RESEARCH

Prognostic analysis of percutaneous vertebroplasty (PVP) combined with ^{125}I implantation on lumbosacral vertebral osteoblastic metastases

Lei Xu[1*†], Xin Huang[1†], Yan Lou[2†], Wei Xie[1†], Jun He[1†], Zuozhang Yang[3*], Yihao Yang[3] and Ya Zhang[3]

Abstract

Objective Lumbosacral vertebral osteoblastic metastasis is treated with percutaneous vertebroplasty (PVP) combined with ^{125}I seed implantation and PVP alone. Compared to PVP alone, we evaluated the effects of combination therapy with PVP and ^{125}I seed implantation on pain, physical condition, and survival and evaluated the clinical value of PVP combined with ^{125}I particle implantation.

Methods We retrospectively analyzed 62 patients with lumbosacral vertebral osseous metastases treated at our hospital between 2016 and 2019. All the patients met the inclusion criteria for ^{125}I implantation, and they were randomly divided into a combined treatment group and a pure PVP surgery group. The visual analog pain scale (VAS), Karnofsky Performance Status (KPS), and survival time were recorded at different time points, including preoperative, postoperative 1 day, 1 month, 3 months, 6 months, 12 months, and 36 months in each group. The variation in clinical indicators and differences between the groups were analyzed using SPSS version 20.0. Correlations between different variables were analyzed using the nonparametric Spearman's rank test. The Kaplan–Meier method was used to estimate the relationship between survival time and KPS score, VAS score, or primary tumor progression, and survival differences were analyzed using the log-rank test. Multivariate analyses were performed using a stepwise Cox proportional hazards model to identify independent prognostic factors.

Results Compared to the PVP treatment group, the pain level in the combined treatment group was significantly reduced ($P = 0.000$), and the patient's physical condition in the combination treatment group significantly improved. Kaplan–Meier analysis showed that the survival rate of the PVP group was significantly lower than that of the combination group ($P = 0.038$). We also found that the median survival of patients in both groups significantly increased with an increase in the KPS score (14 months vs. 33 months) ($P = 0.020$). Patients with more than three transfer sections had significantly lower survival rates than those with one or two segments of the section ($P = 0.001$). Further, Cox regression analysis showed that age ($P = 0.002$), the spinal segment for spinal metastasis ($P = 0.000$), and primary tumor growth rate ($P = 0.005$) were independent factors that affected the long-term survival of patients with lumbosacral vertebral osseous metastases.

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Conclusions PVP combined ^{125}I seeds implantation surgery demonstrated superior effectiveness compared to PVP surgery alone in treating lumbosacral vertebral osseous metastases, which had feasibility in the clinical operation. Preoperative KPS score, spine transfer section, and primary tumor growth rate were closely related to the survival of patients with lumbosacral vertebral osteoblastic metastasis. Age, spinal segment for spinal metastasis, and primary tumor growth can serve as prognostic indicators and guide clinical treatment.

Keywords Lumbosacral vertebral metastases, Osteoblastic, Percutaneous vertebroplasty, ^{125}I seeds, Prognostic analysis

Introduction

Spinal metastases, including osteolytic, osteoblastic, and mixed bone metastases, are common complications of malignant cancers [1, 2]. Osteoblastic metastases occur most commonly in patients with prostate [3–6], gastric [7, 8], bladder [9, 10], lung [11, 12], and breast cancer [13–15]. The incidence of metastatic spinal tumors has gradually increased recently with the increasing prevalence of various tumors worldwide [16]. Pain is the main symptom of osteoblastic spinal metastasis. In severe cases, it can cause complications, such as pathological fractures of the vertebral body, compression of the spinal cord, and paraplegia [17]. Therefore, early diagnosis and appropriate treatment are crucial. It is helpful to minimize bone destruction of the vertebral body caused by spinal metastases, restore the physiological function of the patient's spine as much as possible, and improve the quality of life [18].

In recent years, percutaneous vertebroplasty (PVP) has become a surgical method for the treatment of osteolytic destruction of bone metastases [19–23]. PVP surgery for osteoblastic metastases is rare [21]. Owing to the high rigidity of osteoblastic metastases, the puncture path is hindered [24]. Therefore, spinal osteoblastic metastasis is normally considered a contraindication for PVP [21, 25, 26]. Yang et al. found that the tumor itself and its surrounding areas are the target areas for PVP treatment [27]. Injecting bone cement into these areas can cover the tumor foci, kill them, and reinforce the mechanical strength around the tumor, thereby relieving pain and preventing further destruction of the vertebral body.

^{125}I particles have a long half-life, low energy, persistence, and precise positioning. They target the uncontrolled proliferation of tumor tissue cells and have a tumor-killing effect [28, 29, 21, 30]. The radioactive source is accurately implanted into the target tissue, and the source is reasonably distributed according to the volume, density (half-valent layer) of the target tissue, and relationship with the neighboring important organs. This approach enables 'directed blasting' and maximizes the destruction of cancer cells while minimizing damage to normal tissues and functions. Inspired by the concept of compound technology, Zuozhang et al. [31] first

proposed a combination of PVP and ^{125}I seed vertebral body implantation interstitial brachytherapy (Interstitial Brachytherapy) for the treatment of spinal metastases, with a significant curative effect. Armstrong et al. used ^{125}I seeds to permanently implant 35 patients with paravertebral tumors, and the local control rate at 1 year was 51% [32]. The implantation of ^{125}I seeds in the surgical area can effectively prevent local recurrence after the palliative resection of non-small cell lung cancer. Moreover, 56 patients with liver metastases from colorectal cancer underwent ^{125}I seed permanent implantation. The local control rates at 1, 3, and 5 years were 41%, 23%, and 23%, respectively [33, 34]. All the above results show that the permanent implantation of ^{125}I seeds can better inhibit tumor growth, control local tumor development, significantly reduce the tumor recurrence rate in situ, relieve pain, and significantly prolong survival.

There have been studies on spinal osteoblastic metastases in the thoracic segment; however, few studies have been conducted on the lumbosacral segments [35].

This study retrospectively analyzed the effects of clinical treatment in 62 patients with lumbosacral spinal metastases at our hospital. The correlation between surgical methods and postoperative survival rates was compared. Additionally, we compared the factors affecting the survival of patients with spinal lumbosacral osteoblastic metastases and the selection and efficacy of various surgical procedures.

Material and Methods

Clinical data collection

The subjects of this study were inpatients in the Department of Orthopedics, Chengdu Seventh People's Hospital (Affiliated Cancer Hospital of Chengdu Medical College), between February 2016 and June 2019.

The inclusion criteria were (a) clinical diagnosis of spinal metastases with a pathological diagnosis of the primary tumor or diseased vertebral body, (b) osteogenetic destruction of the lumbosacral vertebrae, (c) Low back pain is the main clinical manifestation, (d) expected survival time > 3 months, (e) Frankel classification of spinal cord function evaluation grade D, Karnofsky Performance Status (KPS) score > 60 points, (f) systemic conditions permit the procedure; no serious diseases

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of the heart and brain and other important organs, and ability to lie in the prone position for 1–2 h (g) persistent pain, no significant improvement with drugs, physical therapy, among others. (h) All patients received conventional chemotherapy and other comprehensive treatments according to the primary tumor regimen after the operation.

The exclusion criteria were as follows: (a) diagnosed as primary malignant tumor of the spine, (b) refused or unable to cooperate with the completion of clinical data collection or follow-up because of objective reasons, (c) patients or their family members refuse surgical treatment, (d) KPS score ≤ 40 or combined with heart, lung and other organ failure and unable to tolerate surgery.

Surgical materials and instruments

(a) Bone cement injection molding instruments and medicines

DOMEStic PVP instruments, including a puncture needle and screw-in syringe pressure device (Shandong Guanlong Company) (Fig. 1). Bone cement: polymethylmethacrylate (PMMA) monomer and polymer type II bone cement were produced by the Tianjin Institute of Synthetic Materials Industry.

(b) Radioactive source

The closed radioactive isotope ^{125}I source was provided by Isotope of China Institute of Atomic Energy (National Medicine Zhunzi H20045969). The radioactive source is cylindrical, and its diameter and height are 0.8 mm and 4.5 mm, respectively. The tissue penetration ability is 1.7 cm, the semivalent layer is 0.025 mmPb, the surface is wrapped in titanium alloy, and the source activity is 0.3–1 mCi. A liquid immersion disinfection method was used, and the benzalkonium bromide (Xinjieerfen) solution was soaked for 30 min.

(c) Contrast agent

We used 76% compound meglumine injection, packaged in 20 mL/15.2 g, with an iodine content of 370 mg/mL as a contrast agent (Schering (Guangzhou) Pharmaceutical Co., Ltd., China).

Research methods

The injection doses of bone cement and I ions, as well as the needle insertion coordinates and depth indications of the applicator, were calculated using the treatment planning system (TPS) software. Specifically, routine preoperative examinations included routine blood tests, blood type, coagulation, blood sugar, liver and kidney function, electrocardiogram, chest radiography, anterior and lateral radiographs of the diseased vertebra, computed tomography (CT), magnetic

Fig. 1 Percutaneous vertebroplasty devices

resonance imaging (MRI), and whole-body bone scans. If conditions permit, a positron emission tomography-computed tomography (PET-CT) examination was performed. Before surgery, CT/MRI images of each patient were scanned into the TPS software for three-dimensional digital image reconstruction. Three-dimensional icons, isodose curves, and absorbed dose indications were accurately formulated and drawn based on the size, location, and relationship with the surrounding normal tissues of the lesion. At the same time, the initial dose of the radiation source required for clinical use, needle insertion coordinates, and depth indications of the applicator are determined, and the treatment plan table is printed out.

The treatment plan was determined based on the tumor source, lesion segment, spinal stability, and degree of intraspinal compression after discussion in the department, and an individualized comprehensive treatment plan was determined. The patients and their families were informed of the treatment plan, and informed consent was obtained from all patients.

Patient grouping
The patients treated with PVP combined with ^{125}I seed implantation were the study group, while the patients treated with PVP alone were the control group.

Clinical data collection
We explained the purpose and significance of the clinical investigation to the patient, solicited their cooperation and trust, determined the initial visual analog pain scale (VAS) and KPS scores, and recorded the results.

Postoperative treatment
Postoperative CT scans were used to observe the distribution of bone cement and particles in the vertebral body, whether there was bone cement leakage, among others; observe the symptoms and signs of the patient, whether there was an infection, among others; and provide preventive anti-inflammatory, hemostasis, dehydration, etc., and nutritional nerve processing.

Postoperative follow-up
The patients were instructed to retest the VAS before surgery and at 1 month, 3 months, 6 months, 1 year, and 3 years after surgery to evaluate recovery. The KPS was monitored before surgery and at 1 month after surgery.

Statistical methods
All data were analyzed using SPSS version 20.0 software (IBM Corp., Armonk, N.Y., USA). A *P* value < 0.05 was considered statistically significant. All patients were randomly divided into two groups, and the VAS score was determined before surgery and 1 month, 3 months, 6 months, and 1 year after surgery. Repeated measures analysis of variance was used to determine whether there was a statistical difference in pain between patients before and after surgery, and the scientific significance and effects of different surgical methods on pain in patients.

All patients in this group were scored using the KPS scoring system before and 1 month after the operation, and a *t*-test was used to determine whether the difference in physical strength between the preoperative and postoperative patients was statistically significant.

Univariate analysis (Kaplan–Meier analysis) was conducted. Patients were divided into groups according to sex, age, location, KPS score, VAS score, primary tumor growth, organ metastasis, and surgical method. Univariate survival analysis was performed between the groups and the Kaplan–Meier method was used to analyze the survival time of patients and determine whether each factor affected survival time.

For each prognostic factor (sex, age, location, KPS score, VAS score, primary tumor growth, organ metastasis, and surgical method), a multivariate Cox proportional hazards regression model was used.

Results
Basic information on the selected patients
In total, 62 patients with lumbosacral bone metastases were randomly divided into a PVP combined with ^{125}I seed implantation group (combined treatment group, *n* = 31) and a PVP alone group (*n* = 31). The clinical data are presented in Table 1, and there was no difference in the factors (all *P* > 0.05). Both groups received conventional chemotherapy according to the primary disease status after surgery.

Evaluation of clinical efficacy
All patients in the combined treatment group were followed up after surgery, and the patients and their families cooperated to complete the evaluation of various efficacy indicators. At the end of the study, 14 of the 31 patients survived. Similarly, all patients in the pure PVP group were followed up after surgery, and they were willing to cooperate in evaluating various efficacy indicators. At the end of the study, five of the 31 patients survived.

Evaluation of treatment effect
We conducted intragroup statistical analyses at different time points for the two groups. As shown in Table 2, the VAS scores of both groups were significantly reduced on the 1st day after the operation. The pain levels in the combined treatment group remained unchanged from 1 to 12 months after surgery. The pain was effectively relieved,

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Table 1 Preclinical data analysis of 62 cases of osteoblastic metastasis in patients with lumbosacral vertebral

Factors	PVP group	Combination therapy group	P value
age	61.35 ± 3.04	60.87 ± 3.68	0.574
Gender			
Male	17	19	0.614
Female	14	12	
Primary tumor			
Prostate cancer	14	15	0.809
Lung cancer	8	7	
Breast cancer	7	8	
Bladder cancer	1	0	
Duodenal papillary adenocarcinoma	1	1	
Metastatic site			
Lumbar spine	10	11	0.878
Sacral spine	9	12	
Lumbar and sacral spine	12	8	
Spinal segment			
1 segment	8	10	0.211
2 segments	10	12	
≥ 3 segments	13	9	
VAS score	8.71 ± 0.34	8.68 ± 0.33	0.734
KPS score	65.29 ± 4.59	67.71 ± 5.89	0.076

while the pain in the simple treatment group was relieved 1 d and 1 month after the operation; however, the pain level gradually increased 3 months after the operation and then remained at a certain level ($P=0.000$). There was a statistically significant difference in the VAS score between preoperative and postoperative patients. Further, we compared between groups, and the pain level in the combined treatment group was significantly lower than that in the PVP treatment group alone ($P=0.000$) (Fig. 2).

We statistically analyzed the preoperative KPS scores of the combined treatment group and the pure PVP group, and the results showed that there was no statistical difference between the two groups (65.3 ± 4.6, 67.7 ± 5.9, $P=0.076$). Additionally, we performed intragroup statistics on the two groups before and 1 month after surgery.

The results showed that the KPS scores of the two groups significantly increased 1 month after surgery, indicating that the physical condition of the patients 1 month after surgery was improved compared with that before the operation (Table 3). We further compared the two groups before and 1 month after surgery and found a significant difference between them ($P=0.000$, Fig. 3).

Univariate analysis
Kaplan–Meier analysis
The log-rank method was used to compare the effects of sex, age, location, KPS score, spinal segment, primary tumor growth, organ metastasis, and surgical method on the survival rate of patients. Survival curves of the survival rates are shown in Table 4 and Fig. 4.

The results showed that there was no significant difference in the survival rate between male and female patients with lumbosacral osteoblastic metastases ($P=0.880$). The difference in survival rate was not statistically significant between patients aged ≤ 60 years and > 60 years old ($P=0.689$). Additionally, there was no statistically significant difference in the survival rates between patients with metastatic sites ($P=0.967$) and those with lumbosacral bone metastases ($P=0.092$) (Fig. 4).

The survival rate of patients with a preoperative KPS score of 60–70 was significantly lower than that of patients with a score of 80–100 ($P=0.002$). A higher KPS score indicated a better prognosis. The survival rate of patients with more than three metastatic segments was significantly lower than that of patients with lumbosacral osteoblastic metastases in one and two segments ($P=0.001$). The survival rate of patients with rapidly growing tumors was significantly lower than that of patients with moderate and slow growth ($P=0.000$), indicating a low degree of malignancy, slow growth, and long survival time. In contrast, the primary tumor was malignant with high severity, rapid disease progression, and short survival time.

To determine the effects of different surgical methods on the progression-free survival rate of patients with lumbosacral osteoblastic metastases, we used the Kaplan–Meier log-rank method for comparison. The

Table 2 VAS score comparisons for the pain of different surgical methods ($\bar{x} \pm s$)

Groups	Cases	Before surgery	After surgery				
			Day 1	1 month	3 months	6 months	12 months
Combination therapy group	31	8.7 ± 0.34	3.0 ± 0.41	2.5 ± 0.23	2.44 ± 0.26	2.38 ± 0.42	2.14 ± 0.31*△
PVP group	31	8.7 ± 0.33	3.1 ± 0.36	3.1 ± 0.28	4.53 ± 0.22	5.68 ± 0.49	5.72 ± 0.52△

△ $P=0.000$ compared with the preoperative and the postoperative
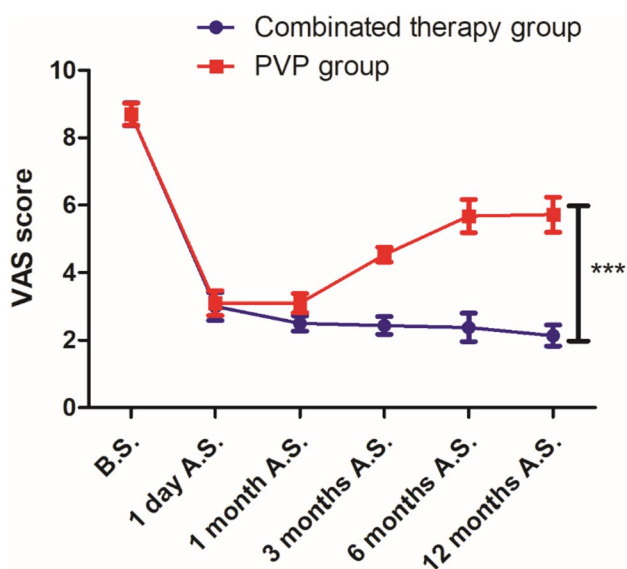
* $P=0.000$, PVP group compared with combination group

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Fig. 2 Pain level trends of different surgical methods

Table 3 Compare KPS score in two groups after treatment ($\bar{x} \pm s$)

Groups	Cases	Before surgery	1 month after surgery
Combined treatment	31	65.3 ± 4.6	87.6 ± 3.9
PVP only treatment	31	67.7 ± 5.9	77.9 ± 4.6
P		> 0.05	< 0.05

survival curves comparing the different surgical modalities are shown in Fig. 4. In the overall comparison, the survival rate of the PVP group was significantly lower than that of the combined treatment group ($P = 0.038$).

Cox regression multivariate analysis

As a multivariate survival analysis model, the Cox regression model can effectively process the final examination data, control various confounding factors, quantitatively analyze the effect strength and direction of the observation indicators, and comprehensively analyze the effect of prognostic factors. To further determine the factors affecting the survival rate of patients with lumbosacral osteoblastic metastases, we analyzed all covariates using the Cox regression equation.

The patient's sex, age, location, preoperative KPS score, spinal segment, primary tumor growth, organ metastasis, and surgical method were included in the multivariate Cox proportional hazards regression model. The variables and their respective values that finally contributed to the effect equation are presented in Table 5.

Cox regression analysis showed that age, primary tumor, and metastatic spinal segment were independent predictors of long-term survival in patients with lumbosacral osteoblastic metastases.

Relative risk (RR value)

For each level of age, the risk of death increased by 3.170 times. Similarly, for each level of the spinal segment, the risk of death increased by 1.909 times, and for each level of primary tumor nature, the risk of death increased by 2.298 times.
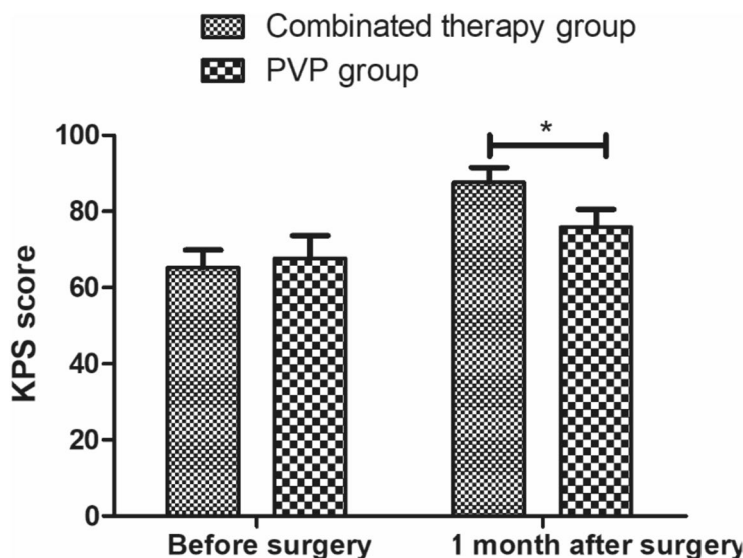

Fig. 3 KPS score changes before and after surgery

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Table 4 Survival time for 62 cases of lumbosacral vertebral osteoblastic metastasis

Groups	n	Survival rate (%)			Median time (months)	95%CI
		6 months	1 year	3 years		
Surgical approach						
Combination therapy group	31	0.839	0.613	0.452	28	-
PVP alone	31	0.839	0.613	0.161	19	9.002~28.998
KPS score before surgery						
60–70	30	0.813	0.656	0.125	14	7.070~20.930
80–100	30	0.867	0.733	0.500	33	14.252~27.748
Primaries						
Slow growth	23	0.957	0.826	0.522	-	-
Moderate growth	19	0.895	0.632	0.316	20	15.653~26.558
Rapid growth	20	0.650	0.500	0.050	12	9.932~18.868
Vertebral segments						
1 segment	17	0.941	0.882	0.588	-	-
2 segments	23	0.826	0.696	0.304	25	18.117~28.231
≥3 segments	22	0.773	0.445	0.091	10	10.986~19.923

The prognostic index (PI) can be calculated according to the prognostic factors determined using the Cox regression model and has important clinical significance. The larger the PI, the worse the prognosis; the smaller the PI, the better the prognosis ($PI = 1.154 \times age + 0.832 \times primary\ tumor + 0.647 \times spinal\ segment$). Typical cases are shown in Figs. 5, 6, and 7.

Discussion

Osteogenic metastatic carcinoma often presents as nodular, spotted, and diffuse multiple lesions on X-ray. Although osteogenic metastasis may manifest as irregular diffusion, the typical osteogenic metastasis is nodular and lacks the sharp shape of bone islands. The treatment methods for spinal lumbosacral osteoblastic metastases include radiotherapy, chemotherapy, surgery, and other comprehensive treatments [23, 36]. Minimally invasive surgery effectively relieves pain, preserves and restores nerve function and spinal stability, and improves quality of life.

Predicting survival and clinical treatment outcomes has always been puzzling for clinicians. Most scholars believe that survival time is related to the malignancy of the tumor, the general condition of the whole body, and metastasis to important organs [37, 38]. Treating osteoblastic metastases requires multidisciplinary cooperation, and the patient's general state, nerve damage, pain, life expectancy, growth rate of the primary tumor, and spinal segment invasion by the tumor must be comprehensively considered before determining the surgical treatment plan and economic conditions [39].

The rational selection of surgical methods is closely related to patient prognosis. However, lumbosacral fusion might narrow the hip joint space and increase the risk of hip osteoarthritis, especially the patients with long-segment lumbosacral fusion [40]. Radiotherapy using ^{125}I seeds implanted between tissues has developed rapidly in recent years and has become a typical example of the best conformal treatment [41, 42]. ^{125}I seed implantation was reported in 239 patients with T1–T2 prostate cancer, and with 5-year and 10-year survival rates of 74% and 66%, respectively [43].

In this study, repeated-measures analysis of variance was used to compare the VAS scores at different time points between the combined treatment and pure PVP surgery groups. The VAS scores for the different surgical methods in the two groups changed over time, and the VAS scores on the 1st day after surgery significantly decreased. The pain of the patients was effectively relieved, while the pain in the simple treatment group was relieved 1 day and 1 month postoperation; however, the pain level gradually increased 3 months after the operation and then remained at a certain level. The pain level in the combined treatment group was significantly lower than that in the PVP group. We conducted a *t*-test on the KPS scores of the combined treatment and pure PVP groups before and 1 month after surgery. The results showed that the KPS scores of the two groups significantly increased 1 month postoperation, indicating that the physical status of all patients improved in the first month after the operation. There was a significant difference between the groups before surgery and 1 month after surgery ($p = 0.000$), and the physical status
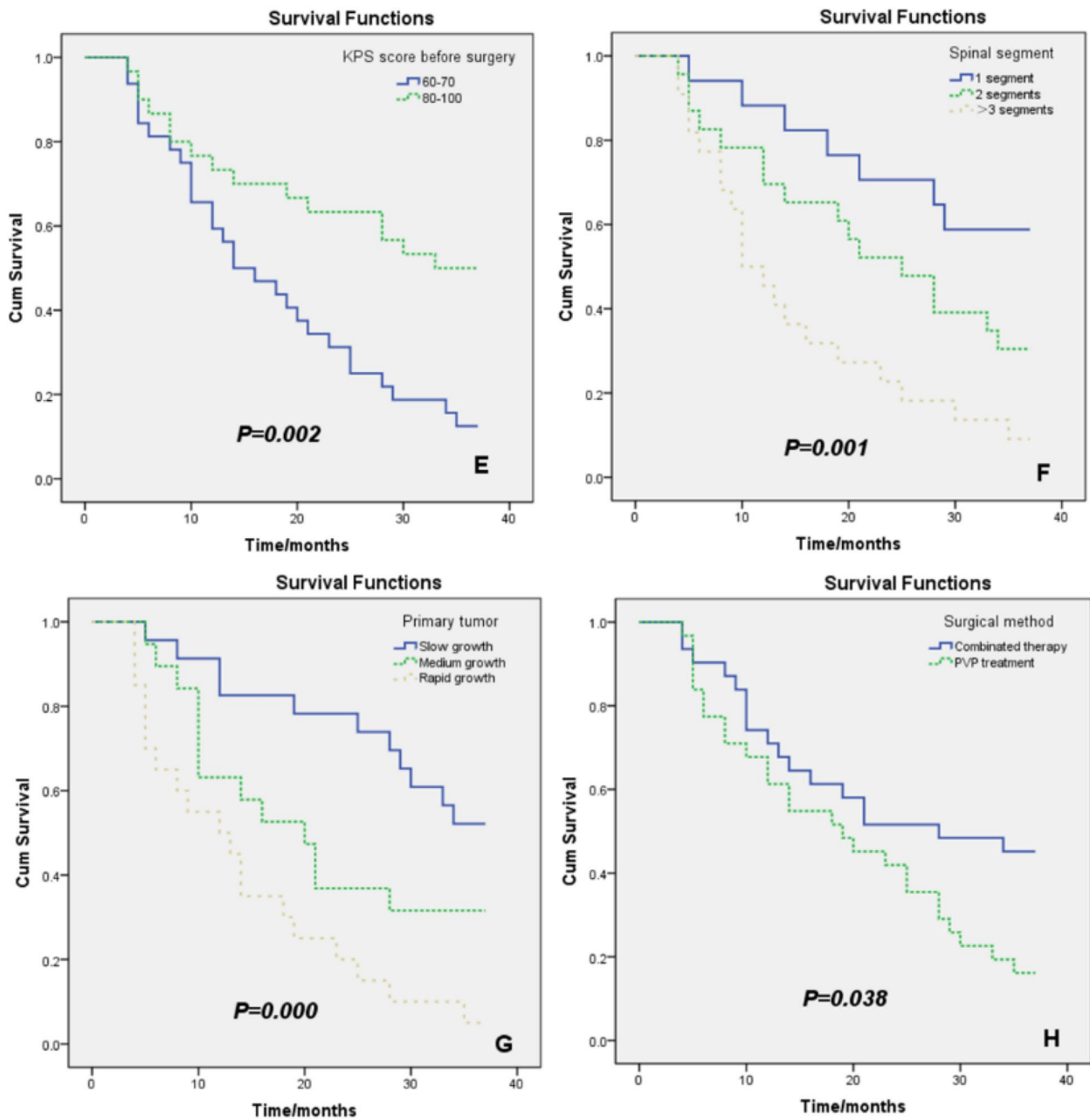
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Fig. 4 Kaplan–Meier analysis and the log-rank test comparing the influence of factors, such as sex, age, tumor metastases, viscera metastasis, KPS score, spine transfer section, and primary tumor growth, surgical approach on patients' survival

Table 5 Sixty-two cases of lumbosacral vertebral osteoblastic metastasis multivariate Cox regression analysis

	B	SE	Wald	Sig	Exp(B)	95.0%CI for Exp(B)
Age	1.154	0.380	9.210	0.002	3.170	1.505 ~ 6.680
Primary tumor	0.832	0.238	12.266	0.000	2.298	1.443 ~ 3.662
Spinal segment	0.647	0.230	7.873	0.005	1.909	1.215 ~ 2.999

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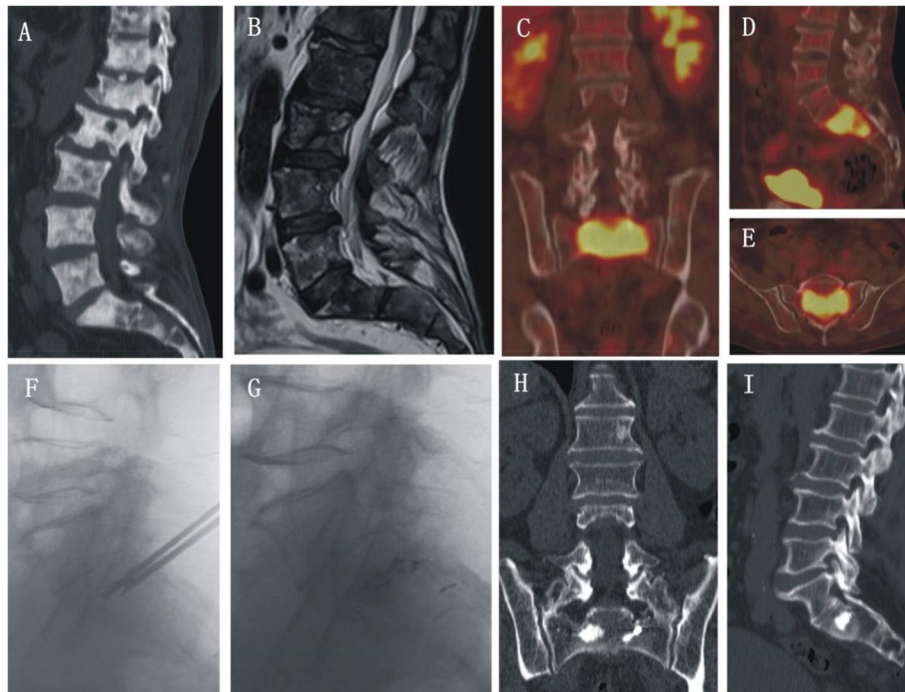
Fig. 5 Male patient, 64 years old, with well-differentiated prostate cancer in February after combined treatment, Back pain 2 weeks preoperative VAS score of 8.7. **A**–**E** Preoperative CT, MRI, and PET-CT show sacral bone destruction and soft tissue mass formation, sacral lesions involving the sacrum, and the corresponding hole. **F**–**G** S2PVP combined with ^{125}I seed implantation. **H**–**I** Postoperative CT showed bone cement and ^{125}I particle distribution in the lesion area, with no leakage of bone cement; Postoperative VAS score, 2.5 points, significant pain relief
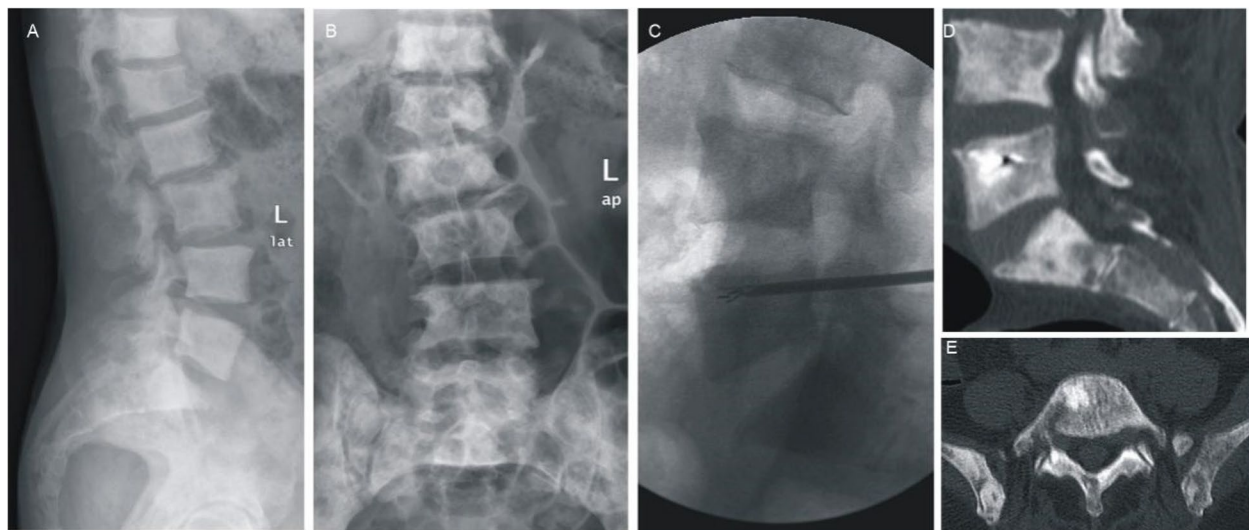
Fig. 6 Male patient, 59 years old, well-differentiated prostate cancer after combined therapy for 1 year, back pain 8 months, preoperative VAS score of 8.5. **A**, **B** Preoperative DR shows multiple bone destruction lumbosacral, and pathological fractures. **C** L5PVP combined with ^{125}I seed implantation. **D**, **E** Postoperative CT showed bone cement and ^{125}I particle distribution in the lesion area, without leakage of bone cement. Postoperative VAS score 2.3 points, significant pain relief

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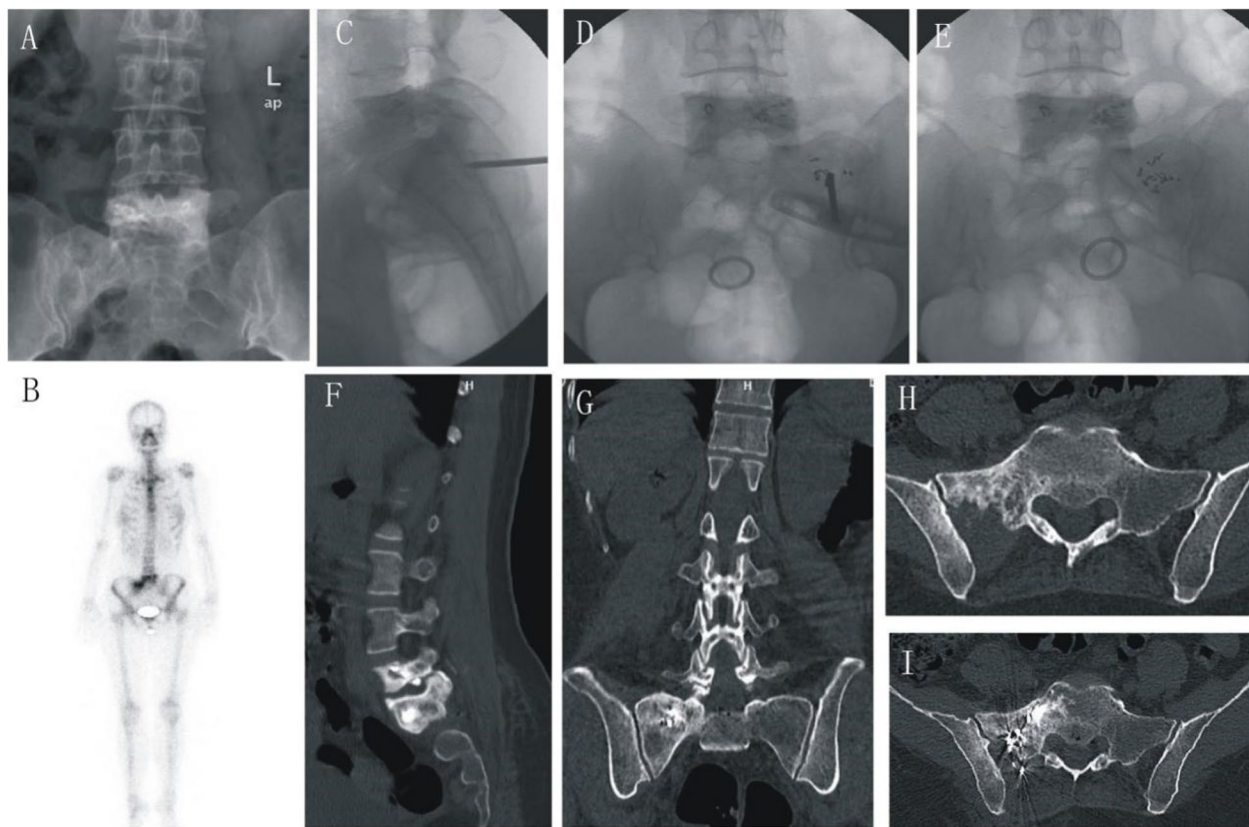
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Fig. 7 Female patients, 4 years after radical resection of the right lung, L5PVP combined with ^{125}I seed 3 years after implantation, Preoperative VAS score 8.7 points. **A** Preoperative DR, CT shows that the right side of the block of S1 vertebrae and the adjacent vertebrae, and right iliac bone increased in inhomogeneity; B: SPECT: To the right sacroiliac joint abnormalities metabolically active, more consideration transferred. **C–E** S1PVP combined with ^{125}I seed implantation. **F–I** Postoperative CT showed bone cement and ^{125}I particle distribution in the lesion area, without leakage of bone cement. Postoperative VAS score 2.7 points, significant pain relief

of patients in the combined treatment group was significantly better than that in the PVP treatment group. Further, univariate statistical analysis revealed that the survival rate of the PVP group was significantly lower than that of the combined treatment group ($P=0.038$). Thus, reasonable selection of the surgical method is closely related to the prognosis of lumbosacral vertebral metastases.

This study showed that the higher the KPS score, the longer the median survival of the patients at 14 and 20 months, respectively, and the difference in survival rate was statistically significant ($P=0.020$). Therefore, KPS is an important indicator for determining the prognosis of patients with spinal lumbosacral bone metastasis. In recent studies, the KPS has been used as an important prognostic factor in the preoperative scoring system for spinal metastases [44, 45], which is consistent with the results of this study. Thus, the preoperative KPS can be used as an important reference indicator for treating lumbosacral osteoblastic metastasis.

Percutaneous bone cement puncture osteoplasty is a minimally invasive surgical technique that enhances the local stability of the bone by injecting bone cement into the damaged area. It is used to treat bone metastases and effectively improves the quality of life of patients after surgery. The injection volume of bone cement is generally 2–9 mL, with an average of 4.5 mL for the thoracic spine and 6.0 mL for the lumbar spine. After the completion of bone cement injection, a waiting period of 15–20 min is observed to allow the polymerization reaction to complete, and then radiography and CT scans were performed for re-examination. There is no interaction between the bone cement and the radioactive iodine ions. ^{125}I seed implantation has attracted widespread attention as an effective technique for interstitial brachytherapy. It involves the implantation of radioactive particles with fixed specifications and activity in the vicinity of the tumor tissue through minimally invasive methods, providing low-dose and long-term irradiation to the tumor tissue, which can improve local control and survival

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rates. Generally, 12–20 ^{125}I particles are implanted, with an average of 16.5 particles.

In tumor epidemiological studies, researchers usually focus on comparing different therapies and identifying factors with independent prognostic value. However, little research has been conducted on patient prognostic categories and their use in choosing the best treatment strategy. A prognostic index (PI) with sufficient prognostic power can help clinicians make scientific and reasonable treatment plans for patients with tumors and largely predict long-term patient survival.

In this study, Cox multivariate regression analysis results further showed that patient age, primary tumor growth, and metastatic spinal segment were independent factors influencing the long-term survival of patients with lumbosacral osteoblastic metastases. We established a risk function equation, and in clinical practice, the PI can be calculated using the model of this study to assess prognosis. In future clinical trials, the rational grouping of patients based on individual prognostic indices may be possible. Additionally, our comparison of PVP alone and PVP combined with ^{125}I seed implantation for treating patients with lumbosacral osteoblastic metastases showed that the treatment effect of PVP combined with ^{125}I seed implantation was better than that of PVP alone. Univariate and Cox multivariate regression analyses confirmed that the preoperative KPS score, segment of spinal metastases, and growth rate of the primary tumor were closely related to the survival rate of patients with lumbosacral osteoblastic metastases. However, the treatment strategy for lumbosacral osteoblastic metastases requires comprehensive multidisciplinary treatment. Based on the patient's condition, an individualized treatment plan should be formulated, incorporating the current prognostic evaluation system and comprehensive evaluation, to develop a practical and effective treatment plan. However, the reliability and accuracy of the results of this study require a large number of case summaries, scientific statistics, and large-scale prospective randomized controlled studies.

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Authors' contributions
Lei Xu and Xin Huang performed the surgical operation. Yan Lou and Wei Xie performed the postoperative follow-up. Jun He and Zuozhang Yang performed statistical analysis. Yihao Yang and Ya Zhang collected the clinical data and performed the preoperative preparation.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

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References
1. Popovic M, Lemke M, Zeng L, Chen E, Nguyen J, Thavarajah N, et al. Comparing prognostic factors in patients with spinal metastases: a literature review. Expert Rev Pharmacoecon Outcomes Res. 2012;12(3):345–56.
2. Linzey JR, Kathawate VG, Strong MJ, Roche K, Goethe PE, Tudrick LR, et al. Patients with progression of spinal metastases who present to the clinic have better outcomes compared to those who present to the emergency department. Cancer Med. 2023;12:20177–87.
3. Zhang X, Jiang P, Wang C. The role of prostate-specific antigen in the osteoblastic bone metastasis of prostate cancer: a literature review. Front Oncol. 2023;13:1127637.
4. Quiroz-Munoz M, Izadmehr S, Arumugam D, Wong B, Kirschenbaum A, Levine AC. Mechanisms of osteoblastic bone metastasis in prostate cancer: role of prostatic acid phosphatase. J Endocr Soc. 2019;3(3):655–64.
5. Lin SC, Lee YC, Yu G, Cheng CJ, Zhou X, Chu K, et al. Endothelial-to-osteoblast conversion generates osteoblastic metastasis of prostate cancer. Dev Cell. 2017;41(5):467–80 e3.
6. Kirschenbaum A, Izadmehr S, Yao S, O'Connor-Chapman KL, Huang A, Gregoriades EM, et al. Prostatic Acid Phosphatase Alters the RANKL/OPG System and Induces Osteoblastic Prostate Cancer Bone Metastases. Endocrinology. 2016;157(12):4526–33.
7. Okazaki J, Muguruma N, Kitamura S, Kimura T, Okamoto K, Miyamoto H, et al. Paraneoplastic hypocalcemia developed in gastric cancer accompanied by osteoblastic metastasis. Intern Med. 2017;56(11):1345–9.
8. Soylu AI, Odabasi E, Gun S, Selcuk MB. Gastric signet ring cell carcinoma presenting with widespread osteoblastic metastasis. J Cancer Res Ther. 2020;16(Supplement):S237–9.
9. Ogasawara T, Tanaka T, Shindo T, Hashimoto K, Fukuta F, Kobayashi K, et al. Two cases of osteoblastic bone metastasis from muscle-invasive bladder cancer with discrepancy in response to chemotherapy: problems and limitations of bone biopsy. Int Cancer Conf J. 2020;9(4):235–9.
10. Zeng W, Swee DS. Severe and refractory hypocalcaemia secondary to osteoblastic bone metastases in bladder signet ring carcinoma: A case report and literature review. Medicine (Baltimore). 2022;101(26):e29731.
11. Garfield D, Cadranel J, Normanno N. Osteoblastic metastases in non-small cell lung cancer and its possible significance. Lung Cancer. 2008;60(1):146–7.
12. Takahara Y, Nakase K, Nojiri M, Kato R, Shinomiya S, Oikawa T, et al. Relationship between clinical features and gene mutations in non-small cell lung cancer with osteoblastic bone metastasis. Cancer Treat Res Commun. 2021;28: 100440.

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13. Haider MT, Holen I, Dear TN, Hunter K, Brown HK. Modifying the osteo-blastic niche with zoledronic acid in vivo-potential implications for breast cancer bone metastasis. Bone. 2014;66(100):240–50.

14. Al-Muqbel KM, Yaghan RJ, Al-Omari MH, Rousan LA, Dagher NM, Al BS. Clinical relevance of 18F-FDG-negative osteoblastic metastatic bone lesions noted on PET/CT in breast cancer patients. Nucl Med Commun. 2016;37(6):593–601.

15. Wu Q, Tian P, He D, Jia Z, He Y, Luo W, et al. SCUBE2 mediates bone metastasis of luminal breast cancer by modulating immune-suppressive osteoblastic niches. Cell Res. 2023;33(6):464–78.

16. Tarawneh AM, Pasku D, Quraishi NA. Surgical complications and re-operation rates in spinal metastases surgery: a systematic review. Eur Spine J. 2021;30(10):2791–9.

17. Smeijers S, Depreitere B. Prognostic scores for survival as decisional support for surgery in spinal metastases: a performance assessment systematic review. Eur Spine J. 2021;30(10):2800–24.

18. Madhavan AA, Eckel LJ, Carr CM, Diehn FE, Lehman VT. Subdural spinal metastases detected on CT myelography: A case report and brief review. Radiol Case Rep. 2021;16(6):1499–503.

19. Koeneman KS, Yeung F, Chung LW. Osteomimetic properties of prostate cancer cells: a hypothesis supporting the predilection of prostate cancer metastasis and growth in the bone environment. Prostate. 1999;39(4):246–61.

20. Antognelli C, Marinucci L, Frosini R, Macchioni L, Talesa VN. Metastatic prostate cancer cells secrete methylglyoxal-derived MG-H1 to reprogram human osteoblasts into a dedifferentiated, malignant-like phenotype: a possible novel player in prostate cancer bone metastasis. Int J Mol Sci. 2021;22(19):10191.

21. Xu S, Liu T, Zhang X, Liu H, Zhao Z, Xu L, et al. Efficacy of percutaneous vertebroplasty for the relief of osteoblastic spinal metastasis pain. Exp Ther Med. 2021;22(1):727.

22. Gravel G, Roussel A, Guth A, Mellot F. Cement leakage during vertebro-plasty: comparison between intact and wall disruption in spinal metasta-ses. Acta Radiol. 2023;64(5):1912–8.

23. Wang L, Zhang C, Liang H, Huang T, Zhong W, Zhao Z, et al. Cement leakage in percutaneous vertebroplasty for spinal metastases: a retro-spective study of risk factors and clinical outcomes. World J Surg Oncol. 2022;20(1):112.

24. Chen L, Ni RF, Liu SY, Liu YZ, Jin YH, Zhu XL, et al. Percutaneous vertebro-plasty as a treatment for painful osteoblastic metastatic spinal lesions. J Vasc Interv Radiol. 2011;22(4):525–8.

25. Saad F, Clarke N, Colombel M. Natural history and treatment of bone complications in prostate cancer. Eur Urol. 2006;49(3):429–40.

26. Amoretti N. Early percutaneous vertebroplasty helps motorsport profes-sionals to resume competition soon after vertebral fracture. Eur Radiol. 2018;28(7):2870–1.

27. Xie L, Chen Y, Zhang Y, Yang Z, Zhang Z, Shen L, et al. Status and pros-pects of percutaneous vertebroplasty combined with (1)(2)(5)I seed implantation for the treatment of spinal metastases. World J Surg Oncol. 2015;13:119.

28. Wu W, Zhang X, Li X, Liu H, Xu L, Liu T, et al. Comparison of the clinical outcomes of percutaneous kyphoplasty for the management of osteo-lytic and osteoblastic-related metastatic vertebral lesions. J Neurointerv Surg. 2022;14(9):938–41.

29. Liu K, Zhang Y, Wang Q, Chen Y, Qin S, Xin P, et al. Differentiation of predominantly osteolytic from osteoblastic spinal metastases based on standard magnetic resonance imaging sequences: a comparison of radi-omics model versus semantic features logistic regression model findings. Quant Imaging Med Surg. 2022;12(11):5004–17.

30. Ando M, Sumitani M, Fuyuki M, Abe H, Shinoda Y, Matsubayashi Y, et al. Imaging features inferring symptom onset due to spinal metastasis progression: a preliminary study. Ann Palliat Med. 2022;11(7):2247–56.

31. Liu X, Yang Z, Xie L, Yuan Z, Ren M, Han L. Advances in the clinical research of the minimally invasive treatment for the posterior edge of vertebral-body defects by spinal metastases. Biomed Rep. 2015;3(5):621–5.

32. Armstrong JG, Fass DE, Bains M, Mychalczak B, Nori D, Arbit E, et al. Paraspinal tumors: techniques and results of brachytherapy. Int J Radiat Oncol Biol Phys. 1991;20(4):787–90.

33. Yang L, Li C, Wang Z, Wu J, Zhou J, Wang R. The clinical efficacy of com-puted tomography-guided (125)I particle implantation combined with

arterial infusion chemotherapy in the treatment of pancreatic cancer. J Cancer Res Ther. 2021;17(3):720–5.

34. Sekiguchi Y, Benjamin CL, Lee EC, Struder JF, Manning CN, Morrissey MC, et al. Effects of heat acclimation following heat acclimatization on whole body heat exchange in trained endurance athletes. Int J Environ Res Public Health. 2022;19(11):6412.

35. Marini C, Morbelli S, Cistaro A, Campi C, Caponnetto C, Bauckneht M, et al. Interplay between spinal cord and cerebral cortex metabolism in amyotrophic lateral sclerosis. Brain. 2018;141(8):2272–9.

36. Rosenberg JE, O'Donnell PH, Balar AV, McGregor BA, Heath EI, Yu EY, et al. Pivotal trial of enfortumab vedotin in urothelial carcinoma after platinum and anti-programmed death 1/programmed death ligand 1 therapy. J Clin Oncol. 2019;37(29):2592–600.

37. Kowalchuk RO, Mullikin TC, Kim DK, Morris JM, Ebner DK, Harmsen WS, et al. Cost-effectiveness of treatment strategies for spinal metastases. Pract Radiat Oncol. 2022;12(3):236–44.

38. Zanaty A, George KJ. Outcomes and efficiency of managing patients admitted for surgery for spinal metastases. Surg Neurol Int. 2022;13:312.

39. Thirunavu VM, Roumeliotis A, Shlobin NA, Kandula V, Shah P, Larkin C, et al. The role of preoperative embolization in the treatment of spinal metastases from renal cell carcinoma. Clin Neurol Neurosurg. 2022;215: 107181.

40. Ulusoy I, Kivrak A. Lumbosacral fusion increases the risk of hip osteoarthri-tis. J Orthop Surg Res. 2023;18(1):452.

41. Mendoza Arnau I, Sanchez Sanchez R, Culianez Casas M, Rebollo Aguirre AC, Gonzalez Jimenez AD, Martinez Meca S. Surgical clips vs. iodine-125 (125I) seeds for marking the location of nonpalpable malignant breast lesions: preliminary results. Radiologia (Engl Ed). 2020;62(1):38–45.

42. Zhou X, Zhang W, Dou M, Li Z, Liu Z, Li J, et al. (125)I seeds inhibit prolif-eration and promote apoptosis in cholangiocarcinoma cells by regulat-ing the AGR2-mediated p38 MAPK pathway. Cancer Lett. 2022;524:29–41.

43. Huang ZM, Pan CC, Wu PH, Zhao M, Li W, Huang ZL, et al. Efficacy of minimally invasive therapies on unresectable pancreatic cancer. Chin J Cancer. 2013;32(6):334–41.

44. Tokuhashi Y, Ajiro Y, Umezawa N. Outcome of treatment for spinal metas-tases using scoring system for preoperative evaluation of prognosis. Spine (Phila Pa 1976). 2009;34(1):69–73.

45. Yang L, Wang F, Zhang H, Yang XG, Zhang HR, Li JK, et al. Patient charac-teristics following surgery for spinal metastases: a multicenter retrospec-tive study. Orthop Surg. 2019;11(6):1039–47.

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