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Original Article

Risk factors for the outcome and prognosis of multiple myeloma patients with pathological fractures undergoing percutaneous vertebroplasty

Haining Xu[1*], Jianliang Tian[2*], Liang Li[3], Fang Liu[4], Yuebing Ren[5], Guangming Guo[6], Qian Peng[7]

[1]Department of Orthopedics, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China; [2]Department of Emergency, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China; [3]Department of Trauma Orthopedics, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China; [4]Dialysis Room, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China; [5]Department of Spine, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China; [6]Department of Trauma Orthopedics, The People's Hospital of Jimo Qingdao, No. 4 Jianmin Street, Jimo District, Qingdao 266000, Shandong, China; [7]Department of Vascular Proctology Surgery, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China. [*]Equal contributors.

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Abstract: This study focuses on the clinical features affecting the outcome and prognosis of multiple myeloma (MM) associated with spinal fractures. We retrospectively analyzed the clinical data of 194 MM patients with pathologic thoracic or lumbar spine fractures admitted to Dongying People's Hospital from April 2005 to February 2021. Patients were categorized into effective and ineffective groups based on post-treatment pain scores and mobility to analyze the influencing factors on the efficacy. Univariate analysis showed that age ≥60 years, number of vertebral fractures ≥2, and conservative treatment were associated with the outcomes. The number of vertebral fractures ≥2 (OR=2.198, *P*=0.034) and conservative treatment (OR=1.685, *P*=0.012) were identified as independent risk factors. In addition, survival curves were depicted using the Kaplan-Meier method, and independent risk factors affecting 2-year survival included efficacy (HR=17.924, *P*<0.001), age (HR=3.544, *P*=0.003) and International Staging System staging (HR=10.770, *P*=0.001). Finally, we constructed a high-accuracy prognostic model for predicting 2-year survival of MM patients with pathologic fractures (AUC=0.756). In conclusion, this study identified independent risk factors affecting the outcome and survival of MM patients with morbid fractures by systematically analyzing clinical characteristics and constructing a survival prediction model, thus providing effective guideline for clinical treatment.

Keywords: Multiple myeloma, fracture, clinical features, effectiveness, prognostic model

Introduction

Multiple myeloma (MM) is a malignant plasma cell disease with a diversity of clinical manifestations [1, 2]. As of 2020, the estimated number of newly diagnosed cases in the United States reached 32,270, with 12,830 new deaths [3]. The data showed [4] that the 10- and 20-year relative survival rates of MM patients showed an increasing trend from 2002 to 2016. In China, the incidence of MM also continued to increase between 2006 and 2016 [5]. In particular, the mortality of MM was on the rise between 2006 and 2014 and stabilized from 2014 to 2016 due to advances in treatment approaches, such as bortezomib, lenalidomide, and hematopoietic stem cell transplantation [6, 7]. The prognosis of MM varies widely, and the survival time of patients may range from a few months to over 10 years [8].

Patients with MM are prone to pathologic vertebral fractures, which may be due to factors such as gravity or minor violence, leading to

decreased spinal stability [9]. This condition often leads to severe pain, inability to erect, stand or walk, and may cause a series of mental disorders such as depression and irritability, or even lead to paralysis, which seriously affects the prognosis and quality of life of patients [10, 11]. Currently, percutaneous vertebroplasty (PVP) has been gradually applied in the treatment for MM combined with pathological spinal fractures to achieve rapid restoration of spinal stability and improvement of neurological dysfunction. However, uncertainty remains regarding the efficacy of PVP and its potential complications, such as cement leakage and increased fracture risks. Some scholars believe that using chemotherapy or radiotherapy alone can also achieve a good therapeutic effect, while surgery increases the risk of adjacent vertebral fracture [12]. Despite therapeutic advances improving survival and quality of life in MM patients, the five-year survival rate is still about 50-60%, and even lower in those with pathologic spinal fractures, as fractures are often indicative of more advanced disease progression and severe bone damage. However, the specific survival rate varies among individuals and treatment outcomes, so effective assessment of the prognosis of MM combined with pathologic fracture patients is beneficial for prioritizing specific treatments and developing individualized treatment plans. Currently, there is insufficient evidence in predicting efficacy and identifying risk factors for this condition [13]. This knowledge gap limits the development of individualized treatment plans and follow-up care.

The purpose of this study is to fill this knowledge gap by retrospectively analyzing data of MM patients. We aimed to identify potential risk factors affecting clinical outcomes. By understanding these factors, we seek to enhance the relevance and effectiveness of treatment strategies, explore emerging treatment patterns, analyze characteristics of patients with poorer prognosis, and establish relevant risk assessment models.

Materials and methods

Ethical statement

The study was approved by the Medical Ethics Committee of Dongying People's Hospital.

Sample source

A retrospective analysis of MM patients treated at Dongying People's Hospital between April 2005 and February 2021 was performed.

Inclusion and exclusion criteria

Inclusion criteria: ① Confirmed diagnosis of MM by MRI or myelocytology; ② Pathologic fracture of the lumbar-thoracic region confirmed by X-ray and CT examination; ③ Presence of lower back pain; ④ Complete clinical data; ⑤ Regular follow-up examinations.

Exclusion criteria: ① Lumbar disc herniation; ② Spinal deformities; ③ Ankylosing spondylitis and foraminal injuries; ④ Concurrent malignancies; ⑤ Expected survival <3 months; ⑥ Subsequent fractures during follow-up with treatment received.

Clinical data collection

Clinical information including gender, age, body mass index (BMI), fracture site, number of vertebral fractures, International Staging System (ISS) [14], disease classification, treatment plan, history of hypertension, history of diabetes mellitus, chemotherapy regimen, and clinical efficacy assessment were collected from electronic medical records, outpatient reviews, and telephone follow-ups. The treatment programs for MM pathologic fractures were conservative treatment and surgical treatment. Conservative treatment used zoledronic acid, and surgical treatment employed zoledronic acid plus PVP. Chemotherapy regimens are categorized into BCD chemotherapy regimens (Bortezomib, Cyclophosphamide and Dexamethasone) [15] and PAD chemotherapy regimens (Bortezomib, Adriamycin and Dexamethasone) [16]. At one month postoperatively, visual analog scale (VAS) [17] was used to evaluate clinical efficacy. Significant response was significantly reduced pain, improved ability to perform daily activities, increased anterior edge of the vertebral body, and VSA score <3. Improvement was defined as mild pain, improved daily activity ability, better front edge of the vertebral body, and the VSA scores ≥3-<6 points. Ineffective response was indicated by severe pain, remained inconvenienced in daily activities, no change in the anterior margin of

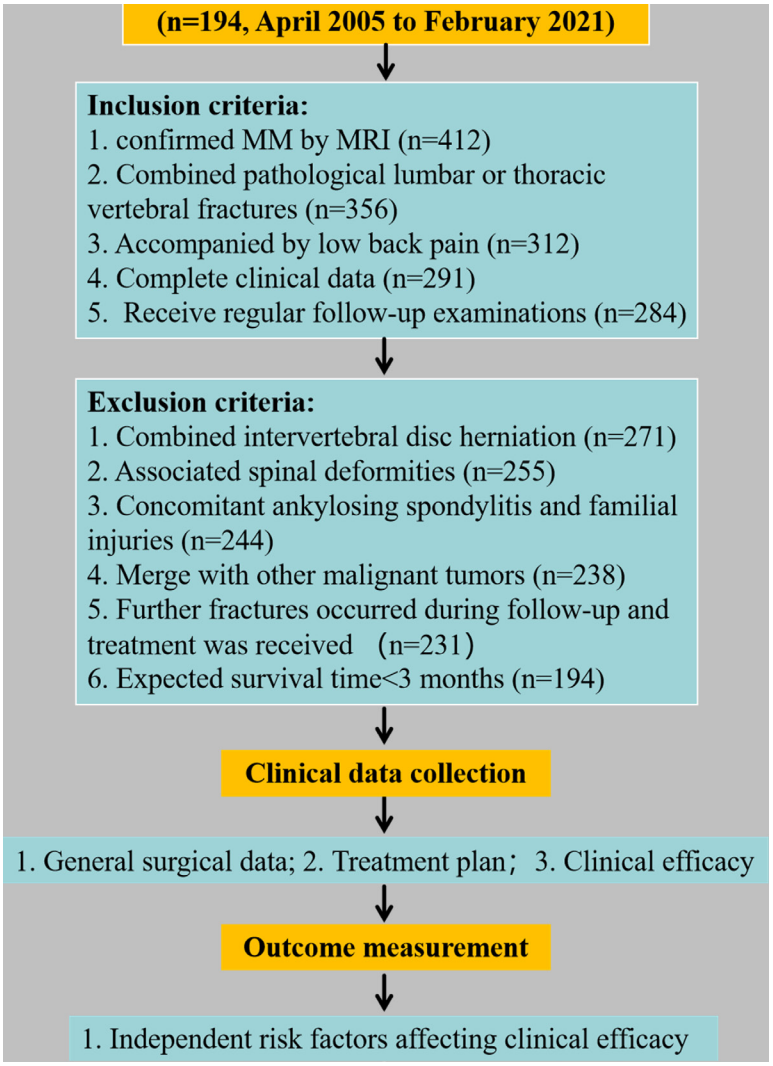

Figure 1. Flowchart of sample inclusion and study content.

the vertebral body, and a VSA score of ≥6 points.

Sample screening and grouping

A total of 194 cases were eligible according to the inclusion and exclusion criteria. Patients with significant response or improvement were categorized into an effective group (n=118) and those with ineffective response into an ineffective group (n=76) according to the criteria for assessing clinical efficacy.

Follow-up

Survival data were collected through telephone follow-ups, which were conducted in January, April, August, and December of each year, over a two-year follow-up period.

Outcome measurement

Independent risk factors affecting clinical outcomes in the patients were analyzed by logistics regression. Cox regression was used to analyze the independent prognostic factors at 2 years. A prognostic model was constructed to predict the 2-year survival in MM patients with pathologic fractures, and its validity and accuracy in clinical prognostic assessment were accessed by ROC curve, calibration curve, and decision curve analysis (DCA). See the flow chart of the study in **Figure 1**.

Statistical analysis

SPSS 26.0 software was used for data processing and analysis. Measurement data were expressed as mean ± standard deviation (mean ± sd), and comparisons between two groups were conducted using independent paired t test. Counting data were expressed as rate (%) and compared using chi-square test. Logistic regression analysis was performed to identify independent risk factors affecting the clinical outcome of the patients. In the process of analyzing the data, we further employed column line graphs to visualize key statistical information in the dataset. In addition, to assess the accuracy of the prediction model, a calibration curve was constructed to understand the consistency between the predicted values of the model and the actual observations. Finally, to evaluate the efficacy of the predictive model in clinical decision making, DCA was applied to calculate and compare the net benefit at different thresholds. Differences were considered statistically significant at a *P* value of less than 0.05.

Table 1. Univariate analysis

Factor	Effective group (n=118)	Ineffective group (n=76)	x^2 value	*P* value
Gender				
Male	36	41	10.61	0.001
Female	82	35		
Age				
≥60 years	70	39	1.204	0.273
<60 years	48	37		
BMI				
≥25 kg/m^2	23	12	0.428	0.513
<25 kg/m^2	95	64		
Fracture site				
Thoracic vertebra	41	30	0.445	0.505
Lumbar vertebra	77	46		
Number of vertebral fractures				
≥2	39	41	8.33	0.004
<2	79	35		
ISS staging				
I	18	9	3.22	0.2
II	36	16		
III	64	51		
Disease classification				
IgG	57	41	1.605	0.448
IgA	30	21		
Other	31	14		
Treatment plan				
Conservative treatment	39	55	28.612	<0.001
Surgical treatment	79	21		
History of hypertension				
Yes	23	9	1.964	0.161
No	95	67		
History of diabetes				
Yes	20	12	0.045	0.832
No	98	64		
Chemotherapy regimen				
BCD chemotherapy regimen	64	41	0.002	0.968
PAD chemotherapy regimen	54	35		

Note: BMI, Body Mass Index; ISS, International Staging System; BCD chemotherapy regimen, Bortezomib, Cyclophosphamide and Dexamethasone; PAD chemotherapy regimen, Bortezomib, Adriamycin and Dexamethasone.

Results

Univariate analysis of factors affecting patient outcomes

We categorized patients into effective (n=118) and ineffective (n=76) groups based on their post-treatment clinical manifestations and VAS scores. A univariate analysis was performed to understand the risk factors affecting patient outcomes. The results showed that patient age ≥60 years, number of vertebral fractures ≥2, and treatment regimen were risk factors affecting patient outcome (**Table 1**, *P*<0.05). After value assignment (**Table 2**), multifactorial logistic regression analysis revealed that the number of vertebral fractures ≥2 (OR=2.198, *P*=0.034) and surgical treatment (OR=1.685, *P*=0.012) were independent risk and protective factors affecting patient outcomes (**Table 3**, *P*< 0.05) (**Figure 2**).

Prognostic factors affecting 2-year survival in MM patients with pathologic fractures

Cox regression was used to analyze the prognostic factors affecting 2-year survival in MM patients with pathological fractures. Efficacy (*P*<0.001), gender (*P*=0.004), age (*P*<0.001), BMI (*P*=0.018), ISS stage (*P*<0.001), disease staging (*P*=0.014), and treatment regimen (*P*=0.045) were found to be correlated with the patient survival at 2-year (**Table 4**). Further, results of Cox multivariate analysis showed that efficacy (HR=17.924, *P*<0.001), age (HR=3.544, *P*= 0.003) and ISS staging (HR= 10.770, *P*=0.001) were independent prognostic factors affecting patients' 2-year survival (**Table 5**; **Figure 3**).

Construction and validation of a 2-year survival prognostic model

A prognostic model for 2-year survival of MM patients with pathologic fractures was constructed, incorporating treatment outcome, patient age, and ISS staging. By converting the total score to a linear predictive value, we were able to estimate the patients' probability of survival over 24 months. The ROC curve analysis

Table 2. Assignment table

Factor	Assignment
Age	≥60 years = 1, <60 years = 0
Number of vertebral fractures	≥2 = 1, <2 = 0
Treatment plan	Conservative treatment = 1, surgical treatment = 0
Efficacy	Effective = 0, ineffective = 1

Table 3. Multivariate logistic regression

Factor	β	Standard error	Chi-square	*P* value	OR value	95% CI	
						Lower limit	Upper limit
Age	0.687	0.356	2.151	0.331	1.673	0.723	2.198
Number of vertebral fractures	0.875	0.361	3.117	0.034	2.198	1.238	2.887
Treatment plan	1.568	0.364	3.562	0.012	1.685	1.286	2.348

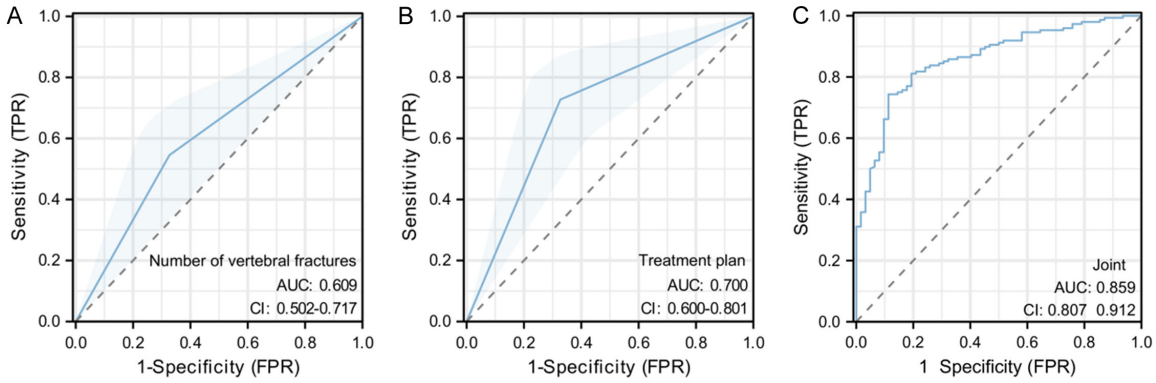

Figure 2. Efficacy of risk factors in assessing patient outcome. A. ROC curves for the assessment of patient outcome by number of vertebral fractures. B. ROC curves for the assessment of patient efficacy by treatment regimens. C. ROC curves for the assessment of patient outcomes by joint prediction. Note: ROC, Receiver Operating characteristic.

Table 4. Cox univariate analysis

Factor	β	Standard error	*P* value	HR	95% CI	
					Lower limit	Upper limit
Efficacy	1.778	0.481	<0.001	5.921	2.306	15.200
Gender	-1.093	0.382	0.004	0.335	0.158	0.709
Age	1.303	0.399	<0.001	3.680	1.682	8.052
BMI	-2.409	1.014	0.018	0.090	0.012	0.656
Fracture site	0.324	0.329	0.324	1.383	0.726	2.633
Number of vertebral fractures	-0.133	0.332	0.688	0.875	0.457	1.678
ISS staging	0.987	0.310	<0.001	2.684	1.461	4.928
Disease classification	0.532	0.216	0.014	1.703	1.114	2.602
Treatment Plan	-0.676	0.337	0.045	0.508	0.263	0.984
History of hypertension	0.403	0.398	0.311	1.497	0.686	3.266
History of diabetes	0.142	0.419	0.735	1.152	0.507	2.618
Chemotherapy regimen	-0.151	0.325	0.641	0.860	0.455	1.624

Note: BMI, Body Mass Index; ISS, International Staging System.

Table 5. Cox multivariate analysis

Factor	β	Standard error	*P* value	HR	95% CI	
					Lower	Upper
Efficacy	2.886	0.625	<0.001	17.924	5.266	61.006
Gender	0.623	0.701	0.374	1.864	0.472	7.359
Age	1.265	0.425	0.003	3.544	1.541	8.148
BMI	-0.764	1.092	0.484	0.466	0.055	3.963
ISS staging	2.377	0.723	0.001	10.770	2.610	44.447
Disease classification	-0.334	0.524	0.523	0.716	0.256	1.999
Treatment Plan	0.476	0.267	0.243	1.754	0.456	2.568
Chemotherapy regimen	0.393	0.386	0.308	1.481	0.696	3.155

Note: BMI, Body Mass Index; ISS, International Staging System.

revealed a high accuracy (AUC=0.756) of the model, indicating good discriminatory ability. The calibration curves confirmed agreement between model predictions and actual observations. DCA demonstrated the clinical utility of the model at multiple probability thresholds, highlighting its relevance for risk stratification in clinical decision-making (**Figure 4**).

Discussion

MM is a common malignancy affecting the hematologic system and quality of life associated with varying degrees of bone pain and fractures [2, 18]. This study aimed to analyze treatment response risk factors in MM patients with pathological fractures, aiming to optimize treatment plans and improve prognosis. By identifying and evaluating these factors, we hope to establish personalized treatment pathways to aid clinical decision-making, improve patient quality of life, and guide management in an aging population with MM.

Our findings indicate that having ≥2 vertebral fractures and receiving conservative treatment were independent risk factors for poor patient outcomes. Conservative treatment, though providing symptomatic relief in some cases, was less effective than surgical intervention in rapidly restoring spinal stability and relieving nerve compression [19]. The presence of multiple vertebral fractures signifies serious spinal instability and widespread disease burden, leading to diminished treatment efficacy, prolonged pain, delayed functional recovery, and increased risk of complications [20]. Thus, our results underscore the importance of tailored treatment strategies and early surgical intervention to improve outcomes.

Previously, a study by Xiang et al. [21] evaluated the risk-benefit ratio of vertebroplasty or vertebral kyphoplasty in MM patients without antimyeloma therapy, revealing a higher incidence of new postoperative vertebral fractures and shorter overall survival in the surgical group. In contrast, our study included patients who were treated conservatively and surgically, and took into account additional variables affecting efficacy, such as number of vertebral fractures. Our study showed that the patients had poorer outcomes when the number of vertebral fractures was ≥2 and when conservative treatment was adopted. These differences emphasize the impact of patient selection, therapeutic approaches, and antimyeloma treatments on outcomes, suggesting that a combination of factors needs to be considered when selecting treatment options. Future studies may require finer categorization of patient selection criteria and introduce more diversity in outcome metrics to fully assess the effects and risks of different treatment options.

The prognosis of MM is influenced by a variety of factors, some of which are related to the disease itself, such as tumor load and genetic abnormalities in tumor cells, and biological features of the disease [22]. Other lifestyle and individual patient factors such as age, gender, overall health, and the presence of comorbidities can also have a significant impact [23]. Patients with MM are often at risk for pathologic fractures, a complication that significantly adds to the burden of disease. Pathologic fractures not only provoke severe pain and impact quality of life, but may also limit mobility, increase treatment complexity, and shorten patient survival [24]. Therefore, prevention and

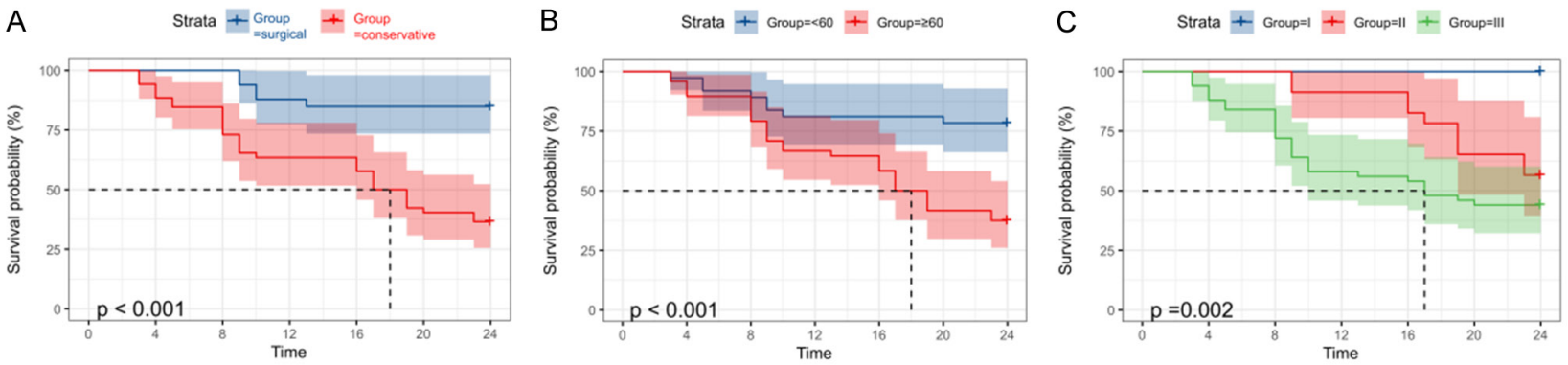

Figure 3. Independent prognostic factors affecting patient survival at 2 years. A. 2-year survival curves in patients with different treatment effects. B. 2-year survival curves in patients of different ages. C. 2-year survival curves in patients of different ISS stages. Note: ISS, International Staging System; MM, Multiple Myeloma.

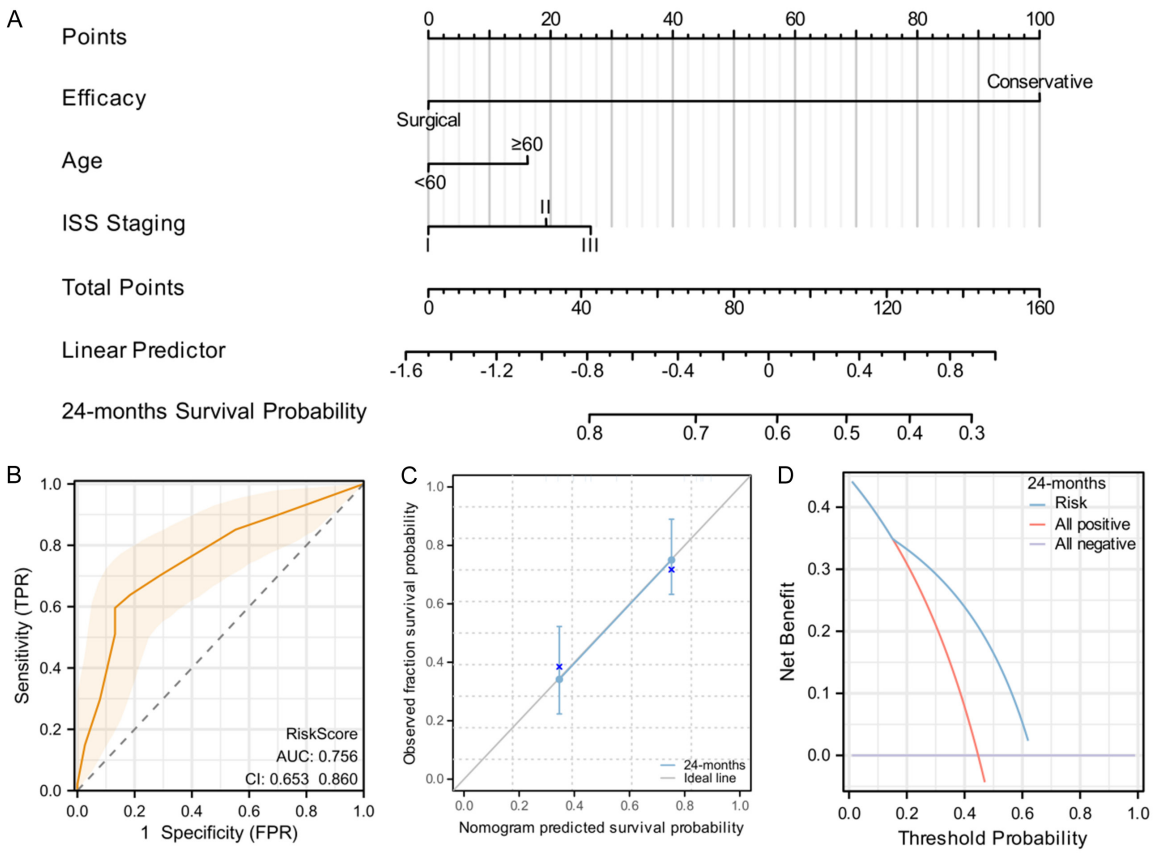

Figure 4. Construction of a prognostic model for predicting pathological fractures in MM. A. Prognostic modeling of MM pathological fractures by column line plots. B. Validation of prognostic models by ROC curves. C. Prognostic calibration curves to validate the accuracy of the prognostic model. D. Clinical utility of the prognostic model assessed by DCA curves. Note: ROC, Receiver Operating Characteristic; DCA, Decision Curve Analysis; MM, Multiple Myeloma.

treatment of fractures is critical for improving the prognosis of patients with MM and requires special attention [25]. Cox regression analysis revealed that ineffective treatment of pathologic fractures, age ≥60 years, and higher ISS stage were independent prognostic factors affecting 2-year survival in patients with MM. These factors reflect the importance of treatment response, the reduced physiologic function of older patients, and the complexities associated with advanced disease stage [26]. Ineffective treatment of pathologic fractures may indicate tumor aggressiveness and treatment resistance, whereas older patients and high ISS staging are associated with increased overall patient health and disease burden [27, 28]. Together, these factors contribute to a significant reduction in survival. Ren et al. [29] provided additional evidence, stating that the systemic inflammatory response index, platelet/lymphocyte ratio, and cytokine IL-8, as independent prognostic factors, contributed to a more accurate prediction of survival outcomes. They constructed a prognostic column chart incorporating inflammatory cells and cytokines and demonstrated better efficacy in predicting the prognosis of MM patients. Besides, Lee et al. [30] showed that high expression of PD-L1 was associated with reduced overall and progression-free survival in patients who did not undergo autologous stem cell transplantation, further emphasizing the importance of molecular and immunological markers in prognosis predication. They also developed a prognostic column chart that combined PD-L1 expression in bone marrow plasma cells and other clinical parameters to effectively predict the prognosis of MM. This suggests that combining these biomarkers with the prognostic factors we identified may help to construct a more accurate predication system.

A notable contribution of this study is that we constructed the first prognostic model for 2-year survival in MM patients with pathologic fractures. By integrating treatment outcomes, patient age, and ISS staging, our model provides, for the first time, a comprehensive scoring system for survival prediction. Our model also showed a strong discriminatory power (AUC=0.756) through ROC curve analysis, demonstrating the ability to accurately identify high- and low-risk patient groups. The excellent results from calibration curves further confirm the high agreement between the predicted survival probability and the actual observed data. DCA confirmed its value in guiding clinical decision-making at different prognostic probability thresholds and provided significant clinical relevance especially in risk stratification. Therefore, our study provides clinicians a tool to tailor treatment regimens for MM patients with pathologic fractures, which help optimize treatment outcomes and improve patient quality of life.

There are several limitations in this study, including small sample size, methodological constraints, theoretical framework constraints, time and geographic location constraints, and technological and resource constraints, which may affect the broad applicability and depth of the study. To address these issues, future research should expand the scope of the sample to increase its representativeness, adopt diversified methodologies to strengthen the reliability of the results, expand the theoretical framework to enhance the depth of the analysis, extend the time span and spatial scope of the study to validate the universality of the conclusions, and at the same time, utilize more advanced technologies and resources to enhance the quality of the study. With these improvements, future research can be expected to provide deeper and broader insights.

In conclusion, this study systematically evaluated clinical characteristics of MM patients with fractures, identified key independent factors affecting outcome and survival, and established a survival prediction model to guide clinical decision-making.

Disclosure of conflict of interest

None.

Address correspondence to: Qian Peng, Department of Vascular Proctology Surgery, Dongying People's Hospital, 317 Dongcheng South 1st Road, Dongying District, Dongying 257091, Shandong, China. E-mail: 278358406@qq.com

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