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Research Paper

Percutaneous vertebroplasty/kyphoplasty contributes to the improved outcome in patients with newly diagnosed multiple myeloma: A single center cohort study

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HIGHLIGHTS:

- Multiple myeloma is the leading cause of destructive bone disease.
- Bone lesions induce pain and fractures, impairing quality of life and survival.
- For myeloma patients, the surgical procedure and timing of surgery are controversial.
- With the onset of bone disease, PVP/PKP combined with biopsy shorten the diagnosis time for MM patients.
- PVP/PKP improves survival in advanced subpopulation or non-transplant MM patients.

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ABSTRACT

Objective: To evaluate the efficacy and prognosis of percutaneous vertebroplasty/kyphoplasty (PVP/PKP) in patients with newly diagnosed multiple myeloma (NDMM).

Methods: Clinical data of NDMM patients who underwent PVP/PKP during front-line regimen at Peking Union Medical College Hospital from January 1, 2003, to June 30, 2023, were analyzed. Patients with comparable bone diseases not receiving orthopedic surgery were selected as controls. Visual analogue scale (VAS) score, progression-free survival (PFS), and overall survival (OS) were compared.

Results: Baseline characteristics were matched between the surgical group (n = 51 with 56 surgeries) and non-surgical group (n = 102), including demographics, tumor load, International Staging System (ISS), bone diseases, cytogenetic abnormalities, first-line treatment, and autologous stem-cell transplantation (ASCT). Bone lesions for PVP/PKP were located at thoracic vertebrae (53.6 %, 30/56) or lumbosacral vertebrae (46.4 %, 26/56). The postoperative VAS score was significantly improved (2.25 ± 0.81 vs 5.92 ± 1.05, $P < 0.001$). The median follow-up time was 51[38–70] months. Kaplan-Meier survival analysis suggested that both PFS (37 [17–89] vs 23[12–61] months, HR 0.648, 95 %CI 0.431–0.973, $P = 0.047$) and OS (not reached vs 66[28-NR] months, HR 0.519, 95 %CI 0.296–0.910, $P = 0.045$) were significantly prolonged in the surgical group. COX multivariate analysis suggested that PVP/PKP was an independent prognostic factor for PFS ($P = 0.021$, HR 0.589, 95 %CI 0.376–0.922) and OS ($P = 0.038$, HR 0.496, 95 %CI 0.255–0.963). Subgroup analysis confirmed that patients with ISS II/III or non-ASCT achieved better PFS and OS in the surgical group (PFS: $P = 0.033$, $P = 0.040$; OS: $P = 0.024$, $P = 0.018$ respectively), while similar survival outcome was observed in patients with ISS I or ASCT between two groups.

Conclusion: For NDMM patients, not only does PVP/PKP alleviate bone pain, meanwhile, it improves the PFS and OS in advanced subpopulation or non-transplant myeloma patients, which suggests that shortening the gap from symptom onset to diagnosis by orthopedic surgery favors clinical prognosis.

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1. Introduction

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by abnormal secretion of monoclonal immunoglobulins with associated organ dysfunction. Bone disease is one of the common complications of MM. About 80 % of patients experience bone pain at the onset of the disease, with a higher proportion of bone destruction during the recurrence stage [1–3]. Myeloma bone disease (MBD) refers to all skeletal-related events (SREs), including osteolytic lesions, refractory bone pain, pathological fractures, hypercalcemia, spinal instability, and spinal cord compression. Some patients underwent percutaneous vertebroplasty/kyphoplasty (PVP/PKP) and were referred to hematologists for a precise diagnosis. Over time, MBD may lead to spinal kyphosis and associated disability, impairing the quality of life and survival [4]. Thus, MBD should be stressed while treating MM. Bisphosphonates are the primary agents for MBD, while denosumab has been approved and demonstrated similar potency, both of which may benefit survival [1,5–8]. In addition to medication, a multidisciplinary collaborative diagnosis and treatment paradigm, including surgery and radiotherapy, are suggested for MBD. For symptomatic vertebral compression fractures, percutaneous vertebroplasty/kyphoplasty is recommended by the International Myeloma Working Group (IMWG) [7,9].

In MM patients, choosing the appropriate surgical methods and determining the right timing for surgery is a crucial issue that often troubles hematologists and orthopedists. If handled improperly, it may lead to delayed diagnosis and treatment, ultimately resulting in a decline in quality of life or even fatal consequences. PVP and PKP are minimally invasive procedures that utilize percutaneous cement augmentation to strengthen and stabilize vertebral body fractures and relieve pain. PVP refers to the injection of polymethylmethacrylate (PMMA) into the pathological void of osteolytic lesions via a transpedicular or extrapedicular approach. PKP, by using inflatable balloons before injection, provides additional benefits of restoring vertebral body height [10–12]. Under the circumstances of emerging antimyeloma drugs with the improvement of survival, as well as effective pain-relief bone-targeted drugs, the impact of PVP/PKP on the efficacy and survival remains uncertain. Therefore, this study aims to analyze the effects of PVP/PKP in myeloma treatment based on the experience of our multi-disciplinary team.

2. Methods

2.1. Patients

Clinical data from the MM database at Peking Union Medical College Hospital were collected and retrospectively analyzed from January 1, 2003, to June 30, 2023. By reviewing their disease diagnosis process, we divided these MM patients into two groups. The surgical group were those who visited the orthopedic department first due to symptoms such as bone pain, and vertebral fractures and then underwent PKP/PVP along with a biopsy for the lesions. After their biopsy results indicated plasmacytoma, they were referred to hematologists. Further examination such as serum protein electrophoresis with immunofixation, and bone marrow aspiration confirmed their MM diagnoses. For patients (1) suffering from severe local pain affecting quality of life, (2) with lytic lesions by imaging in spinal areas consistent with symptoms and physical examination, (3) with suspicion of recent pathological vertebral fracture, and in the absence of spinal cord compression or vertebral posterior wall breakage, PKP/PVP surgery was recommended. Those receiving open spinal surgeries or complicated with severe spinal degeneration (lumbar spinal stenosis, disc herniation) were not eligible. MM patients who were diagnosed by hematologists first and not treated with orthopedic surgeries were selected from the same database as the control group. All patients fulfilled the diagnostic criteria of the 2014 International Myeloma Working Group (IMWG) guidelines[13]. Patients were excluded if tumors or other hematological malignancies were concurrent. Clinical characteristics such as Durie-Salmon (DS) stage, imaging manifestations of bone disease, gender, and age were matched.

This study has been approved by the Ethics Committee of Peking Union Medical College Hospital and was exempt from signing the informed consent forms with approved document No. I-22PJ244.

2.2. Clinical data

Clinical data at baseline were recorded including paraprotein level, biochemical parameters, international staging system (ISS), D-S stage, cytogenetic abnormalities, and imaging changes. Anemia was defined as hemoglobin (Hb) less than or equal to 100 g/L; hypercalcemia as corrected serum calcium greater than 2.75 mmol/L; lactate dehydrogenase (LDH) greater than 250 U/L; and renal impairment as serum creatinine (Cr) greater than 177 mol/L. According to the FISH results, the following cytogenetic abnormalities (CAs) were counted: 1q21+, 17p-, and IgH rearrangements. Amplification of 1q21, t (4;14), t(14;16), and 17p- were defined as high-risk CAs. Imaging-demonstrated osteolytic lesions were counted. Front-line regimens mainly included VRD (bortezomib, lenalidomide, dexamethasone), BCD ± T (bortezomib, cyclophosphamide, dexamethasone, with/without thalidomide), and TCD (thalidomide, cyclophosphamide, dexamethasone). Until June 2023, all patients were followed up by electronic medical records or phone calls.

2.3. Statistical analysis

IBM SPSS 26.0 software and GraphPad Prism 9.3.1 were used for statistical analysis and survival curve construction. The measurement data were analyzed by the independent sample *t*-test, the paired sample *t*-test, or the Wilcoxon rank sum test, and the findings were presented as mean ± standard deviation (x ± SD). The enumeration data were subjected to χ 2 test or Fisher's exact test, and the results were represented as frequency (percentage), i.e., n (%). The OS and PFS were evaluated using the Kaplan-Meier method and the log-rank test and were shown as median [InterQuartile Range]. Cox proportional hazard models were used to examine the risk factors that could affect patients' OS and PFS. $P < 0.05$ was considered a significant difference.

3. Results

3.1. Baseline characteristics

Between January 1, 2003, and June 30, 2023, 1320 MM patients in our database were analyzed, and finally, 153 patients were enrolled. The clinical data at baseline in two groups of patients were summarized in Table 1. Paraprotein levels were lower in the surgical group than in the control group (28.60 ± 18.62 vs 36.42 ± 21.82 g/L, $P = 0.066$). Although the proportion of ISS III and DS III was higher in the control group, yet the difference was not statistically significant. The following characteristics in the two groups were comparable regarding anemia, impaired renal function, hypercalcemia, and elevated LDH. At diagnosis, marrow FISH was not done in 13 patients of the surgical group. Although the non-surgical group had a higher proportion of 1q21+, 17p −, and high-risk IgH CAs than the surgical group (all P values over 0.05), there was a consistent distribution of patients in R-ISS III or R2-ISS IV between the two groups. BCD was the primary front-line regimen in both groups. Ten (19.6 %) patients in the surgical group and twenty-four (23.5 %) in the control group underwent autologous stem-cell transplantation (ASCT).

3.2. Efficacy of surgery

A biopsy of the bone lesion was performed during PVP/PKP, which facilitated the referral to hematologists and shortened the gap of diagnosis. The median time from onset of symptoms to MM diagnosis was 9 weeks in the surgical group and 13 weeks in the non-surgical group ($P =$

Table 1
Demographics and baseline clinical characteristics.[a]

Characteristic	The Surgical group N = 51	The Non-Surgical group N = 102	χ^2/t	P value
Gender			0.000	1.000
Male	31 (60.8 %)	62 (60.8 %)		
Female	20 (39.2 %)	40 (39.2 %)		
Age, years			0.471	0.638
	60.45 ± 10.05	61.24 ± 9.54		
M protein type			0.707	0.872
IgG	31 (60.8 %)	58 (56.9 %)		
IgA	11 (21.6 %)	20 (19.6 %)		
IgD	2 (3.9 %)	5 (4.9 %)		
Light chain	7 (13.7 %)	19 (18.6 %)		
Serum M protein (g/L)	N = 36	N = 78	1.859	0.066
	28.60 ± 18.62	36.42 ± 21.82		
ISS			0.487	0.784
I	17 (33.3 %)	31 (30.4 %)		
II	15 (29.4 %)	27 (26.5 %)		
III	19 (37.3 %)	44 (43.1 %)		
R-ISS	N = 42		0.306	0.858
I	10 (23.8 %)	24 (23.5 %)		
II	25 (59.5 %)	57 (55.9 %)		
III	7 (16.7 %)	21 (20.6 %)		
R2-ISS	N = 38		0.923	0.820
I	9 (23.7 %)	19 (18.6 %)		
II	8 (21.1 %)	21 (20.6 %)		
III	14 (36.8 %)	46 (45.1 %)		
IV	7 (18.4 %)	16 (15.7 %)		
Durie-Salmon stage			1.255	0.534
I	3 (5.9 %)	5 (4.9 %)		
II	8 (15.7 %)	10 (9.8 %		
III	40 (78.4 %)	87 (85.3 %)		
Laboratory Examination				
Anemia	17 (33.3 %)	47 (46.1 %)	2.270	0.132
Renal dysfunction	4 (7.8 %)	13 (12.7 %)	0.827	0.363
Hypercalcemia	6 (11.8 %)	13 (12.7 %)	0.030	0.862
Elevated LDH	6 (11.8 %)	12 (11.8 %)	0.000	1.000
Front-line regimens			3.664	0.160
VRD	10 (19.6 %)	31 (30.4 %)		
BCD	26 (51.0 %)	53 (52.0 %)		
TCD	3 (5.9 %)	9 (8.8 %)		
Others	12 (23.5 %)	9 (8.8 %)		
ASCT			0.303	0.582
Yes	10 (19.6 %)	24 (23.5 %)		
High-risk CAs				
17p-	4/38 (10.5 %)	17/102 (16.7 %)	0.819	0.366
t(4;14)/t(14;16)	4/38 (10.5 %)	13/102 (12.7 %)	0.128	0.721
1q21+	10/38 (26.3 %)	38/102 (37.3 %)	1.470	0.225
Number of the bone lesions				
<3	11 (21.6 %)	16 (15.7 %)	0.810	0.368
≥3	40 (78.4 %)	86 (84.3 %)		

[a] ISS: International Staging System; LDH: lactate dehydrogenase; VRD: bortezomib, lenalidomide, dexamethasone; BCDT: bortezomib, cyclophosphamide, dexamethasone, with/without thalidomide; TCD: thalidomide, cyclophosphamide, dexamethasone; Others: other front-line regimens including VAD (Vincristine, epirubicin, dexamethasone), PAD (bortezomib, epirubicin, dexamethasone), IRD (ixazomib, lenalidomide, dexamethasone), TAD (thalidomide, epirubicin, dexamethasone), VMP (bortezomib, melphalan, prednison). ASCT: autologous stem-cell transplantation; CA: cytogenetic abnormality.

0.037).

The proportion of patients with 3 or greater osteolytic lesions in the surgical group was 78.4 % (40/51), and that of the non-surgical group was 86.3 % (86/102), with no significant difference. The surgical sites included the thoracic vertebrae (53.6 %) and lumbosacral vertebrae (46.4 %). Five patients received two operations. Patients in the surgical group reported significantly improved bone pain. Their VAS score decreased from 5.92 ± 1.05 to 2.25 ± 0.81 (t = 29.60, $P < 0.001$) within two weeks after surgery.

3.3. Prognostic analysis

The overall median follow-up was 51 [38–70] months, and the two groups were comparable (the surgical group: 47[38–57], the control group: 57[38–84], $P = 0.139$).11 deaths occurred in the surgical group compared with 45 deaths for the non-surgical group. The PFS and OS of the surgical group were better than those of the control group (Fig. 1). Median PFS was 37 [17, 89] months for patients undergoing PVP/PKP versus 23 [12,61] months for the non-surgical group (HR 0.648, 95 %CI 0.431–0.973, $P = 0.047$). One-year, 3-year, and 5-year PFS rates were estimated as 86.2 % vs 73.0 %, 52.4 % vs 35.1 %, and 36.3 % vs 25.5 %, which were all better in the surgical group. Median OS was not reached [61, NR] in the surgical group versus 66 [28, NR] months in the control group (HR 0.519, 95 %CI 0.296–0.910, $P = 0.045$). One-year, 3-year, and 5-year OS rates were estimated as 93.3 % vs 91.2 %, 81.8 % vs 68.5 %, and 76.7 % vs 53.2 % respectively.

In the multivariable Cox model for PFS (Table 2), the risk of progression was lower for patients undergoing PVP/PKP (HR 0.589, 95 %CI 0.376–0.922, $P = 0.021$). The data also demonstrated worse PFS for patients with ISS II/III stage ($P = 0.027$) or those without ASCT ($P = 0.023$). Multivariable Cox analysis for OS (Table 3) suggested that ISS II or III (stage II vs I: HR 4.03, 95 %CI 1.592–12.177, stage III vs I: HR 6.218, 95 %CI 2.431–15.903, $P = 0.001$) was risk factors for mortality, and ASCT (HR 0.355, 95 % CI 0.139–0.910, $P = 0.031$) was a strong

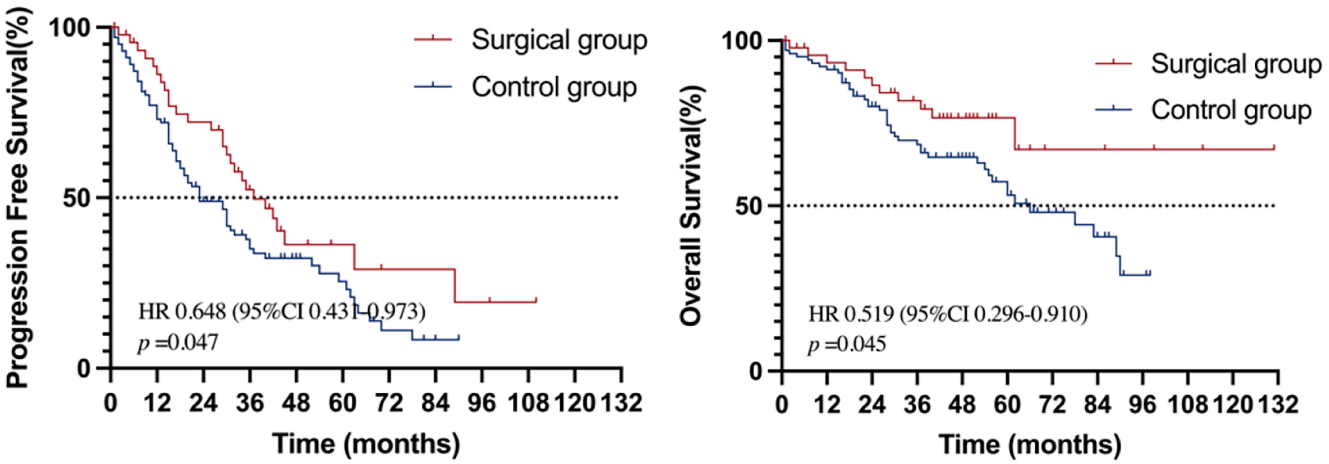

Fig. 1. Kaplan-Meier estimates of progression-free survival and overall survival

Table 2
Univariate analysis and multivariate Cox regression analysis of PFS.

Characteristic	Univariate analysis		Multivariate analysis	
	HR + 95 %CI	P value	HR + 95 %CI	P value
PVP/PKP	0.648[0.431–0.973]	0.047	0.589 [0.376–0.922]	0.021
Age (<65y vs ≥ 65y)	1.431[0.959–2.135]	0.080		
ISS		0.027		0.037
ISS II vs I	1.588 [0.909–2.774]		1.601 [0.915–2.799]	
ISS III vs I	1.933[1.195–3.125]		1.894 [1.163–3.083]	
R-ISS		0.005	/	/
R-ISS II vs I	1.986[1.162–3.393]			
R-ISS III vs I	2.770[1.483–5.174]			
R2-ISS		0.015	/	/
R2-ISS II vs I	1.994[1.000–3.978]			
R2-ISS III vs I	2.678[1.442–4.972]			
R2-ISS IV vs I	2.664[1.246–5.693]			
Durie-Salmon Stage		0.647		
DS stage II vs I	1.437[0.449–4.595]	0.541		
DS stage III vs I	1.588[0.582–4.335]	0.367		
ASCT	0.510[0.299–0.872]	0.014	0.534 [0.311–0.918]	0.023

Table 3
Univariate analysis and multivariate Cox regression analysis of OS.

Characteristic	Univariate analysis		Multivariate analysis	
	HR + 95 %CI	P value	HR + 95 %CI	P value
PVP/PKP	0.519[0.296–0.910]	0.045	0.496 [0.255–0.963]	0.038
Age (<65y vs ≥ 65y)	0.597[0.346–1.032]	0.049	1.303 [0.754–2.252]	0.344
ISS		0.000		0.001
ISS II vs I	4.514[1.634–12.473]		4.403 [1.592–12.177]	
ISS III vs I	6.670[2.613–17.028]		6.218 [2.431–15.903]	
R-ISS		0.001	/	/
R-ISS II vs I	6.513[2.004–21.170]			
R-ISS III vs I	11.065[3.197–38.296]			
R2-ISS		0.005	/	/
R2-ISS II vs I	3.289[0.866–12.482]			
R2-ISS III vs I	6.724[2.063–21.917]			
R2-ISS IV vs I	6.949[1.845–26.182]			
Durie-Salmon Stage		0.767		
DS stage II vs I	1.581[0.318–7.857]			
DS stage III vs I	2.465 [0.408–6.959]			
ASCT	0.298[0.119–0.748]	0.010	0.355 [0.139–0.910]	0.031

protective index. Also, a high correlation between PVP/PKP and better OS (HR 0.496, 95 % CI 0.255–0.963, $P = 0.038$) was revealed. ISS, ASCT, and PVP/PKP were independent risk factors of OS. Due to the small sample size, R-ISS or R2-ISS was not included in the multivariable Cox model.

PVP/PKP also confirmed the prognostic role in subgroup analyses (Table 4). Among patients with ISS II/III (Fig. 2), median PFS was 34 [17,63] months in PVP/PKP group vs 19[8,52] months for the non-

Table 4
Subgroup analysis of PFS and OS.

Characteristics	The Surgical group	The Non-Surgical group	HR (95 % CI)	χ^2	P value
ISS I	N = 17	N = 31			
mPFS (m)	45[32,89]	59[23,67]	0.760 [0.335—1.726]	0.439	0.507
mOS (m)	NR	NR	1.401 [0.215–9.135]	0.138	0.710
ISS II/III	N = 34	N = 71			
mPFS (m)	34[17,63]	19[8,52]	0.584 [0.366–0.931]	4.521	0.033
mOS (m)	NR [37, NR]	54[22,83]	0.451 [0.251–0.812]	5.084	0.024
ASCT	N = 10	N = 24			
mPFS (m)	NR [26, NR]	35[23,64]	0.693 [0.244–1.974]	0.421	0.517
mOS (m)	NR	NR	1.745 [0.246–12.390]	0.399	0.528
non-ASCT	N = 41	N = 78			
mPFS (m)	37[17,63]	19[10.52]	0.617 [0.397–0.959]	4.221	0.040
mOS (m)	NR [62, NR]	60 [26,90]	0.433 [0.242–0.776]	5.612	0.018

surgical group (HR 0.584, 95 %CI 0.366–0.931, $P = 0.033$), while median OS was not reached vs 54[22,83] months (HR 0.451, 95 %CI 0.251–0.812, $P = 0.024$) respectively. Among patients not receiving ASCT (Fig. 3), median PFS and OS were both longer in the surgical group (mPFS: 37[17,63] vs 19[10.52], HR 0.617, 95 %CI 0.397–0.959, $P = 0.040$; mOS: NR vs 60[26,90], HR 0.433, 95 %CI 0.242–0.776, $P = 0.018$).

MM-specific death was the predominant reason in both groups (54.5 % in the surgical group and 73.3 % in the control group, P = 0.424). The causes of deaths were listed in Table 5. Of note, three individuals in the control group died of pulmonary infections within 2 months after diagnosis, whereas no lethal pulmonary infections were observed in the surgical group.

4. Discussion

Bone pain is one of the typical clinical manifestations of MM. Pathological fractures occur in 60 % of MM patients, mainly with vertebral bone involvement [14,15]. MBD results in persistent pain and immobility, therefore increasing the risk of pulmonary infections or other complications, which may interfere with anti-myeloma treatment. The continuous emerging bone-targeted drugs have effectively alleviated

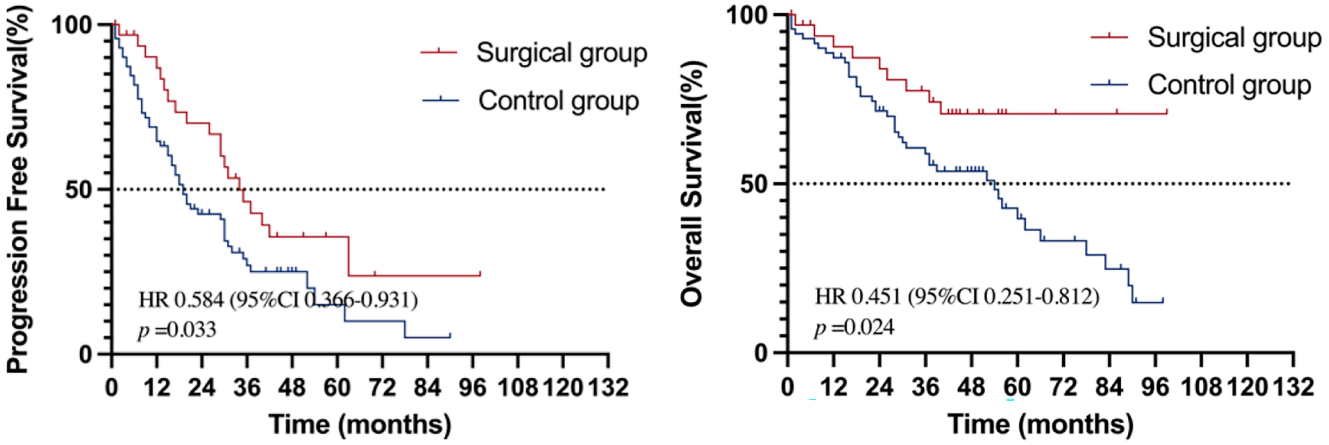

Fig. 2. Kaplan-Meier estimates of progression-free survival and overall survival in the ISS II/III subgroup

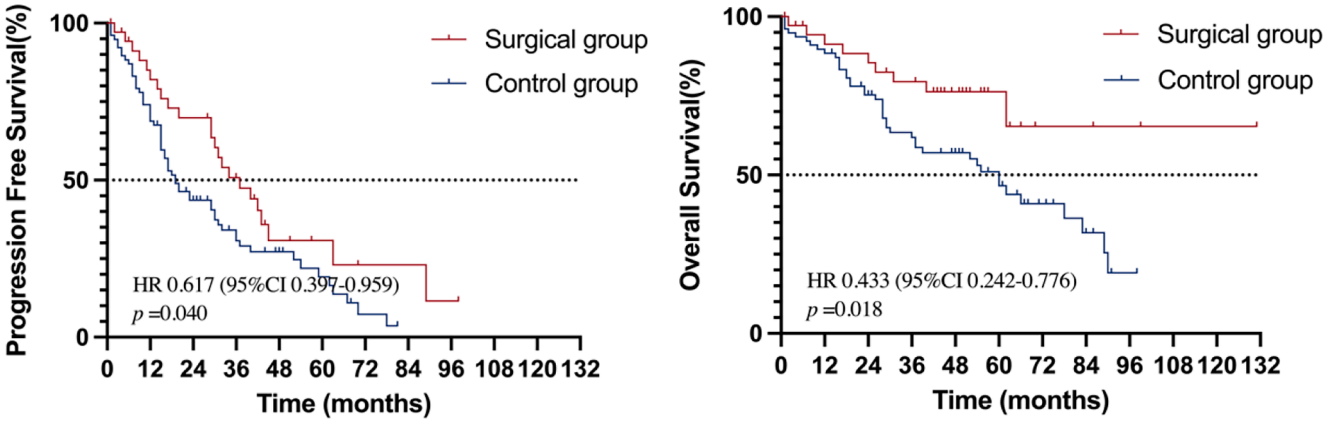

Fig. 3. Kaplan-Meier estimates of progression-free survival and overall survival in the non-ASCT subgroup

Table 5
Causes of Death.

Causes of death	Deaths in the Surgical group (N = 11)	Deaths in the non-Surgical group (N = 45)
Progression of MM	6 (54.5 %)	33 (73.3 %)
Respiratory infections	0	3 (6.7 %)
Genitourinary infections	1 (9.1 %)	1 (2.2 %)
Gastrointestinal infections	1 (9.1 %)	1 (2.2 %)
Coronary artery diseases	1 (9.1 %)	1 (2.2 %)
Neurological diseases	0	2 (4.4 %)
Gastrointestinal hemorrhage	0	1 (2.2 %)
Undetermined causes	2 (18.2 %)	3 (6.7 %)

bone pain and postponed SREs, posing new questions for surgical indications and their impact on response and survival. However, at present, in terms of MBD, the international consensus on the management principles for spinal lesions is limited. Based on the above background, this study analyzed clinical data of newly diagnosed MM patients in a single center, and our experience suggested that PVP/PKP not only alleviated bone pain and improved quality of life, more surprisingly, had a positive impact on front-line response and survival.

In terms of surgical treatment for spinal fractures, PVP/PKP has proven its efficacy in pain relief in patients with osteoporotic spinal fracture [16]. When it comes to severe bone pain associated with cancer, plenty of studies found that PVP/PKP provided sustained pain relief, maintained back support function, improved quality of life, and reduced days of bed rest and analgesic use [9–12,17–23], some of which were conducted from the perspective of orthopedists, focusing on PVP/PKP's role while neglecting the effects of anti-myeloma therapy. Patients treated with PVP/PKP in our study were in the early stage of diagnosis and had not yet started chemotherapy or bone-targeted drugs, which confirmed the efficacy of PVP/PKP in relieving bone pain.

Only a few previous studies considered the potential survival benefits of PVP/PKP. There were no subgroup analysis regarding involved bones (limbs of vertebrae) or surgery patterns with 5-year OS rates varying from 37 % to 63 % [24–27]. These studies suggested that orthopedic surgery of destructive lesions combined with chemotherapies translated into sustained response. In our study, the potential factors contributing to the survival advantages were analyzed.

Multiple real-world studies have revealed that progression of MM was the predominant cause of death in approximately 69–72 % of patients Other potential causes of death include secondary malignancies, infectious diseases, and cardiovascular disorders [28–32]. Rapid recovery from immobility after PVP/PKP may have a beneficial effect on comorbidities. No early lethal infections in the surgical cohort further underscored the potential benefits of PVP/PKP in reducing complications, thereby gaining advances in response and survival.

Further, PMMA, the local injection material for PVP/PKP, is considered to have a potential anti-tumor effect in vivo and in vitro [33,34]. Bone cement possibly starves myeloma cells via isolating blood supply and nutrients from the bone marrow microenvironment. Another primary concern about PVP/PKP was the recurrent fractures at adjacent vertebrae. We demonstrated that five in 51(9.8 %) patients underwent second surgeries due to this, which was relatively low and consistent with the incidence in osteoporotic patients [35–37].

Up to now, the window phase to perform a PVP/PKP after acute bone fractures is still undefined. For acute osteoporotic compression fractures of the vertebrae, most studies recommended within six weeks. The Cancer Patient Fracture Evaluation trial reported that patients who underwent PKP in the first month after vertebral compression have better spine function and fewer analgesic requirements than those receiving delayed surgeries [11]. In the IMWG consensus, PVP/PKP is suggested to be performed within 4–8 weeks for MM patients with severe pain due to fractures [9]. However, systemic anti-myeloma therapy should still be considered first in newly diagnosed MM patients [38–40].

When facing patients with acute vertebral fractures without a definitive diagnosis of MM, orthopedists have to determine whether to perform surgery or wait for tests related to underlying diseases. Despite the emergence of some new non-invasive techniques in recent years, such as liquid biopsy for detecting circulatory tumor cells and cell-free DNA, these techniques are primarily used for predicting prognosis and treatment efficacy, rather than verifying the diagnosis [41–46]. Our study showed that PVP/PKP could both provide evidence for diagnosis and bring benefits in a minimally invasive way. At the same time, a biopsy along with the surgery could shorten the gap to diagnosis in patients whose initial symptoms were SREs. Another study demonstrated that the time to MM diagnosis in 32 patients who underwent PVP/PKP without biopsy was significantly longer compared to those receiving simultaneous biopsy (6.1 months vs 1 month, $P < 0.01$)[47]. Thus, the biopsy of destructive lesions should be performed concurrently with PVP/PKP, which was safe and efficacious.

Our findings provide some potential values for the management of MMBD in real practice, lying in (1) For patients with suspected MBD, presenting with severe symptoms impacting the quality of life, imaging indicating vertebral lytic lesions with concurrent vertebral instability or pathological fractures, it is advisable to undergo PKP/PVP surgery, along with biopsy. (2) For MM patients with spinal involvement, early PKP/PVP intervention may improve quality of life and potentially improve PFS and OS. The close cooperation between orthopedists and hematologists, i.e., multi-disciplinary treatment (MDT), was vital for MM patients with bone diseases, which has been stressed in the guidelines or recommendations [7,8].

Some limitations should be noted. First, our study is limited by its retrospective nature. Although we included patients from the past two decades at our center, the overall cohort remains relatively small, especially for the surgical group. Secondly, some patients lacked cytogenetic data, resulting in an incomplete R-ISS/R2-ISS staging, which could have been discussed in depth. Also, since patients received anti-myeloma therapy and bone-targeted drugs after surgery, we did not analyze the long-term effect in relieving bone pain or recurrent fractures, which may lead to some statistical bias.

5. Conclusion

In conclusion, when there is an onset of bone symptoms with orthopedic indications, PVP/PKP should be performed timely with a concurrent bone biopsy. In newly diagnosed MM patients, PVP/PKP could not only improve the quality of life, but also link to favorable survival due to shortening the gap to diagnosis. Although generations of novel anti-myeloma agents are being developed, multi-disciplinary team still improves patients' outcome comprehensively in the real practice.

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CRediT authorship contribution statement

Fujing Zhang: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization, Software, Validation, Visualization. **Shuzhong Liu:** Methodology, Conceptualization, Formal analysis, Validation, Writing – review & editing. **Xi Zhou:** Investigation, Methodology, Resources, Writing – review & editing. **Wei Wang:** Investigation, Resources. **Congwei Jia:** Investigation, Resources. **Qin Wang:** Investigation, Resources. **Yong Liu:** Writing – review & editing, Supervision, Conceptualization, Investigation, Methodology. **Junling**

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability:

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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