Short Note

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Breaking Back and Bones: A Review on Osteoporotic Vertebral Fracture

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Abstract: Osteoporotic vertebral fracture is the most common fracture from osteoporosis, and are largely undiagnosed due to the mostly asymptomatic nature of the condition. It increases the risk of subsequent fractures and contributes to societal burden. Risk factors for osteoporotic fractures are found in the WHO fracture risk assessment model and used as a tool for monitoring bone health. Vertebral fractures are diagnosed from anteroposterior and lateral spine radiographs and are confirmed with an approximate loss of 20% vertebral height as compared to adjacent vertebrae. One of the most used grading for vertebral fractures is the SQ grading. Mild vertebral fractures could easily be misdiagnosed due to some peculiarities of the vertebral column. CT scan is useful for planning surgical intervention while an MRI scan can provide information about the recency of the fracture and rule out cancer-related fractures. Management depends on the severity of the fracture which could range from conservative management to surgical vertebral augmentation and decompression. Bisphosphonates are used to treat osteoporosis in acute and long-term management of fractures. Osteoimmunological therapies such as denosumab and romosozumab are new therapeutic interventions for osteoporosis while there are many other potential treatment options. Precision medicine provides an individualized treatment approach while regenerative medicine utilizes mesenchymal stem cells for fracture repair.

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Osteoporosis is a public health issue, caused by a reduced rate of bone mineralisation which leads to low bone mass and microarchitectural deterioration contributing to an increased risk of fractures [1]. For the epidemiology of osteoporotic vertebral fracture, it is the most prevalent osteoporotic fracture, which happens in 30 - 50% of the population over 50 [2]. There is no variability between the male and female populations. Instead, there is higher variability in Asia and Latin America as compared to Europe and North America [3]. Most vertebral fractures do not cause any symptoms unless they involve the spinal cord which leads to neurological deficit and is therefore hard to detect. Due to the lack of symptoms, the affected population would not seek any medical attention. The primary complaint is back pain. It could happen without any correlation to trauma and it classically occurs from daily activities such as walking or sitting. It lowers the population's quality of life and causes prolonged immobility, which could lead to social isolation, decreased body mass, and low self-esteem. Having osteoporotic vertebral fractures also has high clinical consequences leading to an increased risk of fractures involving the proximal femoral, radial, sacral, or pelvis, contributing to high societal cost and mortality and is therefore important to be picked up by radiologists [4]. According to Lyritis 1989, these fractures with silent symptomatology are prone to a series of acute back pain that could exceed 20 months in total [5]. Additionally, it may cause a series of adjacent vertebral fractures from altered spinal biodynamics, from a process called "vertebral fracture cascade" [6]. As its presentation is subtle, clues on risk factors for osteoporotic fractures should be obtained to guide its diagnosis and management and prevent further subsequent fractures. The WHO fracture risk assessment model provided a list of risk factors to take into account for future fractures, which includes: current age, gender, prior osteoporotic fracture, parental history

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of hip fracture, femoral neck bone mineral density (BMD), low body mass index (BMI), excessive alcohol intake, current smoking, intake of oral glucocorticoids, rheumatoid arthritis and secondary osteoporosis [7].

According to the World Health Organisation (WHO), osteoporosis is defined as >2.5 standard deviations below peak bone mass of bone mineral density (BMD) measurements [8]. BMD is measured with dual-energy X-ray absorptiometry. Osteopenia, which is a less severe form of osteoporosis, has a BMD value of 1 to 2.5 standard deviations below the average peak bone mass [9]. Severe osteoporosis is described as a status of osteoporosis with osteoporotic fragility fracture. Regardless, having osteoporotic fractures with a normal BMD value or osteopenia is still a pointer for osteoporosis. BMD measurement is periodically reassessed to evaluate the risk for future fractures in low-risk fracture patients. Patients presenting with back pain, risk of fracture, and a high degree of suspicion of vertebral fracture are diagnosed on radiography. Anteroposterior and lateral spine views are obtained to evaluate the spinal column. The most recent consensus is an approximate loss of 20% vertebral height relative to normal-looking adjacent vertebra. These fractures are then graded through the SQ method by Genant et al. [10]. It takes into account the extent of vertebral height loss, in which mild severity has a 20-25% anterior, middle, or posterior height; moderate severity at 25-40%; severe severity at >40% as compared to the adjacent vertebrae. Misdiagnosis could happen for mild vertebral fractures as there were several mimics such as physiological wedging, short vertebral height (SVH), Scheuermann's disease, degenerative scoliosis, Schmorl's nodes, and Cupid's bow deformity. Other imaging modalities include computed tomography scans, magnetic resonance imaging, and bone scintigraphy. CT scans are commonly overused as taking several X-rays could provide the same clinical information due to its inability to distinguish between old or new fractures, however, it is useful in planning for surgical intervention by giving information about the degree of deformity of the fracture as well as the bony composition and surrounding spaces. MRI scans can provide a lot of information to help with the management and prognostication of vertebral fractures from the T1-weighted, T2-weighted, and STIR sequences. STIR sequence allows confirmation of the chronicity of the fracture, whereas a T1-weighted image helps to determine the risk of residual pain. It is also used to distinguish osteoporotic from neoplastic fractures. Bone scintigraphy could suggest a metastatic nature from increased radionuclide uptake in several areas [11].

Conservative and surgical interventions are used for osteoporotic vertebral fractures based on different indications. It is important to treat the fracture and the underlying osteoporosis. Conservative management involves bed rest, pain management, activity modification, bracing, and osteoporosis management. Pain medications are given based on the severity of back pain. Non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, or salicylates are given for mild pain. COX-2 inhibitors are recommended to avoid the risk of gastrointestinal bleeding and renal impairment [12]. For moderate to severe pain, opioids such as oxycodone could be given with low-dose acetaminophen. However, long-term use of opioids is not recommended due to their adverse effects such as constipation, respiratory depression, and opioid dependence [13]. Muscle relaxants are used to relieve painful paravertebral muscle spasms and are most effective for short-term usage as well. Calcitonin could also be given for severe pain providing pain relief by modulating the pain signals while preserving bone health through inhibition of osteoclasts at the same time. Bisphosphonates such as intravenous disodium clodronate were found to provide higher pain relief after the initial management [14]. Bracing is used to stabilise the spine and prevent movement-related pain. The types of brace used depend on the patient's expectations, type and level of fracture, and patient condition. Generally, a thoracolumbar orthosis (TLO) is prescribed for thoracic fractures, while a rigid lumbosacral orthosis (LSO) is used for lower lumbar fractures. Jewett brace is used if hyperextension of the spine is needed, and a Knight-Taylor brace could be considered for flexion, extension, and lateral flexion [15]. Surgical intervention is considered if medical management fails. Vertebral augmentation includes vertebroplasty and kyphoplasty. Vertebroplasty involves direct injection of cement into the fractured vertebrae, however has a high risk of cement extravasation; while kyphoplasty involves inflating a balloon in the affected vertebrae and injecting cement [16], associated with better restoration of kyphotic angle and reduced risk of complications. Both surgical

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procedures provide more pain relief and functional restoration than medical management. Decompression is done when there is a neurological deficit, added with screw implantation and vertebral fixation. Posterior fixation is indicated when there is a burst fracture of the osteoporotic spine, multiple vertebral fractures with large kyphotic deformity, or malunion. Cement may be used as well along with decompression if anterior spinal support is needed.

There are several emerging therapies for osteoporosis to prevent osteoporotic fracture, including in the fields of osteoimmunology, precision medicine, and regenerative medicine. Known osteoimmunology drugs target activating the receptor of nuclear factor-kB ligand (RANKL) monoclonal antibody, which inhibits osteoclast formation and recruitment [17], which is denosumab. It is delivered via subcutaneous injection every 6 months to maintain its anti-resorptive activity of the bone. However, studies have shown that multiple fractures occurred after stopping denosumab therapy, requiring the addition of teriparatide to ensure the maintenance of bone mass. They are without side effects, as prolonged use of denosumab increases the risk of urinary tract infections, hypocalcemia, osteonecrosis of the jaw, and atypical femoral fractures. At the same time, teriparatide is only effective for 2 years. The next potential drugs include sclerostin inhibitors that target the Wnt-β-catenin signalling pathway. Romosozumab is one of the sclerostin inhibitors and is also delivered via subcutaneous injection, has been recently approved by the FDA [18] but is under review by the European Medicines Agency (EMA) due to its cardiovascular complications as observed from the clinical trials. There are other choices of therapy as well that showed potential to treat osteoporosis including growth factors (BMPs, TGF-β, GH, IGF-1), molecules involved in the Wnt pathway (BMP-2, anti-DKK1, TKI), secreted frizzled-related protein 1 (SFRP1), tryptophan hydroxylase 1 (Tph1) inhibitor and Cathepsin K inhibitors (odanacatib). Small molecules, nanoparticles, and natural products like microRNA (miRNA), short interfering RNA (siRNA), bisphosphonate-conjugated iron oxide nanoparticles, vitamin B12, C, D, folate, tart cherry, Zhuanggu Guanjie pill, and BHH10 are effective in osteoporosis therapy too. Precision medicine focuses on tailoring management according to patient's needs. It incorporates preventive care and holistic care such as risk assessment tools, genetic profiling, lifestyle modifications, and pharmacogenomics which could identify interventions that would produce the best response from individual patients. Biomarkers such as serum osteocalcin and C-terminal telopeptide of type 1 collagen are used to estimate and monitor the effectiveness of treatment. Advanced imaging such as high-resolution peripheral quantitative computed tomography is used to obtain specific information about the patient's bone health and estimate future risks of fracture. For regenerative medicine, the exogenous introduction of mesenchymal stem cells targeting a reduced number of resident stem cells in senile osteoporosis has been shown to induce recovery of trabeculae of the vertebrae in mouse models. The advancement of technology, such as digital technology, data science, targeted therapy, genomic data, and increased collaboration between clinicians, researchers, and pharmaceutical companies, will further revolutionize personalized medicine and improve patient outcomes.

Conclusion

Osteoporotic vertebral fracture remains a potentially serious complication of osteoporosis and is mostly undiagnosed due to the lack of symptoms and dilemma from radiographical interpretation. In approaching a patient with back pain, it is important to obtain a history of the risks of osteoporotic fracture and confirm the diagnosis with radiographs. A patient over 50 years of age and of female gender has an increased risk of osteoporotic fracture. Management does not only involve the fracture but also takes into account the osteoporotic nature of the bones. Future management of osteoporosis should incorporate osteoimmunology, precision medicine, and regenerative medicine to further improve patient's bone health, prevent fractures, and reduce mortality.

Ethical Statement: Being a Short note, there were no ethical issues and IRB permission is not required.

Conflicts of interest: The authors declare no conflict of interest.

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