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RESEARCH ARTICLE

Diagnosis of Osteoporosis in Multiple Myeloma: Current Approaches and Perspectives

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PAGE: 79-82

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Abstract

Osteoporosis is one of the most common and clinically significant complications of multiple myeloma (MM), substantially increasing the risk of pathological fractures and adversely affecting patients' quality of life. Over the past decade, diagnostic strategies for skeletal involvement in MM have evolved due to the implementation of highly sensitive imaging modalities and quantitative techniques for assessing bone mineral density. This review summarizes contemporary approaches to the diagnosis of osteoporosis in patients with MM, evaluates their diagnostic performance, strengths, and limitations, and discusses emerging perspectives related to radiomics and artificial intelligence. Emphasis is placed on the importance of a comprehensive and multidisciplinary approach to skeletal assessment in this complex patient population.

KEYWORDS

Osteoporosis; multiple myeloma; bone mineral density; DXA; quantitative computed tomography; MRI; PET/CT.

INTRODUCTION

Osteoporosis is a chronic systemic skeletal disease characterized by decreased bone mineral density (BMD), deterioration of bone microarchitecture, increased bone fragility, and a higher risk of low-energy fractures [1,19]. It represents one of the leading causes of disability among older adults. In patients with multiple myeloma, osteoporosis develops more frequently and progresses more aggressively than in the general population. This phenomenon is driven by both the direct effects of malignant plasma cells on bone remodeling and secondary factors such as prolonged glucocorticoid therapy, chemotherapy, and profound metabolic disturbances [2–4].

According to the International Myeloma Foundation, skeletal involvement is detected in more than 70% of patients at the time of MM diagnosis [3,6]. Conventional radiography, once considered the cornerstone of skeletal assessment, is now recognized as insufficient due to its low sensitivity compared

with modern imaging techniques such as whole-body low-dose computed tomography (WBLDCT), magnetic resonance imaging (MRI), and positron emission tomography combined with CT (PET/CT) [6,7].

The aim of this review is to systematize current diagnostic approaches to osteoporosis in MM, assess their diagnostic accuracy and clinical value, and highlight future directions, including radiomics and artificial intelligence (AI).

Epidemiology of Osteoporosis in Multiple Myeloma

Multiple myeloma is predominantly diagnosed in individuals older than 60 years, and up to 80% of these patients exhibit clinically significant bone involvement. Osteoporosis associated with MM is characterized by rapid progression and a high incidence of pathological fractures involving the spine, hip, and ribs. The socioeconomic impact is substantial, as fractures in MM patients lead to decreased functional independence, increased healthcare expenditures, and higher mortality rates.

Pathophysiology of Osteoporosis in Multiple Myeloma

Bone loss in MM results from a profound imbalance between bone resorption and bone formation. Under physiological conditions, osteoclastic and osteoblastic activities are tightly regulated. In MM, this balance is disrupted by several interrelated mechanisms.

Direct effects of myeloma plasma cells

Myeloma cells secrete multiple osteoclast-activating factors, including receptor activator of nuclear factor κB ligand (RANKL), interleukin-6, and macrophage inflammatory protein-1α, which promote osteoclast differentiation and activity [4,17]. Simultaneously, osteoblast maturation and function are suppressed, resulting in impaired bone formation.

Uncoupled bone remodeling

The dominance of bone resorption over formation leads to so-called "uncoupled remodeling," manifesting as generalized osteopenia, osteolytic lesions, reduced biomechanical strength, and a high risk of compression and pathological fractures [7,18].

Bone marrow microenvironment

Alterations in the bone marrow niche, including dysregulation of Wnt/β-catenin signaling and increased expression of inhibitors such as dickkopf-1 and sclerostin, further exacerbate bone loss [17,35].

Impact of therapy and comorbidities

Long-term glucocorticoid use, cytotoxic and immunomodulatory therapies, vitamin D deficiency, hypocalcemia, and endocrine disorders all contribute to accelerated osteoporosis in MM.

Diagnostic Approaches to Osteoporosis in Multiple Myeloma

Clinical assessment

Initial evaluation includes assessment of age, sex, cumulative glucocorticoid exposure, fracture history, and comorbid endocrine or hematologic conditions. In MM, early and repeated assessment of these risk factors is critical [1,20].

Imaging techniques

Dual-energy X-ray absorptiometry (DXA)

DXA remains the reference standard for BMD measurement, with osteoporosis defined by a T-score ≤ −2.5 [10,22]. However, in MM patients, degenerative spinal changes, vascular calcifications, and osteolytic lesions may compromise accuracy [5,10].

Quantitative computed tomography (QCT)

QCT provides three-dimensional volumetric BMD assessment with separate evaluation of cortical and trabecular compartments [9,21]. It demonstrates higher sensitivity than DXA but is associated with increased radiation exposure and limited availability.

Conventional radiography

Radiography detects bone loss only after ≥30% reduction in bone mass and is therefore inadequate for early diagnosis [1,7].

Ultrasound-based methods

Ultrasound densitometry and radiofrequency echographic multispectrometry (REMS) are radiation-free techniques suitable for fracture risk screening, though they cannot replace DXA or QCT for definitive diagnosis [24].

Advanced imaging in MM

WBLDCT is recommended as the minimum standard for skeletal imaging in MM, enabling detection of small osteolytic lesions and improved fracture risk stratification [3,20,30]. MRI

is highly sensitive for bone marrow infiltration and is valuable for early diagnosis and treatment monitoring [16,32]. PET/CT with ^18F-FDG provides combined anatomical and metabolic information and is essential for assessing disease activity and minimal residual disease [14,33].

Biochemical markers

Markers of bone turnover (β-CTX, P1NP, osteocalcin) and metabolic parameters (calcium, vitamin D, parathyroid hormone) support monitoring but are not diagnostic on their own [20,23].

Radiomics and Artificial Intelligence

Radiomics and AI-based image analysis applied to CT and MRI enable extraction of quantitative texture features that improve diagnostic accuracy, allow detection of early microstructural bone changes, and facilitate fracture risk prediction [8,9,27,29].

Management Considerations

Osteoporosis in MM often coexists with osteolytic lesions and vertebral compression fractures, complicating differential diagnosis with primary osteoporosis [6,26]. Optimal management requires a multidisciplinary approach involving hematologists, radiologists, endocrinologists, and rehabilitation specialists.

CONCLUSION

Osteoporosis is a frequent and clinically significant complication of multiple myeloma. Modern diagnostic strategies integrate quantitative BMD assessment, advanced imaging modalities, biochemical markers, and emerging AI-based tools. A comprehensive, multidisciplinary, and personalized approach is essential for early detection, effective treatment, and fracture prevention in this high-risk population.

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