© 2019 The Authors. Orthopaedic Surgery published by Chinese Orthopaedic Association and John Wiley & Sons Australia, Ltd.

CLINICAL ARTICLE

Patient Characteristics Following Surgery for Spinal Metastases: A Multicenter Retrospective Study

Li Yang, MD^{1,2†}, Feng Wang, MD^{2†}, Hao Zhang, MD², Xiong-gang Yang, MD², Hao-ran Zhang, MD², Ji-kai Li, MD², Rui-qi Qiao, MD², Guo-chuan Zhang, MD, PhD³, Yong-cheng Hu, MD, PhD¹

¹Department of Bone Tumor, Tianjin Hospital and ²Graduate School, Tianjin Medical University, Tianjin and ³Department of Musculoskeletal Tumor, Third Hospital of Hebei Medical University, Hebei, China

Objectives: To summarize the epidemiological characteristics of patients following surgery for spinal metastases retrospectively and make a univariate analysis to identify independent variables that could affect the operation decision making.

Methods: This was a multicenter retrospective review of patients with spinal metastasis who were treated with surgery from 1 January 2007 to 31 July 2019. Basic clinical data were analyzed retrospectively by univariate analysis to identify independent variables that could affect the decision of operation modalities, including gender, age, spinal metastatic site, Frankel score, Karnofsky performance score (KPS), spinal instability neoplastic score (SINS), visual analogue scale (VAS), Tokuhashi score, urinary and fecal incontinence, spinal pathological fracture, primary tumor, extraspinal metastasis, visceral metastasis, si, and bone lesion (osteolytic, osteoblastic or mixed).

Results: A total of 580 patients including 332 males and 248 females were enrolled in the study with an average age of 58.26 years old (range, 13–86 years old). The most common spinal metastatic level was the thoracic vertebra (190 [32.76%]), followed by the lumbar vertebra (146 [25.17%]), cervical vertebra (47 [8.10%]), and sacral vertebra (35 [6.03%]). Metastases involving more than two sites of the cervical, thoracic, lumbar, and sacral vertebrae arose in 162 (27.93%) patients. For primary tumor, there were 198 (34.14%) cases of lung cancer, 41 (7.07%) cases of kidney cancer, 39 (6.72%) cases of breast cancer, 38 (6.55%) cases of gastrointestinal cancer, 35 (6.03%) cases of lymphoma and myeloma, 25 (4.31%) cases of prostate cancer, 24 (4.14%) cases of liver cancer, 23 (3.97%) cases of mesenchymal tissue sarcoma, 20 (3.45%) cases of thyroid cancer, and 84 (14.48%) cases were tumor with unknown origin. Sixty-three (10.86%) patients received minimally invasive surgery, 460 (79.31%) patients received palliative surgery, and the remaining 57 (9.83%) received tumor resection. According to the univariate analysis, the KPS score, SINS score, VAS score, Tokuhashi score, urinary and fecal incontinence, spinal pathological fracture, and bone lesion (osteolytic, osteoblastic or mixed) were independent and favorable factors affecting the surgery modalities.

Conclusions: Surgical treatment for spinal metastases was mainly to relieve pain, rebuild spinal stability, improve nerve function, control local tumors, and improve the quality of life of patients. For middle-aged and elderly patients with good general conditions, severe pain, spinal pathological fracture, spine instability and without urinary and fecal incontinence, early surgical treatment should be actively carried out.

Key words: Epidemiological study characteristics; Spinal metastases; Surgical treatment; Univariate analysis

Address for correspondence Guo-chuan Zhang MD, PhD, Department of Musculoskeletal Tumor, Third Hospital of Hebei Medical University, Hebei, China Email:anewing@sohu.com Yong-cheng Hu, MD, PHD; Department of Bone Tumor, Tianjin Hospital; No. 406, Jiefang Southern Road, Hexi District, Tianjin, China 300211 Tel: 008613920006965; Fax: 0086-22-28241184; Email: yongchenghu@126.com

Disclosure: This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration: All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

[†]These authors contributed to the work equally and should be regarded as co-first authors.

Received 9 September 2019; accepted 10 September 2019

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Orthopaedic Surgery Volume 11 • Number 6 • December, 2019 PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

Introduction

S pinal metastases are the most common type of bone metastases with a prevalence of 30%-70% in cancer patients and 5%-10% metastases may be associated with epidural spinal cord compression (ESCC) leading to impaired mobility, neurologic deficits, and decreased quality of life¹⁻⁴.

In order to relieve pain, improve nerve function, control local tumors, and improve quality of life for patients, surgery is more and more widely performed, including minimally invasive surgery, palliative surgery, or radical surgery. In turn, the majority of studies report a significant clinical effect for carefully selected spinal metastatic patients⁵⁻⁷. Flavio Tancioni et al.⁸ reported 25 consecutive patients with a diagnosis of ESCC from solid primary tumors. These patients were treated with minimally invasive surgery, with 96% clinical remission of pain and 88% improvement of neurological deficit after 2 weeks. Masuda et al.⁹ assessed the surgical outcomes of 44 patients treated with posterior decompression and stabilization and reported that the Frankel score and Eastern Cooperative Oncology Group performance status (ECOG-PS) improved in all patients after surgery. Boriani et al.¹⁰ also applied total en-bloc spondylectomy for 165 patients, and reported that all patients had neurologic deficits improvement and the local recurrences recorded were just 15.28% after 25 years.

However, there still remains some problems when treating spinal metastasis with surgery. Complications must be considered after surgery, such as intra-operation bleeding, spinal cord injury, and hematoma^{11,12}. Furthermore, the purposes for spinal metastasis treatment are usually different from visceral metastases, which makes the treatment concept, preoperative evaluation, and treatment strategy of spinal metastasis become irregular and arbitrary^{13,14}. At the same time as the rapid development of immuno-therapy, endocrine therapy, radiotherapy, and chemotherapy (especially targeted therapy), a multidisciplinary combined therapy of spinal metastasis has become a trend^{15–17}. Therefore, indications and contraindications for spinal metastasis surgery treatment should be clearly understood.

Accordingly, a multicenter retrospective study was performed with the aim of: (i) summarizing the epidemiological characteristics of patients following surgery for spinal metastases; (ii) making a subgroup analysis to identify independent and favorable factors which could affect the surgery selection; and (iii) helping clinicians make a more appropriate surgery decision for patients with spinal metastasis.

Patients and Methods

Participants

This was a multicenter retrospective review of patients with spinal metastasis who were treated with surgery from 1 January 2007 to 31 July 2019. All patients met the following inclusion criteria: (i) patients diagnosed with spinal metastasis precisely by clinical imaging examination (CT, MRI, ECT or PET-CT) or pathological examination; (ii) patients with hematological malignancy spinal metastasis, including lymphoma and myeloma; (iii) patients who were treated by surgical intervention; and (iv) patients whose observation indicators below could be retrospectively analyzed.

Exclusion criteria for this review were: (i) patients with impaired spinal cord function due to other diseases, such as primary spinal tumors, spinal tuberculosis, or spinal degenerative diseases; (ii) outpatients; (iii) patients with another spinal surgery aside from the metastatic tumor; and (iv) patients undergoing biopsies as the only surgical intervention.

Operation Category

Operations applied for patients were mainly divided into minimally invasive surgery and aggressive surgery based on the operation invasiveness.

Minimally invasive surgery was defined as techniques which had lower associated soft tissue damage and shorter hospital lengths of stay, including percutaneous vertebroplasty (PVP) or percutaneous kyphoplasty (PKP).

For aggressive surgery, palliative surgery was applied for the purpose of improving impaired mobility, neurologic function, and quality of life, but the tumor was not resected completely. Posterior laminectomy decompression and subtotal corpectomy (combing with vertebroplasty and microwave ablation or not) were included.

For the purpose of removing the tumor completely, radical surgery was performed for patients, including total or piecemeal vertebrectomy, piecemeal or total en-bloc spondylectomy.

Observation Indicators

Indicators were collected including gender, age, primary malignancy type, spinal metastatic level, spinal pathological fracture, urinary and fecal incontinence, extraspinal metastasis, visceral metastasis, bone lesion, Frankel score, Karnofsky performance score (KPS), visual analogue scale (VAS), spinal instability neoplastic score (SINS), and Tokuhashi score.

Primary malignancy type was defined as the origin of spinal metastatic tumor, such as lung cancer, breast cancer, and kidney cancer, among others.

Spinal metastatic level was defined as the location where the metastatic tumor existed. Based on the anatomical structure of the spine, it was divided into the cervical vertebra, thoracic vertebra, lumbar vertebra, sacral vertebra, and trans-segmental metastasis.

Spinal pathological fracture was defined as vertebral body or appendix fractured due to the tumors based on examinations with X-rays, CT, or MRI.

Extraspinal metastasis was defined as patients with bone metastasis other than that occurring in the spine (such as rib, femur, tibia, fibula).

Bone lesion was identified based on the function of osteoblasts and osteoclasts, including osteolytic, osteoblastic, and mixed, through examinations with X-rays or CT.

Frankel score classification provided an assessment of spinal cord function, which was divided into five grades of A, B, C, D, and E based on the degree of spinal cord injury. Grade A meant complete neurological injury with no motor and

PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

sensory function, Grade B meant preserved sensation only, Grade C meant preserved nonfunctional motor, Grade D meant preserved functional motor, and Grade E meant normal motor and sensory function¹⁸.

KPS score was used to assess the functional status of patients. From 0 to 100, patients with no symptoms were scored at 100, patients who died were scored at 0. Generally speaking, KPS score above 80 was considered to be self-care level, 50–70 was considered into half self-care level, and 50 was considered patients needing help from others¹⁹.

VAS score was a measure of pain intensity and it was a continuous scale comprised of a horizontal (called horizontal visual analog scale) or vertical (called vertical visual analog scale) scale. For pain intensity, the scores could be from 0-10, which was determined by measuring the distance (mm) on the 10 cm line between the "no pain" anchor and the patient's mark²⁰.

SINS score was applied for assessing the spinal instability. It contained the lesion location, mechanical pain, bone lesion, radiographic spinal alignment, vertebral body collapse, and posterolateral involvement. The total score was 18 (1–6 meant stable, 7–12 meant potentially stable, and 13– 18 meant unstable)²¹. Tokuhashi score was a prognostic evaluation of patients which was based on KPS score, numbers of extraspinal metastasis, numbers of vertebra bodies, visceral metastasis, primary malignancy type, and spinal cord palsy. The score was from zero to 15, usually divided into 0–8 with overall survival less than 6 months, 9–11 with overall survival between 6 and 12 months, and 12–15 with overall survival more than 12 months²².

Statistical Analysis

Measurement data (age, intra-operation bleeding, and operation time) were expressed as their mean, with the minimum and maximum values compared with the *t*-test. Counting data (gender, primary tumor, and neurological assessment etc.) were compared using the χ 2-test. All statistical analyses were performed using IBM SPSS Statistics 22.0, and a two-tailed *P* < 0.05 was considered significant difference statistically.

Results

Cohort Characteristics

As shown in Table 1, a total of 332 male and 248 female patients were enrolled in the study with an average age of 58.26 years old (range, 13–86 years old), an average intra-operation bleeding of 1334.98 mL (range, 5–9000 mL), and an average operation time of 216.31 min (range, 60–680 min).

The most common spinal metastatic level was the thoracic vertebra (190 [32.76%]), followed by the lumbar vertebra (146 [25.17%]), cervical vertebra (47 [8.10%]), and sacral vertebra (35 [6.03%]). Metastases involving more than two sites of the cervical, thoracic, lumbar, and sacral vertebrae arose in 162(27.93%) patients. Among these patients, only one single segment metastasis was presented in 270 (46.55%) patients and two or more segment metastases were presented in 310 (53.45%) patients (Fig. 1).

For primary tumors, there were 198 (34.14%) cases of lung cancer, 41 (7.07%) cases of kidney cancer, 39 (6.72%) cases of breast cancer, 38 (6.55%) cases of gastrointestinal cancer, 35 (6.03%) cases of lymphoma and myeloma, 25 (4.31%) cases of prostate cancer, 24 (4.14%) cases of liver cancer, 23 (3.97%) cases of mesenchymal tissue sarcoma, 20 (3.45%) cases of thyroid cancer, and 84 (14.48%) cases were with unknown origin of tumor (Fig. 2).

Four hundred and seventy one (81.21%) patients presented unbearable pain with an average VAS score of 7.12 (range, 0–9). As for neurological impairment, 90 (15.52%) patients presented paralysis including Frankel A in 27 patients, Frankel B in 13 and Frankel C in 50 patients. Furthermore, 485 (83.62%) patients presented spinal instability and the average SINS score of 8.02 (range, 7–18). More details were presented in Fig. 3.

Operation Category and Univariate Analysis

In this cohort study, 63 (10.86%) patients received minimally invasive surgery (including 58 PVP and five PKP). Four hundred and sixty (79.31%) patients received palliative surgery (including 290 posterior laminectomy, 155 subtotal corpectomy, 15 subtotal corpectomy combined with microwave ablation and vertebroplasty) and 57 (9.83%) patients received radical surgery (including 36 total vertebrectomy and 21 total en-bloc spondylectomy). The results of univariate analysis were shown in Table 2, with KPS score, SINS score, VAS score, Tokuhashi score, urinary and fecal incontinence, spinal pathological fracture, and bone lesion (osteolytic, osteoblastic or mixed) being independent and favorable factors affecting the surgery treatment.

KPS Score

The KPS score was divided into three groups (10-40, 50-70, 80-100) (P = 0.017). For group 10–40, no patients received minimally invasive surgery, 30 (5.17%) patients received palliative surgery, and three (0.52%) patients received radical surgery. For group 50–70, 21 (3.62%) patients received minimally invasive surgery, 209 (36.03%) patients received palliative surgery, and 34 (5.86%) patients received radical surgery. For group 80–100, 42 (7.24%) patients received minimally invasive surgery, 221 (38.10%) patients received palliative surgery, and 20 (3.45%) patients received radical surgery.

SINS Score

Three groups (1-6, 7-12, 13-18) (P < 0.001) were included for the SINS score. For group 1–6, eight (1.38%) patients received minimally invasive surgery, 84 (14.48%) patients received palliative surgery and three (0.52%) patients received radical surgery.

1042

Orthopaedic Surgery Volume 11 • Number 6 • December, 2019 PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

	Lung	Kidney	Breast	Prostate	Thyroid	Liver	Colorectal	Gastric	Myeloma and	Mes	enchymal
	cancer	cancer	cancer	cancer	cancer	cancer	cancer	cancer	lymphoma	tissue	e sarcoma
Gender											
Male	120	35	0	25	5	20	10	15	19		9
Female	78	6	39	0	15	4	11	2	16		14
Age (year)											
≤44	24	3	10	0	0	2	1	1	2		8
45-59	79	13	18	4	10	9	11	6	11		6
60–74	89	21	10	15	8	13	8	8	22		9
75–89	6	4	1	6	2	0	1	2	0		0
pinal metastatic site	0	4	Ŧ	0	2	0	1	2	0		0
Cervical vertebra											
		-	0	0	4	4	0	0	0		4
Single segment	14	5	0	2	1	4	0	0	0		1
Multiple segment	5	0	2	0	1	1	0	0	0		0
Thoracic vertebra											
Single segment	30	9	9	4	3	3	5	5	8		5
Multiple segment	25	8	7	7	4	4	3	3	5		5
Lumbar vertebra											
Single segment	39	6	5	2	6	3	6	2	9		6
Multiple segment	16	2	2	1	0	1	1	0	5		2
Sacral vertebra	8	1	0	3	1	3	3	1	0		3
Trans-segmental	61	10	14	6	4	5	3	6	8		1
metastasis	~1			-	,	~	-	5	5		-
xtraspinal metastasis											
Yes	96	17	14	14	8	9	7	7	14		6
No	102	24	25	11	12	15	14	10	21		17
isceral metastasis			-		_	_		-	_		_
Yes	31	6	3	2	5	6	9	2	0		5
No	167	35	36	23	15	18	12	15	35		18
pinal pathological fract	ure										
Yes	69	15	21	9	6	8	8	5	20		9
No	129	26	18	16	14	16	13	12	15		14
Sone lesion											
Osteolytic	67	15	11	8	5	7	4	8	24		9
Osteoblastic	5	0	0	1	0	0	0	0	0		0
Mixed	1	0	0	1	0	0	0	0	0		1
Unknown	125	26	28	15	15	17	17	9	11		13
	-										
		Unknown origin	Rep	roductive syst tumors	em	Esophageal cancer		dder Icer	Pancreas cancer	Others	Totally (n)
							,				
lender		10		6		_			-	~	
Male		48		2		7		3	5	9	332
Female		36		10		2	3	3	0	12	248
ge (year)											
≤44		8		2		0		L	1	7	70
45–59		27		7		2	2	2	2	10	217
60–74		38		3		7	3	3	2	3	259
75–89		11		0		0)	0	1	34
pinal metastatic site											
Cervical vertebra											
Single segment		4		0		1	()	0	1	33
Multiple segment		4		0		0)	0	0	33 14
		2		0		0	(,	0	0	14
Thoracic vertebra		-		0		2			2	~	~~
Single segment		7		2		3		L	3	2	99
		14		0		1	-	L	1	6	91
Multiple segment											
Lumbar vertebra		16		3		1		2	0	5	111
Lumbar vertebra Single segment						0	()	0	0	35
Lumbar vertebra		7		0		0	,		0		
Lumbar vertebra Single segment				0 2		0		L	0	3	35
Lumbar vertebra Single segment Multiple segment		7					2	L			
Lumbar vertebra Single segment Multiple segment Sacral vertebra		7 8		2		0	2		0	3	35
Lumbar vertebra Single segment Multiple segment Sacral vertebra Trans-segmental metastasis		7 8		2		0	2		0	3	35
Lumbar vertebra Single segment Multiple segment Sacral vertebra Trans-segmental metastasis xtraspinal metastasis		7 8 26		2 5		0 3	-	L	0 1	3 4	35 162
Lumbar vertebra Single segment Multiple segment Sacral vertebra Trans-segmental metastasis Xtraspinal metastasis Yes		7 8 26 32		2 5 3		0 3 2		L 2	0 1 0	3 4 5	35 162 237
Lumbar vertebra Single segment Multiple segment Sacral vertebra Trans-segmental metastasis Extraspinal metastasis Yes No		7 8 26		2 5		0 3		L	0 1	3 4	35 162
Lumbar vertebra Single segment Multiple segment Sacral vertebra Trans-segmental metastasis Xtraspinal metastasis Yes		7 8 26 32		2 5 3		0 3 2		L 2	0 1 0	3 4 5	35 162 237

1043

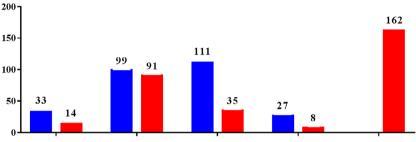
Orthopaedic Surgery Volume 11 • Number 6 • December, 2019 PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

	Unknown	Reproductive system	Esophageal	Bladder	Pancreas		Totally
	origin	tumors	cancer	cancer	cancer	Others	(n)
Spinal pathological fracture							
Yes	29	3	3	2	2	3	212
No	55	9	6	4	3	18	368
Bone lesion							
Osteolytic	23	3	4	3	2	2	195
Osteoblastic	2	0	0	0	0	0	8
Mixed	0	0	0	0	0	0	3
Unknown	59	9	5	3	3	19	374

Fig. 1 Spinal metastatic level among the 580 patients. The most common spinal metastatic site was the thoracic vertebra (190 [32.76%]), followed by the lumbar vertebra (146 [25.17%]), cervical vertebra (47 [8.10%]), sacral vertebra (35 [6.03%]) and trans-segmental metastasis (162 [27.93%]). Only one single segment metastasis was presented in 247 (42.59%) and two or more segment metastasis was in 333 (57.41%).

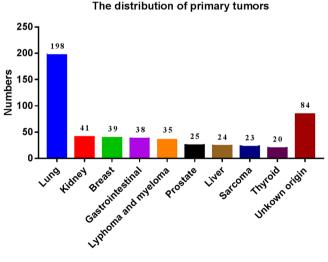
Single segment (one segment)

Multiple segment (two or more segment)



Cervical vertebra Thoracic vertebra Lumbar vertebra Sacral vertebra Trans-segmental

For group 7–12, 42 (7.24%) patients received minimally invasive surgery, 327 (56.38%) patients received palliative surgery, and 24 (4.14%) patients received radical surgery. For group 13–18, 13 (2.24%) patients received minimally invasive surgery,



13 (2.24%) patients received radical surgery, 10 group 13–16,

Fig. 2 Distribution of the primary tumors in 580 patients with spinal metastasis treated with surgery. Lung cancer was the most one in 198 (34.14%) cases. Kidney cancer, breast cancer, gastrointestinal cancer, lymphoma, and myeloma did not show significant difference. Prostate cancer, liver cancer and mesenchymal tissue sarcoma were nearly at the same. 84 (14.48%) cases were with unknown origin of tumor but with clear pathological examinations.

49 (8.45%) patients received palliative surgery, and 30 (5.17%) patients received radical surgery.

VAS Score

The VAS score was divided into three groups (0-3, 4-6, 7-10) (P = 0.009). For group 0-3, six (1.03%) patients received minimally invasive surgery, 93 (64.58%) patients received palliative surgery, and 10 (1.72%) patients received radical surgery. For group 7–12, 26 (4.48%) patients received minimally invasive surgery, 223 (38.45%) patients received palliative surgery, and 36 (6.21%) patients received radical surgery. For group 13–18, 31 (5.34%) patients received minimally invasive surgery, 144 (24.8%) patients received palliative surgery, and 11 (1.90%) patients received radical surgery.

Tokuhashi Score

The Tokuhashi score was divided into three groups (0-8, 9-11, 12-15) (P = 0.021). For group 0-8, 15 (2.59%) patients received minimally invasive surgery, 72 (12.41%) patients received palliative surgery, and five (0.86%) patients received radical surgery. For group 9-11, 31 (5.34%) patients received minimally invasive surgery, 221 (38.10%) patients received palliative surgery, and 20 (3.45%) patients received radical surgery. For group 12-15, 17 (2.93%) patients received minimally invasive surgery, 167 (28.79%) patients received palliative surgery, and 32 (5.52%) patients received radical surgery.

Urinary and Fecal Incontinence

Among these 580 patients, 64 (11.03%) patients presented urinary and fecal incontinence including 58 (10.00%) patients

PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

Orthopaedic Surgery Volume 11 • Number 6 • December, 2019

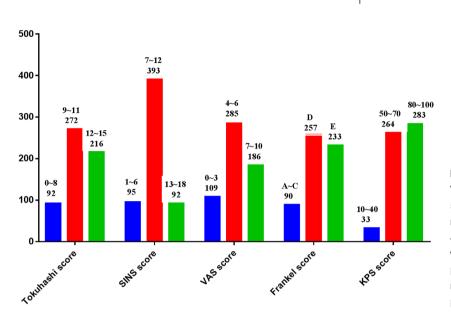


Fig. 3 Distribution of Tokuhashi score, SINS score, VAS score, Frankel score and KPS score in 580 patients treated with surgery. Tokuhashi score more than nine was shown in 488 (84.14%) patients; 485 (83.62%) patients presented spinal instability with SINS score more than 7; 471 (81.21%) patients presented pain with VAS score more four. As for neurological impairment, 90 (15.52%) patients presented paralysis.

receiving palliative surgery and six (1.03%) patients receiving radical surgery. The remaining 516 (88.97%) patients were with no urinary and fecal incontinence, 63 (10.86%) patients received minimally invasive surgery, 402 (69.31%) patients received palliative surgery, and 51 (8.79%) patients received radical surgery. The difference was significant among groups (P = 0.028).

Spinal Pathological Fracture

Two hundred and twelve (36.55%) patients presented spinal pathological fracture, and among these patients 35 (6.03%) patients received minimally invasive surgery, 155 (26.72%) patients received palliative surgery, and 22 (3.79%) patients received radical surgery. And while spinal pathological fracture did not occur in 368 (63.45%) patients, 28 (4.83%) patients received minimally invasive surgery, 305 (52.59%) patients received palliative surgery, and 35 (6.03%) patients received radical surgery. The difference was significant among groups (P = 0.002).

Bone Lesion (Osteolytic, Osteoblastic, or Mixed)

Totally, 192 (33.10%) patients presented with osteolytic lesions through imaging examinations and received surgery treatment. Thirty-one (5.34%) patients received minimally invasive surgery, 153 (26.38%) patients received palliative surgery, and eight (1.38%) patients received radical surgery. For patients with osteoblastic lesions, only eight (1.38%) patients received palliative surgery and one (0.17%) patient received radical surgery. For patients with mixed lesions, just one (0.17%) patient received minimally invasive surgery and two (0.34%) patients received palliative surgery. The difference was significant among groups (P < 0.001).

Discussion

S pinal metastases are the most common type of bone metastasis with a prevalence of 30%–70% in cancer patients; 5%–10% of metastases may be associated with ESCC leading to impaired mobility, neurologic deficits, and decreased quality of life. However, there is still no consensus

regarding the best treatment modality for these lesions. In this multicenter study, a total of 580 patients with an average age of 58.26 years (range, 13–86 years old) were enrolled in the study to summarize and analyze the epidemiological characteristics and independent variables affecting surgical modalities for spinal metastases.

Among these 580 patients, the epidemiological characteristics were analyzed. Three hundred and thirty two male and 248 female patients were enrolled with a ratio of 1.34:1, and most patients were at middle or elderly age between 45 years and 74 years. For primary lesion, the most common were lung cancer, followed by kidney cancer, breast cancer, gastrointestinal cancer, lymphoma and myeloma, prostate cancer, mesenchymal tissue sarcoma, and thyroid cancer. Especially, lung cancer was the top one leading to spinal metastasis either in males or females, which was different from data published abroad (prostate cancer in males and breast cancer in females). It may be due to the regional and cultural differences²³. The most common spinal metastatic site was the thoracic vertebra (190 [32.76%]), followed by the lumbar vertebra (146 [25.17%]), and metastases involving more than two sites of the cervical, thoracic, lumbar, and sacral vertebrae arose in 162 (27.93%) patients, that was the same as in the report by Bollen et al.²⁴.

As shown in Table 2, the KPS score, SINS score, VAS score, Tokuhashi score, urinary and fecal incontinence, spinal pathological fracture, and occurrence of bone lesion (osteolytic, osteoblastic or mixed) were independent and favorable factors affecting the surgery modalities. It could be determined that patients who received minimally invasive surgery preferentially should have a good general condition, the KPS score was more than 70 without urinary and fecal incontinence and visceral metastasis. Spinal metastatic sites showed no significant difference, but subgroup of vertebral body metastasis and appendix metastasis was not analyzed. However, some investigators pointed out that the minimally invasive surgery should be carefully selected for patients with

1045

Orthopaedic Surgery Volume 11 • Number 6 • December, 2019

PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

TABLE 2 Univariate analysis to identify independent variables that could affect the operation modality (P < 0.05 was identified with significant difference; n = number)

cant difference; n = number)				
	Minimally invasive surgery n = 63 (10.86%)	Palliative surgery n = 460 (79.31%)	Radical surgery n = 57 (9.83%)	P value
Gender				
Male	36	258	36	
Female	27	202	21	P = 0.120
Age (year)	21	202	21	F = 0.120
Age (year) ≤44	6	59	3	
<u>≥44</u> 45–59	21	167	31	
60-74	32	203	23	
75–89	4	31	23	
	4	31	0	P = 0.059
Spinal metastatic site Cervical vertebra	0	40	F	
		42	5	
Thoracic vertebra	17	152	21	
Lumbar vertebra	16	122	8	
Sacral vertebra	3	28	4	D 0.070
Trans-segmental	27	116	19	<i>P</i> = 0.078
metastasis				
Frankel score	2			
A–C	3	75	12	
D	33	195	29	
E	27	190	16	P = 0.067
KPS score	_			
10–40	0	30	3	
50–70	21	209	34	
80–100	42	221	20	P = 0.017
SINS score				
1–6	8	84	3	
7–12	42	327	24	
13–18	13	49	30	P < 0.001
VAS score				
0–3	6	93	10	
4–6	26	223	36	
7–10	31	144	11	P = 0.009
Tokuhashi score				
0–8	15	72	5	
9–11	31	221	20	
12–15	17	167	32	P = 0.021
Urinary and fecal incontinence				
Yes	0	58	6	
No	63	402	51	P = 0.028
Primary tumor				
Slow growth	16	113	12	
Moderate growth	23	182	18	
Rapid growth	24	165	27	P = 0.335
Extraspinal metastasis				
Yes	30	185	22	
No	33	275	35	P = 0.385
Visceral metastasis		2.0		
Yes	0	70	9	
No	54	390	48	<i>P</i> = 0.971
Spinal pathological fracture	U r	000	-0	, _ 0.01 I
Yes	35	155	22	
No	28	305	35	<i>P</i> = 0.002
Bone lesion	20	505	35	F = 0.002
Osteolytic	31	153	8	
Osteoblastic				
	0	8	1	
Mixed	1	2	0	D + 0 004
Unknown	31	297	48	P < 0.001

vertebral body posterior wall and pedicle involvement²⁵, so further analyses were needed to determine minimally invasive surgery indications for different spinal metastatic sites.

improvement of symptoms.^{26–29} That is to say, surgeons must consider the patients' overall health, as well as the imaging examination of the vertebral metastases. In this study, 460 (79.31%) patients received palliative surgery including 290 posterior laminectomy, 155 subtotal

Unlike primary spinal tumors, the goal of surgery for spinal metastases is not cure but an overwhelming

corpectomy, and 15 subtotal corpectomy combined with microwave ablation and vertebroplasty. Most of them presented severe pain and spinal instability but the general conditions were good with KPS score more than 60 and Frankel score in D and E. The revised Tokuhashi score have suggested that surgery only be considered in patients with a life expectancy of more than 6 months^{30,31}, meaning that patients, especially those with aggressive primary tumor metastasis, are ineligible for surgical symptom palliation^{29,32}. However, in this multicenter case series, lung cancer was the most common metastasis, as seen in 198 patients. Rapid development of radiotherapy and chemotherapy, especially targeted therapy, may help to improve patients' life expectancy.

Radical surgery was also performed for spinal metastasis, but the complex anatomical structure of the spine made the operation very difficult and bleeding occurs frequently during the operation. Therefore, indications and contraindications should be strictly clear. The indications for spinal metastatic tumor resection are generally as follows: single-level metastatic tumors of thoracic and lumbar vertebra with well-controlled primary lesions susceptible to chemotherapy or targeted therapy; without vital visceral metastasis; patients with longer life expectancy; no more than two adjacent segment lesions; Tokuhashi score at a range of 12~15^{22,33,34}. Only 57 (9.83%) patients who received tumor resection containing 36 total vertebrectomy and 21 total en-bloc spondylectomy were enrolled in this retrospective study, most of them were met with the indications above. In addition, univariate analysis identified that patients with spinal pathological fracture and spinal instability

1. Barzilai O, Laufer I, Yamada Y, et *al.* Integrating evidence-based medicine for treatment of spinal metastases into a decision framework: neurologic, oncologic, mechanicals stability, and systemic disease. J Clin Oncol, 2017, 35: 2419–2427.

2. Barzilai O, McLaughlin L, Amato MK, *et al.* Predictors of quality of life improvement after surgery for metastatic tumors of the spine: prospective cohort study. Spine J, 2018, 18: 1109–1115.

3. Moussazadeh N, Laufer I, Yamada Y, Bilsky MH. Separation surgery for spinal metastases: effect of spinal radiosurgery on surgical treatment goals. Cancer Control, 2014, 21: 168–174.

4. Witham TF, Khavkin YA, Gallia GL, Wolinsky JP, Gokaslan ZL. Surgery insight: current management of epidural spinal cord compression from metastatic spine disease. Nat Clin Pract Neurol, 2006, 2: 87–94.

5. Yao A, Sarkiss CA, Ladner TR, Jenkins AL 3rd. Contemporary spinal oncology treatment paradigms and outcomes for metastatic tumors to the spine: a systematic review of breast, prostate, renal, and lung metastases. J Clin Neurosci, 2017, 41: 11–23.

6. Lau D, Chou D. Posterior thoracic corpectomy with cage reconstruction for metastatic spinal tumors: comparing the mini-open approach to the open approach. J Neurosurg Spine, 2015, 23: 217–227.

7. Daniel JW, Veiga JC. Prognostic parameters and spinal metastases: a research study. PLoS One, 2014, 9: e109579.

8. Tancioni F, Navarria P, Pessina F, *et al.* Early surgical experience with minimally invasive percutaneous approach for patients with metastatic epidural spinal cord compression (MESCC) to poor prognoses. Ann Surg Oncol, 2012, 19: 294–300.

9. Masuda K, Ebata K, Yasuhara Y, Enomoto A, Saito T. Outcomes and prognosis of neurological decompression and stabilization for spinal metastasis: is assessment with the spinal instability neoplastic score useful for predicting surgical results. Asian Spine J, 2018, 12: 846–853.

10. Boriani S, Gasbarrini A, Bandiera S, Ghermandi R, Lador R. En bloc resections in the spine-the experience of 220 cases over 25 years. World Neurosurg, 2017, 98: 217–229.

(SINS score at a range of 13–18) could also be treated with tumor resection which should be considered for indications.

The limitations of this retrospective study include: lack of non-surgical patients enrolled as control group; spinal metastatic sites are just on the basis of cervical vertebra, thoracic vertebra, lumbar vertebra, sacral vertebra, and transsegmental metastasis, however, another subgroup containing vertebral body and appendix should also be considered; and surgery modalities are not divided into the subgroup of operation combining with or without radiotherapy, chemotherapy and targeted therapy.

Conclusions

Surgical treatment for spinal metastases is mainly to relieve pain, rebuild spinal stability, improve nerve function, control local tumors, and improve the quality of life of patients. With the rapid development of radiotherapy, chemotherapy (especially targeted therapy), immunotherapy and endocrine therapy, the level of surgical treatment of spinal metastases has been greatly improved. For middle-aged and elderly patients with good general conditions, severe pain, spinal pathological fracture, spine instability and without urinary and fecal incontinence, early surgical treatment should be actively carried out.

Acknowledgments

The authors are grateful for support from the Library of Tianjin Medical University. We would also like to thank the friends who gave us help in the creation and revision of the article.

References

11. Mesfin A, El Dafrawy MH, Jain A, Hassanzadeh H, Kebaish KM. Total en bloc spondylectomy for primary and metastatic spine tumor. Orthopedics, 2015, 38: e995–e1000.

12. Salame K, Regev G, Keynan O, Lidar Z. Total en bloc spondylectomy for vertebral tumors. Isr Med Assoc J, 2015, 17: 37–41.

13. Bollen L, Wibmer C, Van der Linden YM, *et al.* Predictive value of six prognostic scoring systems for spinal bone metastases: an analysis based on 1379 patients. Spine (Phila Pa 1976), 2016, 41: E155–E162.

14. Wibmer C, Leithner A, Hofmann G, et *al.* Survival analysis of 254 patients after manifestation of spinal metastases: evaluation of seven preoperative scoring systems. Spine (Phila Pa 1976), 2011, 36: 1977–1986.

15. Patchell RA, Tibbs PA, Regine WF, *et al.* Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet, 2005, 366: 643–648.

16. Park S, Kim KH, Rhee WJ, Lee J, Cho Y, Koom WS. Treatment outcome of radiation therapy and concurrent targeted molecular therapy in spinal metastasis from renal cell carcinoma. Radiat Oncol J, 2016, 34: 128–134.

17. Cazzato RL, Garnon J, Caudrelier J, Rao PP, Koch G, Gangi A. Percutaneous radiofrequency ablation of painful spinal metastasis: a systematic literature assessment of analgesia and safety. Int J Hyperthermia, 2018, 34: 1272–1281.

18. van Middendorp JJ, Goss B, Urquhart S, Atresh S, Williams RP, Schuetz M. Diagnosis and prognosis of traumatic spinal cord injury. Global Spine J, 2011, 1: 1–8.

19. Terret C, Albrand G, Moncenix G, Droz JP. Karnofsky performance scale (KPS) or physical performance test (PPT)? That is the question. Crit Rev Oncol Hematol, 2011, 77: 142–147.

20. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). Arthritis Care Res (Hoboken), 2011, 63: S240–S252.

ORTHOPAEDIC SURGERY VOLUME 11 • NUMBER 6 • DECEMBER, 2019

PATIENTS FOLLOWING SURGERY FOR SPINAL METASTASES

21. Fisher CG. DiPaola CP. Ryken TC. et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. Spine (Phila Pa 1976), 2010, 35: E1221-F1229

22. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine (Phila Pa 1976), 2005, 30: 2186-2191.

23. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin, 2015, 65: 87-108.

24. Bollen L, van der Linden YM, Pondaag W, et al. Prognostic factors associated with survival in patients with symptomatic spinal bone metastases: a

retrospective cohort study of 1,043 patients. Neuro Oncol, 2014, 16: 991-998.

25. Goetz MP, Callstrom MR, Charboneau JW, et al. Percutaneous image guided radiofrequency ablation of painful metastases involving bone: a multicenter study. J Clin Oncol, 2004, 22: 300–306.

26. Yang SB, Cho W, Chang U. Analysis of prognostic factors relating to postoperative survival in spinal metastases. J Korean Neurosurg Soc, 2012, 51:

127-134

27. Sohn S, Kim J, Chung CK, et al. A nationwide epidemiological study of newly diagnosed spine metastasis in the adult Korean population. Spine J, 2016, 16: 937-945

28. Vanek P. Bradac O. Trebicky F. Saur K. de Lacy P. Benes V. Influence of the preoperative neurological status on survival after the surgical treatment of symptomatic spinal metastases with spinal cord compression. Spine (Phila Pa 1976) 2015 40: 1824-1830

29. Pennington Z, Ahmed AK, Molina CA, Ehresman J, Laufer I. Sciubba DM. Minimally invasive versus conventional spine surgery for vertebral metastases: a systematic review of the evidence. Ann Transl Med, 2018, 6: 103.

30. Kaloostian PE, Yurter A, Zadnik PL, Sciubba DM, Gokaslan ZL. Current paradigms for metastatic spinal disease: an evidence-based review. Ann Surg Oncol, 2014, 21: 248-262.

31. Zadnik PL, Hwang L, Ju DG, et al. Prolonged survival following aggressive treatment for metastatic breast cancer in the spine. Clin Exp Metastasis, 2014, 31: 47-55.

32. Goodwin CR, Sankey EW, Liu A, et al. A systematic review of clinical outcomes for patients diagnosed with skin cancer spinal metastases. J Neurosurg Spine, 2015, 24: 837-849.

33. Murakami H, Kawahara N, Demura S, Kato S, Yoshioka K, Tomita K. Total en bloc spondylectomy for lung cancer metastasis to the spine. J Neurosurg Spine, 2010 13:414-417

34. Oka S, Matsumiya H, Shinohara S, et al. Total or partial vertebrectomy for lung cancer invading the spine. Ann Med Surg (Lond), 2016, 12: 1-4.