



Predictors of survival in patients with surgical spine multiple myeloma metastases



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ABSTRACT

Background: Multiple myeloma (MM) is the most common primary malignant tumor of the spine and bone. Spinal metastases are part of the evolution and progression of the MM disease. Therefore, this study aims at investigating prognostic factors associated with overall survival (OS) in patients with symptomatic spine MM metastases.

Methods: Consecutive spine surgery procedures were performed in the largest series reported to date and comprising 51 patients with osteolytic vertebral compression fractures resulting from MM, diagnosed by either bone marrow or tumor biopsy.

Results: The mean age of patients was 61.1 years and mean follow-up was 31.9 months. Through univariate analyses, ISS stage ($p < 0.0001$), preoperative spine instability (SINS score) ($p < 0.03$), posterior osteosynthesis fixation ($p < 0.002$), preoperative adjuvant therapy ($p < 0.02$), postoperative adjuvant treatment ($p < 0.001$), bone marrow transplant ($p < 0.03$) and newly MM diagnosed ($p < 0.03$) emerged as powerful predictors of survival. Cox multivariate proportional hazard model indicated that only ISS Stage and stabilization surgery such as osteosynthesis were two independent predictive factors for OS [hazard ratio (HR): 0.268, 95% confidence interval (CI) 0.07–0.536; $p < 0.006$ for the former and HR: 0.184, 95% confidence interval (CI) 0.03–0.89; $p < 0.04$ for the latter].

Conclusion: Stabilization surgery combined to ISS staging should be considered as an important prognostic survival factor for patients with symptomatic MM spine metastases.

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1. Introduction

Multiple myeloma (MM) is a heterogeneous disease, with survival duration ranging from a few months to more than 10 years. The International Staging System (ISS) is a simple risk stratification algorithm based on two parameters; serum β_2 -microglobulin and albumin levels. This score, defined in 2005, identifies three patient groups with different prognoses: the median overall survival (OS) was 62 months in the ISS stage I, 44 months in the ISS stage II, and 29 months in the ISS stage III groups ($P < 0.001$) [1]. Although a large number of biologic or genetic prognostic markers have been described in MM, the identification of other prognostic factors that could explain the heterogeneity seen in this disease remains

controversial, particularly when the disease is progressive and reaches skeletal localization. The spine is the most frequently affected skeletal site in MM [2] and such localization is present in up to 60% of patients at diagnosis [3]. Affected vertebral bodies may become weakened with progressive bone destruction or defect in the posterior wall and pedicles, which means that fracture may compromise spinal stability and therefore neurological function. Spinal cord compression has been reported to develop in 11–24% of myeloma patients [4,5]. Successful treatment and management of spinal myeloma disease requires control of the myeloma with systemic chemotherapy [6,7], regional spine treatment with radiotherapy [8] and surgery or orthopedic management (corset) to reduce the risk of further spinal bone destruction or permanent deformity/neurological dysfunction [9].

A number of new therapies have been approved for the treatment of myeloma in the last decade, with a resultant improvement in outcome. However, considerable heterogeneity exists in the survival outcomes among patients diagnosed with MM, especially

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when metastatic bone lesions have been identified. In spine metastases, it has been demonstrated that surgery must not be considered except when structural instability and neurological compromise exist [10]. In contrast, another study argued that surgical management of myeloma spinal disease was similar to the management of spinal metastases in solid cancers [11]. To date, little is known about the surgical treatment and long-term prognosis of these patients. Therefore, through the largest surgical series to date, this study aims at identifying prognostic factors associated with overall survival (OS) in patients with surgery for spine myeloma metastases.

2. Materials and methods

2.1. Study population

Fifty-one patients underwent spine surgery for MM spinal cord compression or instability between January 2004 and July 2014. Patients with spine metastasis who were evaluated by axial computed tomography, and magnetic resonance (MRI) spine, as well as bone scintigraphy were included in this study. These exams were standardized in order to diagnose and stage the patients. All patients included in this study were aged at least 18 years and presented with histologically confirmed MM with metastases localized in the spine diagnosed by either bone marrow or tumor biopsy.

2.2. Details of procedure

When laminectomy was isolated, a single medial incision at the pathological vertebra was made. After disinsertion of paraspinal muscles, the posterior arch was resected using a diamond bur and lateral decompression was achieved with bone scissors. When laminectomy was associated with osteosynthesis, the incision was extended two levels above and below the pathological vertebra. The instrumentation consisted of a simple fixation, without associated bone graft, and a drain was introduced for 24 h. The correct position of the screws in the pedicles was controlled by a post-operative CT scan. The 10 patients who had benefited from a simple fixation without any associated decompression underwent percutaneous (5; 50%) or open surgery (5; 50%). The operating management for patients with open surgery was identical to that described previously.

All patients with neurological symptoms were operated in emergency by decompressive laminectomy with or without osteosynthesis according to their level of instability. In our surgical institution patients with a Spine Instability Neoplastic Score (SINS) > 8 benefited from a posterior fixation. Patients with a compressive epiduritis or posterior compression but not yet symptomatic had simple or stepped laminectomy and the same SINS criteria were applied to determine indication of fixation.

Pathological fractures of the cervicothoracic junction (C7-T1: one) or thoracolumbar (T12-L1: seven, 13.7%) areas were the only ones in which osteosynthesis, independently of SINS, was systematic to avoid any progressive deformation. For other vertebral levels, the surgical decisions was based on neurological impairment and SINS.

2.3. ISS score

International staging system (ISS) stage I was defined as serum β 2-microglobulin levels \leq 3.5 mg/L and serum albumin levels \geq 3.5 g/dL. ISS stage II included all patients with neither stage I nor stage III disease. ISS stage III was defined as serum β 2-microglobulin levels \geq 5.5 mg/L, irrespective of serum albumin

levels [1].

2.4. Statistical analysis

Demographic, clinical outcomes, treatment data were analyzed with an alpha risk level of 5%. χ^2 Pearson tests were used for analyses. Univariate and multivariate analyses were used to identify factors associated with Overall Survival (OS). Survival was evaluated by the Kaplan–Meier method and differences were analyzed by log-rank test. Factors with p values \leq 0.1 were subjected to multivariate analysis for survival rate by multivariate Cox proportional hazard analysis. p values \leq 0.05 were considered statistically significant. All statistical analyses were performed using SPSS program for Windows V17.0 (SPSS, Chicago, IL, U.S.A). Data are presented as the mean \pm standard deviation. For all analyses, a p-value of <0.05 was considered statistically significant.

3. Results

As presented in Table 1, there were 33 (64.7%) patients were males and 18 (35.3%) patients were females, with a median age of 61.09 years (range 37.7–76.9 years). The mean follow-up of our series was 34.9 months (SD: 12.7). The median ASA was 2 (Range 1–4). Median Karnofsky Performance Score (KPS) at surgery was 80 (SD: 16.5). At presentation, physical examinations showed neurological deficits or palsies resulted from spinal cord compression for 16 patients (31.4%), radiculargia for 5 patients (9.8%) and pain for the other 30 (58.8%).

This retrospective study analyzed 51 cases of spinal MM metastases surgically managed in a single institute, Nantes University Hospital, over a 14-year period (2000–2014). Twenty-four patients (47%) had ISS stage I, 18 (35.3%) had ISS stage II, and 9 (17.7%) had ISS stage III. The overall median survival of our patients with myeloma was 40.6 months (Fig. 1A). The median survival duration since surgery in our series was: ISS stage I (77.2 months; SD 16.9), ISS stage II (40.6 months; SD 19.2) and ISS stage III (7.9 months; SD 4.9), $p < 0.0001$ (Fig. 1B and Table 2). Eight patients (15.7%) died at 1-month follow-up, and 14 (27.4%) within 1 year of surgery. 2 patients were diagnosed as plasmocytoma, with median survival of

Table 1

Summary of patients' clinical and demographic characteristics for 51 consecutive cases of spinal multiple myeloma metastases.

Characteristic	Value N (%) or [SD]
Age (years)	61.09 [12.09]
Gender	
Male	33 (64.7)
Female	18 (35.3)
Median Karnofsky (KPS)	80 [16.5]
ASA score	2 [0.6]
International staging system	
ISS stage I	24 (47)
ISS stage II	18 (35.3)
ISS stage III	9 (17.7)
Presentation examinations	
Neurological deficits/palsies	16 (31.4)
Radiculargia	5 (9.8)
Pain	30 (58.8)
Number of lesions	
1	17 (33.3)
2	15 (29.4)
\geq 3	19 (37.3)
Level	
Cervical	8 (15.7)
Thoracic	31 (60.8)
Lumbar	12 (23.5)
Length of stay in days	8.8 [15.4]

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