Original Study

Stability of Spinal Bone Lesions in Patients With Multiple Myeloma After Radiotherapy—A Retrospective Analysis of 130 Cases

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Abstract

This retrospective analysis evaluated the response regarding bone density and stability of patients with osteolytic spinal bone lesions due to multiple myeloma after palliative radiotherapy. The rate of unstable lesions decreased from 51% to 24%, and the bone density showed a significant increase 6 months after radiotherapy. Palliative radiotherapy is an effective method resulting in a significant increase for local response and stability without severe RT-related toxicity.

Background: The objective of the present retrospective analysis was the response evaluation regarding bone density and stability of patients with osteolytic spinal bone lesions due to multiple myeloma after palliative radiotherapy (RT). **Patients and Methods:** Patients with multiple myeloma who had undergone spinal RT from March 2003 to May 2016 were analyzed before and 3 and 6 months after RT. Assessment of spinal stability and bone density was performed using the internationally recognized Taneichi scoring system and measurement of bone density using computed tomography imaging-based Hounsfield units. For statistical analysis, we used the Bowker test, McNemar test, and κ statistics to detect possible asymmetries in the distribution of the Taneichi score over time. We used the Student *t* test for comparison of the density values (Hounsfield units) before and after treatment. Toxicity was evaluated using the Common Terminology Criteria for Adverse Events, version 4.0. Additionally, overall survival was calculated using the Kaplan-Meier method. **Results:** We evaluated 130 patients (69% male; 31% female) with multiple myeloma and a median age of 58 years. The median follow-up period was 41 months. Before treatment, 51% of the lesions were classified as unstable. At 3 and 6 months after RT, this rate had decreased to 41% ($P = .0047$) and 24% ($P = .2393$), respectively. The computed tomography measurements showed a significant increase in bone density at 3 and 6 months after RT. Acute RT-related grade 1 and 2 complications were detected in 34% of patients. Late side effects (grade 1-2) were detected in 23% of the patients. No severe grade 3 or 4 acute or late toxicities were identified. The median overall survival was 19.7 months for all patients and 6.6 months for patients with a Karnofsky performance score of $\leq$ 70%. **Conclusion:** To the best of our knowledge, ours is the first report to analyze the bone density and stability in patients with multiple myeloma after RT using a validated scoring system and computed tomography imaging. Palliative RT is an effective method resulting in a significant increase in bone density for local response and stability without severe RT-related toxicity. Furthermore, recalcification could already be detected at 3 months after treatment.

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Introduction

Multiple myeloma (MM) accounts for 10% of all hematologic malignancies and 1% of all cancer cases. The annual incidence is 4 to 6 cases per 100,000 persons.[1] Osteolytic lesions are a major feature of MM; 70% to 80% of patients will have osteolytic lesions at the initial diagnosis and ≤ 90% will develop general osteolytic lesions during the disease course.[2] The typical symptoms include pain, pathologic fractures, and/or spinal cord compression, which often strongly affect patients' quality of life and lead to persistent immobilization.

The standard treatment of patients with MM includes corticosteroids and chemotherapy, with or without stem cell transplantation, depending on the patient's age and performance status. The main aim of systemic treatment is the induction of remission with consecutive rapid symptom control to further prevent complications.

Palliative percutaneous radiotherapy (RT) represents one of the most important treatment options for bone lesions (40% of patients). Previous studies have reported a reduction of neurologic symptoms in 50% of cases,[3] improvements in stability caused by recalcification in 40% to 50% of patients,[4,5] and a reduction in the risk of pathologic fractures.[6] Pain reduction using RT can be achieved in ≤ 90% of patients.[5]

Many previous studies have shown that approximately two thirds of patients required the use of RT during the course of their disease.[7] For spinal disease, orthopedic corsets or RT can be used to prevent vertebral fractures and spinal cord compression.[7] Although plasma cells are very radiosensitive, and RT is considered an effective and curative treatment for plasmacytoma,[8,9] the use of RT is mainly a palliative option for MM.[10] In addition, bisphosphonates should be used in combination with anti-MM therapy because they reduce bone resorption and prolong patient survival.[11]

The use of a validated scoring system to assess the stability of spinal bone lesions could be useful to prevent the overdiagnosis of instability by physicians and to classify the stability after treatment to allow for the implementation of early mobilization for these patients. Thus, the objective of the present retrospective analysis was to evaluate the response after palliative RT for osteolytic bone lesions in MM regarding bone density and stability.

Patients and Methods

Patient and Treatment Characteristics

The data from 130 patients with MM and osteolytic lesions of the vertebral column were retrospectively analyzed (Table 1). These patients had been treated at the radiation oncology department at the University Hospital of Heidelberg from March 2003 to May 2016. We collected the patient data from the Heidelberg NCT Cancer Registry. Patients underwent regular follow-up examinations, including computed tomography (CT) before and 3 and 6 months after RT.

Assessment of spinal stability and bone density was performed using the internationally recognized Taneichi scoring system[12] and measurement of Hounsfield units (HU) on CT scans (Figure 1). The CT scans were assessed before and 3 and 6 months after RT. In patients with > 1 treated lesion, we selected the lesion with the greatest probability of collapse according to the Taneichi score. Accordingly, osteolytic lesions with subtypes A to C were classified as stable and those with subtypes D to F as unstable (Table 2).

Table 1 Patient Characteristics

Characteristic	n (%)
Patients	130 (100)
Age (y)	
Median	57.6
Range	28.7-86.3
Sex	
Male	90 (69.2)
Female	40 (30.8)
Karnofsky performance score	
60	6 (4.6)
70	16 (12.3)
80	90 (69.2)
90	18 (13.9)
Durie-Salmon stage	
IA	3 (2.3)
IB	0 (0)
IIA	7 (5.4)
IIB	1 (0.8)
IIIA	94 (72.3)
IIIB	25 (19.2)
Bone lesions	
1	10 (7.69)
2-5	39 (30.0)
>5	81 (62.3)
Spinal involvement	
Cervical	33 (25.4)
Thoracic	66 (50.8)
Lumbar	31 (23.9)

A positive response was defined as a change from unstable to stable at 3 or 6 months after RT.

Toxicity was evaluated using the Common Terminology Criteria for Adverse Events, version 4.0. The present study was performed in accordance with the ethical standards of the Declaration of Helsinki. The Heidelberg ethics committee approved the study (approval date, October 22, 2012; approval no. S-513/2012). Because of the retrospective study design, informed patient consent was not required. The data used in our analysis were from publications available in the public domain.

Radiotherapy

All treatment was performed at the radiation oncology department of University Hospital Heidelberg. After the planning CT scan had been performed, the patients underwent either 3-dimensional conformal RT (97%) or intensity-modulated RT (3%). The planning target volume covered the affected vertebral body and the one above and below. The patients received a median single dose of 3 Gy (range, 2-3 Gy) and a median total dose of 30 Gy (range, 20-40 Gy). The dose was applied in 5 fractions per week. The individual and total doses were calculated separately for each individual patient and depended on the patient's general state of health, the current disease stage, and their prognosis. The treatment characteristics are listed in Table 2.