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Original Article

The Future of Fracture Risk Assessment in the Management of Osteoporosis

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Abstract

There have been many advances in the field of osteoporosis that add to a greater understanding of skeletal integrity and the adverse effects menopause and aging have on bone. The World Health Organization, the International Osteoporosis Foundation, and numerous additional governmental and privately sponsored organizations, societies, and their respective task forces have provided guidance for the use of appropriate fracture assessment methodologies and fracture risk assessment tools, and for the prevention and management of osteoporosis. Despite these worldwide efforts, a majority of patients at high risk of fracture have not had bone density testing and are not diagnosed or offered osteoporosis treatment before or even after sustaining a fragility fracture. The future of fracture risk assessment and, in general, osteoporosis management requires health-care systems to develop customizable electronic medical record (EMR) systems that incorporate the tools necessary to identify patients at high fracture risk. As provided in the example of an advanced health-care osteoporosis model, an EMR can be fully customizable to identify fractures and patients at high risk of fracture, to assist clinicians in selecting the most efficacious osteoporosis treatments, and to provide long-term follow-up with or without serial bone density testing. Future fracture risk assessment models will likely be further refined by incorporating advanced fracture predictive technologies for integration into algorithms that have improved discrimination, calibration, risk reclassification capabilities, and clinical utility. These models will include accurate and reproducible bone biomarkers and genomic testing that will be automatically integrated into worldwide EMR systems for screening large numbers of at-risk populations and younger patients for future prediction and prevention of disease. The integration of this type of a fracture prediction model into future electronic medical record systems will result in the prevention of osteoporosis fractures.

Key Words: Fracture liaison service; fracture risk; primary fracture prevention; risk assessment tool; secondary fracture prevention.

Introduction

It is estimated that 1 in 2–3 women and 1 in 4–5 men in developed countries are expected to sustain an osteoporosis fracture that is associated with significant morbidity, mortality, and adverse psychological, social, and financial consequences for the affected individual family and society *(1–3)*. There are 200 million women who have osteoporosis worldwide, with 1.6 million women sustaining an osteoporotic hip fracture annually. As the world population ages, it is estimated that by 2050, the annual number of hip fractures will increase to between 4.5 and 6.3 million *(1–3)*. The importance of fracture risk assessment has been discussed at length by all the contributing coauthors to this volume *(4)*. The assessment of fracture risk is the keystone to the prevention and management of osteoporosis.

There are 2 different but interdependent discussion points that should be considered when taking into account an effective model for the identification and treatment of

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patients at risk for osteoporosis fractures. The first is concerned with the technologies available for the measurement of bone mass and skeletal integrity and the algorithms that integrate clinical risk factors (CRFs) for fracture with these measurements into a highly predictable fracture tool. An in-depth review of the present and future evolution of the technologies available for the measurement of bone mass and skeletal integrity and available fracture risk algorithms, including their respective and comparative performance measures (discrimination, calibration, reclassification, and clinical utility), have been discussed at length elsewhere in this volume of the *Journal of Clinical Densitometry (4)*. The second discussion point is concerned with the importance of integrating the results of skeletal measurement technologies and osteoporosis algorithms into worldwide health-care systems that will not burden the clinician but rather assist in identifying patients at high fracture risk for consideration of medical intervention. The following discussion will further address the integration of both concepts into an effective model for the evaluation and treatment of osteoporosis.

The discussion of the future of osteoporosis fracture risk assessment begins with the characterization of osteoporosis. Osteoporosis is characterized by reduced bone mass, disrupted bone architecture, and increased risk of fragility fractures *(5)*. The diagnosis of osteoporosis can be made clinically after an individual sustains a fragility fracture or is defined by the World Health Organization (WHO) diagnostic criteria as a bone mineral density (BMD) *T*-score of less than or equal to –2.5 standard deviations below a young Caucasian reference population performed by dual-energy X-ray absorptiometry (DXA) at the spine, the hip, or the forearm *(6,7)*. The choice of the T-2.5 threshold for the DXA BMD diagnosis of osteoporosis was based on the prevalence of BMD at or below this threshold in postmenopausal women measured at the spine, the hip, and the forearm that correlated with the lifetime risk of fractures at the 3 anatomical sites *(6,7)*. There are significant limitations to the use of the *T*-score for the diagnosis of osteoporosis and as a treatment threshold inclusive of the fact that the majority of osteoporosis fractures occur in patients who do not have osteoporosis but rather osteopenia or normal BMD. The definition has been more recently updated by the WHO to include the femoral neck region (DXA) *(8)* that is presently being used with fracture algorithms (tools) to improve fracture prediction *(9–12)*. National guidelines that use DXA BMD *T*-score thresholds alone for the diagnosis and pharmacological treatment of osteoporosis imply that osteoporosis is a monofactorial disorder with the T-2.5 threshold being found to have low sensitivity and low positive predictive value for osteoporotic fractures *(13–17)*. There are additional reasons that a T-2.5 cannot be considered as a worldwide diagnostic and therapeutic intervention threshold. Two important reasons are the 10-fold difference in fracture rates worldwide and numerous CRFs that are known to influence fracture risk independent of BMD *(18,19)*.

Alternatives to DXA *T*-Scores for the Assessment of Fracture Risk

There have been many advances in the technologies that measure and explain skeletal integrity and the adverse effects menopause and aging have on bone as discussed in this volume of the *Journal of Clinical Densitometry (4)*. I would refer the reader to these excellent reviews and the potential use of each technology for fracture risk assessment. Although there will be significant advances in the technologies that measure skeletal integrity and predict future fractures, there will always be the fact that osteoporotic fractures are multifactorial in origin and are associated with many CRFs that may or may not directly impact the quantitative measurement of BMD or other measurement parameters. An important example of a non-BMD-dependent CRF that is associated with increased osteoporotic fractures is high falls risk associated with severe arthritis of the weight-bearing joints, metabolic and neurological diseases that affect position sense and neuromuscular functioning, uncorrectable visual loss, and many others that have been comprehensively reviewed by one of the coauthors in this volume *(4)*. Because of the limitations of bone mass and skeletal integrity measurements alone to precisely predict an individual's fracture risk, algorithms have been designed to incorporate CRF for fractures with or without BMD resulting in improved hip, spine, forearm, humerus, and any future fracture prediction *(9–12)*. Fracture risk algorithms using absolute rather than relative risk estimates are being used worldwide in national guidelines to determine which patients are at the highest fracture risk and should be considered for treatment as has been comprehensively reviewed in this special edition *(4,20–24)*.

Worldwide Prevention Efforts Using Fracture Risk Stratification and the Fracture Liaison Service (FLS) Model

The WHO, the International Osteoporosis Foundation, and numerous governmental and privately sponsored national organizations have not only provided osteoporosis educational resources for the public, medical profession, and government but have also provided guidance for the use of appropriate fracture assessment methodologies, fracture risk assessment tools, and guidelines for the prevention and management of osteoporosis *(24)*. Despite these worldwide efforts, a majority of patients at high risk of fracture have not had bone density measurement by any available technology and are not diagnosed or offered osteoporosis treatment before or even after sustaining a fragility fracture *(20–25)*.

There are many challenges inherent in the universal implementation of a risk stratification-treatment model to appreciably reduce the risk of an initial osteoporosis fracture (primary fracture prevention) or an identification-treatment model for patients who have previously sustained an osteoporotic fracture (secondary fracture prevention).