLUSION

In people with SCI, various ABPTs enhance neuromuscular advantages and use-dependent neuroplasticity. Regardless of the skeletal site studied, no known ABPT completely stops bone loss that happens in the lower limbs during the acute/subacute post-SCI phase. Furthermore, no ABPT has demonstrated universal efficacy in raising BMD at the high-fracture-risk areas around the knee. However, a limited fraction of trials evaluating FES modalities found reduced BMD loss in the distal femur and/or proximal tibia in people with acute to subacute SCI and increased BMD in people with chronic SCI, implying that such regimens could be beneficial. Furthermore, a small sample of studies that used weight-bearing ABPTs without FES revealed BMD improvements elsewhere but no changes at the knee.

References:

1. McClelland J.A., et al.: Total knee arthroplasty with computer-assisted navigation more closely replicates normal knee biomechanics than conventional surgery. The Knee. 2017;24:651-.656. CrossRef Google Scholar
2. Gothesen O., et al.: Computerized navigation: a useful tool in total knee replacement. JBJS Essent Surg Tech. 2020;10:e0022. CrossRef Google Scholar
3. Singisetti K., et al.: Navigation-assisted versus conventional total knee replacement: no difference in patient-reported outcome measures (PROMs) at 1 and 2 years. Arch Orthop Trauma Surg. 2015;135:1595-1601. CrossRef Google Scholar
4. Engh GA.: Surgical technique of the midvastus arthrotomy. Clin Orthop. 1998;351:270-274. Crossref Google Scholar
5. Hube R., Sotereanos N.G., Reichel H.: The midvastus approach for total knee arthroplasty. Orthop Traumatol. 2002;10:235-244. CrossRef Google Scholar
6. Abdel M.P., et al.: Effect of postoperative mechanical axis alignment on survival and functional outcomes of modern total knee arthroplasties with cement: a concise follow-up at 20 Years. JBJS. 2018;100:472-478. CrossRef Google Scholar
7. Liu H.W., et al.: Surgical approaches in total knee arthroplasty: a meta-analysis comparing the midvastus and subvastus to the medial peripatellar approach. J Arthroplasty. 2014;29:298-304. CrossRef Google Scholar
8. Matziolis G., et al.: A prospective, randomized study of computer-assisted and conventional total knee arthroplasty: three-dimensional evaluation of implant alignment and rotation. JBJS. 2007;89:236-243. CrossRef Google Scholar
9. Lotke P.A., Ecker M.L.: Influence of positioning of prosthesis in total knee replacement. J Bone Joint Surg Am. 1977;59:77-79. Google Scholar CrossRef
10. Pearle A.D., Kendoff D., Musahl V.: Perspectives on computer-assisted orthopaedic surgery: movement toward quantitative orthopaedic surgery. J Bone Joint Surg Am. 2009;91:7-12. CrossRef Google Scholar