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REVIEW ARTICLE



# Current concepts in the management of bone lesions in multiple myeloma

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## ABSTRACT

**Introduction.** Bone lesions remain a serious, unresolved issue in patients with multiple myeloma. The management of myeloma-related bone disease involves a multimodal approach, including chemotherapy, bone antiresorptive agents (bisphosphonates), radiotherapy, pharmacological pain management, minimally invasive percutaneous orthopedic procedures, and invasive surgical interventions.

**Material and methods.** A bibliographic search was conducted using databases such as *PubMed, Hinari, SpringerLink, the National Center for Biotechnology Information, and Medline*. Articles published between 2000 and 2025 were selected using the following keywords: "bone lesions in multiple myeloma" in combination with terms such as "conservative treatment," "surgical treatment," "orthopedic surgery," and "minimally invasive techniques" to maximize the search yield. Based on the established search criteria, a total of 286 full-text articles were identified. The final bibliography includes 42 relevant sources, deemed representative of the literature published on the topic of this review article.

**Results.** Bisphosphonates or denosumab should be considered the standard of care for the treatment of bone disease in patients with multiple myeloma. Cement augmentation (polymethylmethacrylate) is effective in managing painful vertebral compression fractures (percutaneous vertebroplasty, balloon-assisted percutaneous kyphoplasty). Radiotherapy is recommended for uncontrolled pain in cases of spinal cord compression or pathological fractures of long bones, especially in patients who show no response or minimal response to systemic treatment for multiple myeloma. Surgery should be used to prevent and repair pathological fractures of long bones, spinal instability, and spinal cord compression caused by bony fragments. Postoperative radiotherapy should be considered, particularly for long bone fractures, to achieve local disease control and prevent implant failure.

**Conclusions.** The current concept in the management of patients with multiple myeloma and bone lesions is based on developing an individualized approach that takes into account anatomical, biological, radiological, and social factors. The selection of surgical techniques must be tailored to each patient, based on general medical condition, quality of life and life expectancy, prior response to chemotherapy, fracture location, number, size and distribution of bone lesions, extent of bone invasion, neurological status, and patient expectations.

**Keywords:** multiple myeloma, bone lesions, conservative treatment, surgical treatment, orthopedic surgery, minimally invasive methods.

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## Key messages

### What is not yet known about the issue addressed in the submitted manuscript

Despite continuous improvements in outcomes for patients with multiple myeloma due to the increasing availability of effective treatments, skeletal-related complications remain a significant issue, imposing a substantial burden on both patients and health-

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care systems. Therefore, preventing these complications is of paramount importance.

**The research hypothesis**

The analysis and synthesis of contemporary literature reveal a clear association between the appropriate application of surgical indications and improved clinical outcomes in patients with multiple myeloma and bone lesions.

**The novelty added by the manuscript to the already published scientific literature**

This article provides a synthesis of the most recent international publications concerning the characteristics and effectiveness of current medical and surgical treatment methods for bone complications in patients with multiple myeloma. The study's findings will contribute to improving treatment protocols for managing and optimizing therapeutic approaches in patients with multiple myeloma.

## Introduction

Bone disease – one of the major complications of multiple myeloma (MM) – is characterized by severe bone loss and the development of osteolytic lesions, frequently leading to pathological fractures. Bone lesions occur in approximately 80% of patients with newly diagnosed symptomatic MM and in over 90% during the course of the disease, being associated with significant patient morbidity and mortality. The axial skeleton, particularly the spine, and the proximal long bones are most commonly affected, although any bone may be involved [1-13].

The spine is the most frequently affected site due to myeloma-induced osteoporosis, osteolysis, or vertebral compression fractures (VCFs), accounting for about 60% of bone lesions present at diagnosis and 15–30% of newly developed lesions. These patients have an increased risk of skeletal-related events – including pain, VCFs, spinal instability and spinal cord compression, hypercalcemia, and pathological fractures of long bones – that often require radiotherapy and surgical intervention. All of these factors negatively impact quality of life and significantly reduce overall patient survival [1-13].

The treatment of bone lesions remains a serious, unresolved issue in patients with MM. The management of myeloma bone disease involves a multimodal approach that includes chemotherapy, bone antiresorptive agents (bisphosphonates), radiotherapy, pain management (aspirin, nonsteroidal anti-inflammatory drugs), minimally invasive percutaneous orthopedic interventions (percutaneous vertebroplasty – VP, balloon-assisted kyphoplasty – BKP), and invasive surgical procedures. However, optimal management depends on the individual nature of bone involvement – primarily spinal involvement – and requires careful evaluation and appropriate intervention throughout treatment [1, 2, 5, 11-15].

In this context, this article aims to provide a narrative synthesis of the most recent data regarding the characteristics and effectiveness of modern medical and surgical management strategies for patients with multiple myeloma and bone lesions.

## Material and methods

To achieve the stated objective, an initial search of scientific publications was conducted using specialized databases, including *PubMed, Hinari (Health Internet Work Access to Research Initiative), SpringerLink, the National Center for Biotechnology Information, and Medline*. The selection criteria for articles focused on contemporary data regarding pharmacological management, minimally invasive percutaneous orthopedic interventions, and invasive surgical treatments for bone disease in patients with multiple myeloma. The following keywords were used: "bone lesions in multiple myeloma," combined in various ways with terms such as "conservative treatment," "surgical treatment," "orthopedic surgery," and "minimally invasive methods" to maximize search efficiency.

For the advanced selection of bibliographic sources, the following filters were applied: full-text availability, English language, and publication years ranging from 2000 to 2024. After a preliminary analysis of titles, original research articles, editorials, narrative reviews, systematic reviews, and meta-analyses were selected – those that included relevant information and contemporary concepts regarding the effectiveness of various medical and surgical management strategies in patients with MM and bone lesions. Additionally, the reference lists of the selected articles were reviewed to identify further relevant publications not captured in the initial database search.

The information from the included publications was collected, categorized, evaluated, and synthesized to highlight the key aspects of current perspectives on medical and surgical treatment methods for bone disease in MM.

To minimize the risk of systematic bias in the study, comprehensive database searches were performed to identify the maximum number of relevant publications. Only studies meeting validity criteria were included, and reliable exclusion criteria were applied to eliminate irrelevant articles.

## Results

Following the processing of information identified from databases such as PubMed, Hinari, SpringerLink, the Na-

tional Center for Biotechnology Information, and Medline, and according to the defined search criteria, a total of 286 articles were found addressing the topic of managing patients with MMBD (multiple myeloma bone disease). After a primary title screening, 58 articles were deemed potentially relevant for this synthesis. Upon further in-depth review of these sources, a final selection of 42 publications was made. These 42 articles were included in the final bibliography, being considered representative of the literature published on the topic of this review article.

Publications whose content did not align with the subject, despite being identified by the search algorithm, as well as articles that were not freely accessible via *HINARI* or through the scientific medical library of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, were subsequently excluded from the list.

***Current non-operative*** interventions for the treatment of vertebral compression fractures (VCFs) include oral and parenteral analgesics, corticosteroids, bisphosphonates, spinal orthoses, and radiotherapy [16].

Bisphosphonates (zoledronic acid and pamidronic acid) are specific inhibitors of osteoclastic activity administered intravenously and represent the cornerstone of treatment and prevention of bone disease in newly diagnosed multiple myeloma (MM), with or without associated bone involvement. These agents inhibit osteoclast activity and induce osteoclast apoptosis, thereby reducing bone resorption and, consequently, decreasing and delaying skeletal complications associated with MM. Bisphosphonates are effective in reducing VCFs and pain; however, they do not completely prevent osteolytic lesions, fail to promote new bone formation or repair of existing lesions, and their role in improving survival remains unclear [2, 3, 5, 7, 9-13, 15, 17-20].

The International Myeloma Working Group (IMWG) experts recommend zoledronic acid for all newly diagnosed MM patients, regardless of the presence of bone disease. Once patients achieve a very good partial response or a good response, following monthly administration of zoledronic acid for at least 12 months and up to 24 months, the treating physician may consider reducing the frequency or discontinuing the treatment [3, 18]. Zoledronate is superior to first-generation bisphosphonates (etidronate) in improving outcomes related to vertebral compression fractures (VCFs) [2, 12, 17, 18].

Although bisphosphonates represent the initial treatment of choice, their long-term use is limited due to adverse effects. These include nephrotoxicity, requiring dose adjustment in hospitalized patients with renal insufficiency, flu-like symptoms, gastrointestinal disturbances during administration, atrial fibrillation, and atypical femoral fractures [9, 10, 12, 15, 18-20]. A critical factor to consider when prescribing high-dose bisphosphonates is the risk of osteonecrosis of the jaw, which can occur in approximately 3–4% to 11.0–11.8% of patients [3, 5, 12, 18].

Current treatments aim to prevent MM-induced bone disease through the use of antiresorptive therapy. New drugs are being developed that act specifically on bone pathology. At present, the use of zoledronic acid or denosumab is recommended at the initiation of treatment in newly diagnosed MM patients with bone lesions [3, 7, 9, 10, 12, 18, 19, 21].

Denosumab is a monoclonal IgG2 antibody and is considered an effective alternative to bisphosphonates for managing bone lesions in MM [2, 12, 13, 18, 20]. Denosumab is effective in preventing systemic osteolytic events and, importantly, improves quality of life in MM patients. A key advantage of denosumab is its significantly lower risk of renal toxicity, making it preferable to zoledronate for patients with MM who have renal dysfunction and hypercalcemia [2, 3, 12, 13, 18, 20].

Drug combinations targeting both myeloma cells and the bone marrow microenvironment may be potentially useful in inducing disease response and halting bone resorption. In this context, thalidomide and lenalidomide represent a new treatment paradigm due to their alternative mechanisms of action, which include disruption of the interaction between plasma cells and bone marrow stromal cells, inhibition of cytokine secretion, anti-angiogenic activity, and immunomodulatory effects, resulting in significant improvement in overall survival [11].

Recent advances in understanding the pathogenesis of bone lesions in multiple myeloma offer new therapeutic approaches and potential targets. There is a growing need for new therapeutic targets that not only prevent but also repair bone destruction, which may enhance treatment outcomes and, most importantly, improve the quality of life in MM patients. Bone anabolic agents (parathyroid hormone, anti-Dkk-1, anti-sclerostin, etc.) show strong potential utility in the treatment of bone lesions in MM. Increasing evidence of the benefits of these agents brings promise for improving the management of bone disease in multiple myeloma patients [19].

The primary indication for radiotherapy is the treatment of bone pain. Other indications include the prevention of pathological fractures, spinal cord compression, or alleviation of symptoms associated with tumor mass. In MM, spinal radiotherapy is typically used in patients with uncontrolled pain or in cases of impending vertebral compression fracture (VCF) or spinal cord compression. Studies conducted on small patient cohorts have demonstrated that complete pain relief (76.4–84%), as well as improvements in quality of life and motor function, were achieved in a considerable proportion of treated cases [3, 11-13, 15, 18, 20, 21].

However, radiotherapy may be associated with an increased risk of vertebral compression fractures (VCFs), which could significantly impact both survival and quality of life. Overall, within a 3-year period, approximately 30.7% of patients reported new VCFs or progression of existing fractures. The analgesic effect of radiotherapy is typically delayed by 10–15 days, and its impact on bone reconstruction is partial, requiring several weeks to fully develop. Therefore, in cases of severe pain, neurological complications, or spinal instability, surgical intervention may be considered [3, 12, 13, 18, 21].

Analgesics are commonly used in multiple myeloma management and include simple analgesics (paracetamol), nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and diclofenac, weak opioids (co-codamol, dihydrocodeine), and strong opioids (morphine, oxycodone, fentanyl) [9, 10].

Thus, bisphosphonates and denosumab remain the standard first-line therapy for MM patients to prevent skeletal-related events. New agents targeting various molecular pathways involved in bone metabolism restoration are under development, and some are currently undergoing clinical trials [13, 20].

***Orthopedic surgery*.** The main objectives of orthopedic surgery in bone lesions among patients with multiple myeloma (MM) are to reduce pain, alleviate symptoms, improve mobility, prevent pathological fractures, restore bone and spinal stability, decompress the spinal cord and nerve roots, enhance quality of life, and support subsequent systemic treatment.

Studies have confirmed the effectiveness of surgical intervention in metastatic spinal disease for improving quality of life and clinical outcomes. Surgery is typically reserved for cases where conservative treatment has failed or when structural integrity and function are severely compromised [6, 8-10, 12, 20, 22-25].

When considering surgical intervention in patients with multiple myeloma (MM), several factors must be included in the decision-making process: potential neurological deterioration, disease stage and prognosis, overall patient condition, lesion location and number, as well as the patient's preferences and expectations. To improve quality of life, the primary objective of surgical treatment is to preserve mobility by reducing pain, maintaining neurological function, and ensuring structural stability [20].

As previously mentioned, MM is often successfully treated with non-surgical methods, including chemotherapy and radiotherapy. In cases of MM without neurological compromise or instability, radiotherapy is considered the treatment of choice. However, when pathological fractures of the extremities or spine are unstable, or when neurological deficits result from nerve compression by tumor masses, surgical intervention is required before radiotherapy or systemic therapy [12, 21, 23, 26, 27].

Indications for surgical treatment in MM include: spinal instability; actual or impending pathological fracture caused by MM; progressive neurological impairment due to spinal cord or nerve root compression by MM; intractable pain attributable to MM; solitary bone plasmacytoma; soft tissue plasmacytoma involving the limbs or spine; actual or impending long bone fracture; and needle or open biopsy providing pathological evidence that supports further treatment [8, 25, 27].

Contraindications to surgical treatment of MM include: poor physical condition; severe cardiac, pulmonary, or renal dysfunction; significant coagulopathy that is difficult to correct; and uncontrolled severe infection [8].

The spectrum of surgical treatment options for the extremities ranges from composite osteosynthesis using bone cement and implants, with stable extramedullary plates or intramedullary nails, to endoprosthetic systems. In spinal surgery, minimally invasive procedures (vertebroplasty, balloon kyphoplasty), selective decompressions, spinal fusion (spondylodesis), and vertebral body replacement procedures are commonly employed. The choice of surgical method and timing of treatment must be individualized based on the risk profile and prognosis of the patient with MM. Postoperative local radiotherapy should always be administered after intralesional tumor resection and surgical stabilization to prevent tumor progression [12, 15, 23, 28, 29].

Current surgical treatment options for the proximal femur include osteosynthesis (intramedullary fixation with nails, intramedullary implants, open reduction and internal fixation with plates and screws), as well as reconstructive options (hemiarthroplasty or total hip arthroplasty and endoprosthetic reconstructions) [25, 30, 31].

***Vertebral Lesions.*** Multiple myeloma (MM) commonly affects the spine, particularly the vertebral bodies. The most frequent site of vertebral compression fractures (VCFs) in MM is the thoracic spine, followed by the lumbar and cervical regions. Bone lesions lead to bone pain, pathological fractures, and spinal cord compression, potentially resulting in neurological deficits. Surgical intervention is indicated when >50% of the vertebral body or the posterior vertebral elements (posterior margin, pedicles) are destroyed, and the tumor has invaded the spinal canal. Sudden-onset neurological deterioration and mechanical instability are the main indications for surgical intervention [16, 32].

When VCFs cause significant pain (with vertebral height loss exceeding one-third and kyphotic spinal deformity), minimally invasive procedures – vertebroplasty (VP) or balloon kyphoplasty (BKP) – may be considered to stabilize the spine and relieve pain [8, 33]. Minimally invasive treatment strengthens the vertebrae, significantly reduces pain, provides mechanical stability, and improves functional outcomes and quality of life [8, 11, 14, 18].

In cases of spinal cord compression from lesions within the spinal canal or unstable spinal fractures, open surgery is often necessary for spinal cord decompression and restoration of spinal stability [8, 11, 21].

Recommended surgical interventions include:

- ***Laminectomy***, used solely for targeted decompression and posterior reconstruction, aiming to preserve the integrity of neurological structures while providing adequate mechanical stability of the spine. In the past, decompressive laminectomy via a posterior surgical approach was considered the treatment of choice; however, it is now rarely used, as it may lead to spinal destabilization and consequently worsen pain and neurological deficits.
- ***Extracapsular intralesional excision*** of the neoplastic mass in cases resistant to chemotherapy and radiotherapy.
- ***Vertebral body reconstruction*** according to the biomechanical needs of the spine (using a prosthesis, acrylic cement – polymethylmethacrylate, autologous bone graft, or vertebral body stent).

- ***Vertebroplasty (VP)*** *or* ***balloon kyphoplasty (BKP)*** – minimally invasive percutaneous procedures –reserved for patients who, after pharmacologic and/or radiotherapeutic treatment, are left with a cavity in the vertebral body that poses a high risk of fracture [8-12, 17, 23, 29, 33, 34].

Although traditional non-operative treatment may provide pain relief, it does not stabilize vertebral compression fractures or minimize progressive kyphotic deformity – outcomes that can only be achieved through vertebral augmentation procedures such as VP and BKP [16].

***Vertebroplasty (VP) and Balloon Kyphoplasty (BKP)*** are minimally invasive procedures used as local treatments for vertebral lesions to rapidly reduce pain and prevent deformity. These procedures are well tolerated and associated with early clinical pain relief, significant reduction in the use of analgesic medications, shorter hospital stays, lower complication rates, improved quality of life, and a favorable platform for subsequent treatment. In addition, they are characterized by low approach-related morbidity and faster recovery, which may accelerate the initiation of adjuvant systemic therapies – making them especially suitable for lesions without major instability. VP involves the percutaneous injection of bone cement (polymethylmethacrylate) into the fractured vertebral body to stabilize it and destroy nerve endings to relieve pain. BKP involves the insertion of a balloon to restore vertebral height, realign the sagittal profile, and create a cavity that can be easily filled with high-viscosity bone cement under low pressure [11, 12, 15, 16, 34-38].

Vertebroplasty (VP) is a minimally invasive, simple, safe, and effective procedure for the treatment of painful vertebral compression fractures (VCFs) in patients with multiple myeloma (MM). The technique was first described in 1987 for the treatment of painful vertebral collapses caused by hemangiomas and osteolytic spinal tumors. The main advantages include immediate stabilization of the fractured vertebral body, significant and long-lasting pain relief (both at rest and during activity), a marked increase in vertebral strength and quality of life, thereby reducing the risk of fracture in the treated vertebra or new collapses in adjacent vertebral bodies. Subjective scores showed sustained improvement – approximately 65% of patients required fewer analgesics post-VP, and 70% experienced improved mobility, with discharge occurring within 2-4 hours. The procedure can be repeated at multiple levels, and the pain relief effect is virtually permanent [16, 37, 38].

A study conducted on a cohort of 4,547 patients (3,211 women and 1,336 men) with a mean age of 70.2 years reported a total of 13,437 treated vertebrae. The authors concluded that VP is an effective and safe procedure for managing vertebral fractures, significantly alleviating pain within 48 hours. No major neurological complications were reported, while minor complications were observed in 32.9% of cases [36].

***Balloon Kyphoplasty (BKP)*** is a minimally invasive procedure used to treat painful vertebral compression fractures (VCFs) caused by primary or secondary osteoporosis, osteolytic lesions due to multiple myeloma (MM), bone metastases, or trauma. The goal of BKP is to reduce and stabilize the fracture while restoring vertebral body height, thereby providing immediate and sustained pain relief, improved physical function, and enhanced quality of life, while also preventing subsequent VCFs. After balloon removal, the created intravertebral cavity is filled with cement (polymethylmethacrylate) or bone graft to restore vertebral height [9, 10, 12, 15, 26, 33, 39].

BKP is a well-tolerated, relatively safe, and effective technique in patients with painful neoplastic spinal fractures, including VCFs caused by MM. The procedure results in rapid pain relief and functional improvement, significant restoration of vertebral height, and reduction of segmental kyphosis, helping to prevent further vertebral height loss and reducing the risk of kyphotic deformities. BKP provides long-term benefits in terms of pain and disability. However, potential procedural disadvantages include incomplete fracture reduction or significant loss of reduction after balloon deflation, prior to cement injection [35, 39, 40].

Cement leakage into adjacent neural and vascular spaces is the most commonly reported complication of vertebroplasty (VP) and balloon kyphoplasty (BKP), but it occurs more frequently after VP. Although in most cases cement leakage is clinically insignificant, in extreme situations it can lead to serious complications such as pulmonary or cerebral embolism, neurological deficits, myelopathy, radiculopathy, and, in rare cases, death [16, 38, 40].

VP is associated with a very high incidence of cement extrusion, with reported leakage rates ranging from 30% to 75%, and even up to 85.7% in cases with posterior vertebral wall osteolysis. Moreover, VP does not attempt to restore lost vertebral height or correct the resulting spinal deformity. Kyphotic spinal curvature may compromise spinal biomechanics and increase the risk of subsequent fractures in adjacent vertebrae. Consequently, BKP - developed from VP techniques in the 1990s - was introduced as a more effective treatment option in MM. BKP helps restore lost vertebral height, correct spinal deformities, stabilize the spine, and reduce the incidence of cement leakage. The absence of cement-related complications may be attributed to: (1) the use of high-viscosity cement; (2) the selection of BKP in appropriate cases; and (3) the injection of relatively small volumes of cement (2-8 mL) [16, 35, 37, 39, 40].

Serious complications associated with BKP – such as inflammation, epidural hematoma, rib fractures, cement leakage, pulmonary embolism, and systemic toxicity – are rare. The most frequently reported complication is cement leakage (extrusion), occurring in 7-9% of cases. The vast majority of these events are asymptomatic. Symptomatic cement leakage is reported in only 0.04-1.3% of cases. New VCFs following BKP have been reported in 14.1-17% of patients over a follow-up period ranging from one month to three years [10, 11, 26].

A systematic review of the literature included 23 studies (9 on BKP, 12 on VP, and 2 on both procedures), totaling 923 patients with vertebral fractures due to multiple myeloma

(MM). The authors concluded that both BKP and VP were equally effective in reducing postoperative pain scores and analgesic medication use, with low treatment-related complication rates. However, complications generally occurred more frequently after VP compared to BKP. Both procedures demonstrated similar safety and efficacy profiles [40].

A new procedure called "vertebral body stenting" uses a specially designed stent mounted on a catheter, which can be implanted and expanded within the vertebral body, leading to a significant increase in overall vertebral height. This innovative technique enables complete reduction of VCFs and helps maintain the restored height through the use of the stent. Recently, small-scale studies have shown the effectiveness of a spinal implant – an expandable intravertebral titanium device – that provides long-term pain relief and restoration of hemovascularization in VCFs secondary to MM and other etiologies [16].

Open surgical approaches include direct anterior, posterior, and combined anterior-posterior approaches. The goals of surgical intervention are maximal tumor resection, decompression, spinal reconstruction, and internal fixation. Suitable internal fixation systems include titanium plates, spinal systems with pedicle screws, and lateral mass screw fixation systems. Appropriate reconstructive implants include artificial vertebral bodies, titanium mesh, bone cement, and bone allografts [8].

Spinal surgery plays a fundamental role in cases of vertebral involvement in multiple myeloma (MM) that are partially or entirely unresponsive to pharmacologic and radiotherapy treatments, particularly in cases of disease progression or relapse. Surgical intervention in selected MM patients with spinal involvement and neurological deficits is associated with favorable clinical outcomes, neurological recovery, and an acceptable complication rate. Furthermore, the improved efficacy of medical therapies has led to increased life expectancy, reinforcing the consistent and undisputed utility of spinal surgery – especially regarding functional status [17, 32].

Surgical intervention serves a supportive role in MM management and is performed with the intent to stabilize imminent or existing pathological fractures in cases of refractory pain, neurological complications, or spinal instability. The objectives of surgery include decompression of neural structures, pain control, restoration of spinal stability, and correction of coronal and sagittal spinal alignment. The goal of tumor excision is the partial or complete removal of neoplastic tissue surrounded by healthy tissue. Surgery for vertebral MM lesions is a valuable option for carefully selected patients [17, 41].

According to a U.S. national database, vertebral augmentation (9,643 cases, 65.7%) was the most commonly performed procedure, followed by spinal stabilization with or without decompression (4,176 cases, 28.4%), and decompression alone (868 cases, 5.9%). The study highlighted a growing trend in the use of spinal surgery for inpatient MM management, while the rate of vertebral augmentation procedures is decreasing [14].

However, postoperative complication rates remain high after spinal surgery in patients with multiple myeloma (MM). The overall complication rate has been reported to range between 22.4% and 35.0%, which aligns with complication rates observed after spinal surgery for spinal metastases in the broader literature, ranging from 14% to 34%. Approximately 20% of patients underwent at least one reoperation within 2.5 years following the initial spinal surgery. The most common indications for reoperation were adjacent-level fractures (53%), wound dehiscence and/or infected hardware (19%), and tumor recurrence or spinal cord compression at the operated site (15%) [14, 41].

Thus, balloon kyphoplasty (BKP) and vertebroplasty (VP) are both safe and effective surgical procedures for the treatment of vertebral compression fractures (VCFs). BKP provides comparable long-term pain relief, functional outcomes, and rates of new adjacent VCFs to VP. However, BKP is superior to VP in terms of cement volume injected, short-term pain relief, short- and long-term correction of the kyphotic angle, and lower cement leakage rates. On the other hand, BKP is associated with a longer operative time and higher material costs than VP.

A combination of open surgery and minimally invasive spinal surgery is often used to treat patients with multiple spinal lesions, as it provides the benefits of both approaches - reducing blood loss and other complications [8].

*Long Bone Lesions*. In MM, long bone fractures are relatively less common than VCFs but typically require hospitalization for early intervention via fixation or replacement of the affected segment. The benefits of surgical treatment for pathological fractures of long bones in the limbs include pain relief, restoration of bone continuity and limb function, and improved quality of life [2, 6, 8, 28].

Pathological fractures of long bones should be operated on as soon as possible, especially in the lower limbs due to weight-bearing demands. Procedures include resection of the affected segment, augmentation with polymethylmethacrylate, internal fixation (using screws, plates, or intramedullary nails in carbon – fiber-reinforced or titanium implants), or replacement with conventional prostheses or megaprostheses [2, 6, 8, 28, 30, 31].

The selection of the fixation system and surgical procedure depends on the patient's general condition, quality of life, and life expectancy; prior response to chemotherapy; fracture location; the number, size, and distribution of lesions; extent of bone invasion; neurological status; and patient expectations [8, 24, 30, 31].

Complications associated with surgical treatment methods for bone lesions in multiple myeloma (MM) have been broadly classified into four main categories:

- Hematoma-related (cauda equina syndrome, lower limb weakness, sudden paraplegia).
- Wound-related (hematoma, wound dehiscence).
- Surgical complications (implant failure or dislodgement, rod breakage, screw loosening, inaccurate screw placement, pathological fracture).
- Medical complications (deep vein thrombosis, acute

renal failure, acute respiratory failure, pulmonary embolism, intraoperative hyperthermia) [17, 27, 31].

To date, there is no consensus on the surgical complication rate in patients with multiple myeloma (MM), with various studies reporting significantly different rates, ranging from 3.9% to 35% [22].

Given that patients with MM and bone lesions are often in advanced stages of the disease with terminal organ dysfunction, one study analyzed the types and incidence of perioperative medical and surgical complications. The overall complication rate following surgery among 58 patients with bone disease in MM was 74.03%, with 45.45% of patients experiencing two or more complications. Surgical complications were reported in only 20.78% of cases (e.g., bleeding or hematomas, adjacent segment fractures, surgical site infections). Among medical complications, the most frequent were moderate to severe anemia requiring transfusion (28.57%), acute renal failure (25.97%), infections (24.68%), and hypercalcemia (10.39%) [4].

*Surveillance and Prognosis.* Surgical intervention in patients with MM-related bone lesions has been shown to improve overall survival and reduce the rate of postoperative complications [42].

According to a recent study, 58 patients treated for MM-related bone disease were followed for a mean period of 6.13 years, and 37.93% experienced a new fracture during follow-up. The median overall survival after surgical intervention was 32.9 months (ranging from 11.6 to 49.0 months). The estimated overall survival rates at 1, 3, and 5 years postoperatively were 81.17%, 57%, and 34.11%, respectively [4].

According to multivariate logistic regression analysis, patient age, disease duration, International Staging System (ISS), preoperative Karnofsky performance status, hemoglobin <90 g/L, and systemic treatment are independent prognostic factors influencing outcomes in MM patients following surgical treatment of bone lesions [22].

Thus, bisphosphonates or denosumab should be considered the standard of care for the treatment of skeletal disease in patients with multiple myeloma (MM). The choice of a specific agent should take into account several factors such as cost, convenience, patient preference, and toxicity profile. The International Myeloma Working Group (IMWG) recommends zoledronic acid as the preferred treatment option for patients without imaging-confirmed bone disease related to MM, while denosumab is preferred for patients with renal insufficiency.

Cement augmentation (polymethylmethacrylate) is effective in the treatment of painful vertebral compression fractures (VP, BKP). Radiotherapy is recommended for uncontrolled pain in cases of spinal cord compression or pathological fractures of long bones, particularly in patients with absent or minimal response to systemic treatment for multiple myeloma (MM). Surgery should be employed to prevent and repair pathological fractures of long bones, address spinal instability, and decompress the spinal cord in cases involving bony fragments. Postoperative radiotherapy should be considered, especially for long bone fractures, to achieve local disease control and to prevent implant failure. This approach is particularly important in patients who demonstrate minimal or no response to systemic MM treatment.

## Conclusions

1. The current therapeutic landscape for bone complications in multiple myeloma supports the individualized use of antiresorptive agents, emphasizing the need for a patient-centered approach based on clinical and practical considerations.
2. Minimally invasive procedures such as balloon kyphoplasty and vertebroplasty remain valuable options for managing vertebral fractures, with specific procedural advantages that can guide surgical decision-making.
3. An integrated therapeutic strategy combining radiotherapy and surgical intervention plays a critical role in managing structural complications, particularly in refractory cases, supporting both symptom relief and disease control.

## Competing interests

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