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ORIGINAL ARTICLE

Retrospective Study

Prognostic factors and its predictive value in patients with metastatic spinal cancer

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Abstract

BACKGROUND

The spine is the most common location of metastatic diseases. Treating a metastatic spinal tumor depends on many factors, including patients' overall health and life expectancy. The present study was conducted to investigate prognostic factors and clinical outcomes in patients with vertebral metastases.

AIM

To investigate prognostic factors and their predictive value in patients with metastatic spinal cancer.

METHODS

A retrospective analysis of 109 patients with metastatic spinal cancer was conducted between January 2015 and September 2017. The prognoses and survival were analyzed, and the effects of factors such as clinical features, treatment methods, primary lesions and affected spinal segments on the prognosis of patients with metastatic spinal cancer were discussed. The prognostic value of Frankel spinal cord injury functional classification scale, metastatic spinal cord compression (MSCC), spinal instability neoplastic score (SINS) and the revised Tokuhashi score for prediction of prognosis was explored in patients with metastatic spinal tumors.

RESULTS

Age, comorbidity of metastasis from elsewhere, treatment methods, the number

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of spinal tumors, patient's attitude toward tumors and Karnofsky performance scale score have an effect on the prognosis of patients (all $P < 0.05$). With respect to classification of spinal cord injury, before operation, the proportion of grade B and grade C was higher in the group of patients who died than in the group of patients who survived, and that of grade D and grade E was lower in the group of patients who died than in the group of patients who survived (all $P < 0.05$). At 1 mo after operation, the proportion of grade A, B and C was higher in the group of patients who died than in the group of patients who survived, and that of grade E was lower in patients in the group of patients who died than in the group of patients who survived (all $P < 0.05$). MSCC occurred in four (14.3%) patients in the survival group and 17 (21.0%) patients in the death group ($P < 0.05$). All patients suffered from intractable pain, dysfunction in spinal cord and even paralysis. The proportion of SINS score of 1 to 6 points was lower in the death group than in the survival group, and the proportion of SINS score of 7 to 12 points was higher in the death group than in the survival group (all $P < 0.05$). The proportion of revised Tokuhashi score of 0 to 8 points and 9 to 11 points were higher in the death group than in the survival group, and the proportion of revised Tokuhashi score of 12 to 15 points was lower in the death group than in the survival group (all $P < 0.05$). Frankel spinal cord injury functional classification scale, MSCC, SINS and revised Tokuhashi score were important factors influencing the surgical treatment of patients with metastatic spinal cancer (all $P < 0.05$).

CONCLUSION

Frankel spinal cord injury functional classification scale, MSCC, SINS and revised Tokuhashi score were helpful in predicting the prognosis of patients with metastatic spinal cancer.

Key Words: Metastatic spinal tumors; Frankel spinal cord injury functional classification scale; Metastatic spinal cord compression; Spinal instability neoplastic score; Revised Tokuhashi score

Core Tip: Early detection and prompt management usually ensure a better prognosis for cancer patients. It is important to examine the prognostic factors that influence the prognosis of patients with metastatic spine tumors in order to determine the optimal treatment strategy. The present study showed that age, comorbidity of metastasis from elsewhere, therapies, number of spinal tumors, patient attitude toward tumors and Karnofsky performance score significantly influenced prognosis of patients with metastatic spine tumors. Moreover, Frankel spinal cord injury functional classification scale score, metastatic spinal cord compression, spinal instability neoplastic score and revised Tokuhashi score were important factors influencing the prognosis of this disease and the treatment selection.

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INTRODUCTION

Although human societies develop rapidly and technology progresses with each passing day, the pace of human evolution is slow, far slower than that of societies and technology. Human beings still cannot adapt to the changes in life habits and natural environment, and the incidence of malignant tumors is increasing[1-3]. A majority of patients with malignant tumors may experience bone metastasis[4-6]. Spine, second only to lung and liver, is one of the most common sites for distant metastases of

malignant tumors[7]. The symptoms of spinal cord compression frequently occur in patients with metastatic spinal cancer including severe spinal pain, weakness of both legs, hypoesthesia, *etc*., which are leading causes of decrease in quality of life and survival[8,9]. Clinically, the most common therapies for metastatic spinal cancer include subtotal corpectomy combined with internal fixation and decompression and minimally invasive percutaneous spine surgery. Percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) were widely used minimally invasive procedures for metastatic spinal cancer. PVP can effectively increase vertebral strength, relieve pain and improve quality of life[10]. PKP can effectively restore the height of vertebral body, strengthen the strength of vertebral body and improve the safety of surgery[11,12]. The present study enrolled 109 patients with spinal metastatic cancer, including 60 patients undergoing subtotal corpectomy and internal fixation and decompression, and 49 patients undergoing minimally invasive percutaneous spine surgery (33 patients undergoing PVP and 16 patients undergoing PKP). Prognosis and survival were analyzed. Effects of factors such as clinical characteristics, therapies, primary lesions and spinal segment on the prognosis were analyzed. Diagnostic value of Frankel spinal cord injury functional classification scale, metastatic spinal cord compression (MSCC), spinal instability neoplastic score (SINS) and revised Tokuhashi score for predicting of prognosis in patients with metastatic spinal cancer was evaluated in patients with metastatic spinal tumors.

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MATERIALS AND METHODS

General information

A retrospective analysis was conducted in 109 patients with metastatic spinal tumors who were admitted to hospital between January 2016 and September 2019. Inclusion criteria were as follows: (1) patients diagnosed with metastatic spinal cancer confirmed by pathologic, cytologic and imaging diagnostic results; (2) patients with spinal tumors exhibited; (3) patients whose spinal body was confirmed with osteolytic bone destruction or mixed osteolytic destruction; (4) patients whose cortical structure of posterior margin of spinal body was intact without symptoms of radiculopathy; (5) patients whose survival period was ≥ 5 mo; and (6) patients whose complete clinical data were available. Exclusion criteria included: (1) patients with poor basic performance status; and (2) patients with severe coagulation disorders.

Methods

Renal function, electrocardiogram, complete blood count and routine coagulation tests were performed in all patients before the surgery. In addition, imaging tests, such as X-ray, computed tomography and magnetic resonance imaging, were used to determine the damage state of spinal body based on which appropriate therapy was selected[13]. Sixty patients in the subtotal corpectomy group underwent subtotal corpectomy of metastatic spinal tumors and fixation and decompression.

First, a Y-shaped incision was made in the skin to expose spinous process and laminectomy. The erector spinae muscle was horizontally cut off, and distal and proximal muscle was pulled away. Second, parapophysis was exposed and removed. Anterolateral vertebral body was exposed, and peripheral tissues were push away and stripped. Third, tumor tissues in the spinal body were cut out. Posterior margin of vertebral body was conserved as a marker, and a stripper was inserted between the posterior margin of a vertebra and a thecal sac. The posterior margin of the vertebral body was pushed and pressed forward. Cartilage that covers the bone were cleaned, and contralateral tumors were cut out. Bone blocks and bone strips were taken out with an appropriate size as a substitute based on the circumstances of bone defect and were anterolaterally inserted through thecal sac and erected in the place where there was a defect. After the surgery, spinal reconstruction stability was achieved. Stop incision bleeding and gentamicin containing normal saline was used to wash the incision and sew layer by layer[14,15]. Of the 49 patients undergoing minimally invasive percutaneous spine surgery, 33 patients underwent PVP and 16 patients underwent PKP. In terms of PKP, patients lay on their back. After sterilization and anesthesia, the direction of the needle and the needle position were ensured under the guidance of X-ray machine. The stylet was removed when the aspirating needle reached spinal body passing through pediculus arcus vertebrae. Electrodes were selected based on the size and position of tumors. Needle electrode penetrated into the position affected where a balloon was placed through the same passage under the

guidance of imaging. Pressure injection of iohexol was given to the patients under the detection of imaging, and the injection was stopped until the balloon was inflated. Bone cement was prepared, and the balloon was withdrawn at the dough stage. Under the guidance of imaging, bone cement was injected into the vertebral cavity. For bone cement, the dosage used was usually 2 to 4 mL. Stylet was embedded and was removed together with channel tube, and antiseptic dressing was used. After the procedure, patients were allowed to lie flat for 8 h, and electrocardiography machines were used to monitor their vital signs. For PVP treatment, the operation was comparable with that of PKP except that the affected vertebral body was filled with bone cement through percutaneous pediculus arcus vertebrae or extrapedicular approach. Vertebral body was observed closely, and recovery after spine surgery was closely monitored postoperatively.

Measures

First, a univariate analysis of outcomes was performed in patients with metastatic spinal tumors. Patients were divided into different groups based on their survival. Patients with survival of 3 years or over 3 years were enrolled in a survival group, and patients with survival under 3 years were enrolled in a death group. Clinical indices were compared between the two groups, and a univariate analysis of outcomes was performed[16]. Second, Frankel spinal cord injury functional classification scale score was determined. Frankel spinal cord injury functional classification scale score was estimated before the operation and at 1 mo after the operation. Death was classified as grade A. Five-grade scale was introduced for classifying spinal injury based on the sensory and motor function below the affected plane. Grade A: Complete loss of deep and light sensory and motor functions below the affected plane; Grade B: Motor function sparing and only sensation in some sacral region below the affected plane; Grade C: Some motor function and lack of function of interest below the affected plane; Grade D: Motor dysfunction below the affected plane and ability to walk only with assistance; and Grade E: Complete deep and light sensory and motor functions with possible pathologic reflexes. Third, MSCC was determined. MSCC means that the epidural metastatic lesion causes true displacement of the spinal cord from its normal position in the spinal canal. It usually causes spinal cord compression and cauda equina syndrome with severe pain and sensory and motor dysfunction below the affected plane and sphincter of Oddi dysfunction. Fourth, spinal instability neoplastic score (SINS) was determined. SINS scale generally evaluates six aspects: Location, pain, bone lesion, radiographic spinal alignment, vertebral body collapse and posterior spinal element involvement. The total score of SINS was 0 to 18 points. A score of 0 to 6 points denotes stability, 7 to 12 points denotes potential instability, and 13 to 18 points denotes instability. If SINS was 7 or beyond 7, surgical intervention is recommended. Fifth, revised Tokuhashi score was determined. To be specific, total score of 0 to 8 points, 9 to 11 points and 12 to 15 points indicates expected survival was < 6 mo, 6 to 12 mo and > 12 mo, respectively.

Statistical analysis

SPSS22.0 software was used for all statistical analyses. Measurement data are expressed as mean ± SD and inter-group difference was compared using Student's *t* test. Enumeration data are expressed as % and inter-group difference was compared using χ^2 test. Logistic analysis was used to conduct a univariate analysis of influential factors for the prognosis and to estimate their value for prediction of the prognosis. $P < 0.05$ represented a significant difference.

RESULTS

Univariate analysis of influential factors for the prognosis of patients with metastatic spinal tumors revealed that age, comorbidity of metastasis from elsewhere, therapies, number of spinal tumors, patient attitude toward tumors and Karnofsky performance score have an effect on the prognosis of patients with metastatic spinal tumors ($P < 0.05$, Table 1).

In terms of Frankel spinal cord injury functional classification scale score, the proportion of grade B and grade C patients were higher in the death group than in the survival group, and the proportion of grade D and grade E patients were lower in the death group than in the survival group (all $P < 0.05$, Table 2). At 1 mo after the surgery, the proportion of grade A, grade B and grade C patients were higher in the death group than in the survival group and the proportion of grade E patients were

Table 1 Univariate analysis of influential factors for the prognosis of patients with spinal metastatic tumors

Clinical characteristics	*n*	Survival group, *n* = 28	Death group, *n* = 81	χ^2 value	*P* value
Gender				0.981	0.456
Male	68	16	52		
Female	41	12	29		
Age in yr				34.542	0.001
20 to 39	23	10	13		
40 to 59	61	15	46		
60 to 89	25	3	22		
Comorbidity of metastases from elsewhere				45.890	0.001
Yes	65	7	58		
No	44	21	23		
Types of primary lesions				2.342	0.108
Lung cancer	27	8	19		
Gastric cancer	23	4	19		
Thyroid cancer	20	5	15		
Breast cancer	19	7	12		
Intestinal cancer	13	3	10		
Other cancers	7	1	6		
Therapies				19.221	0.001
Subtotal resection combined with internal fixation and decompression	60	12	48		
Minimally invasive percutaneous spine surgery	49	16	33		
Number of spinal tumors				5.762	0.041
1 to 2	47	16	31		
≥ 3	62	12	50		
Patient attitudes toward tumors				4.093	0.046
Face it positively	29	9	20		
Accept it	41	14	27		
Deny it	12	2	10		
Resist it	27	3	24		
Karnofsky performance score				13.674	0.001
10 to 30	6	0	6		
30 to 50	25	4	21		
50 to 70	54	10	44		
70 to 90	24	14	10		

lower in the death group than in the survival group (all $P < 0.05$).

Comparison of MSCC in patients with metastatic spinal tumors of different outcomes revealed that MSCC occurred in four patients (14.3%) in the survival group and 17 patients (21.0%) in the death group ($P < 0.05$). Patients usually had symptoms of refractory pain, spinal nerve disorders and even paralysis. With regard to SINS score in patients with metastatic spinal tumors who had different survival outcomes, the proportion of patients who reported 1 to 6 points for SINS was lower in the death group than in the survival group and the proportion of patients who reported 7 to 12 points for SINS was higher in the death group than in the survival group (all $P < 0.05$, Table 3).

Table 2 Frankel spinal cord injury functional classification scale score in patients with spinal metastatic tumors of different outcomes, *n* (%)

Groups	*n*	Time points	Frankel spinal cord injury functional classification scale score				
			Grade A	Grade B	Grade C	Grade D	Grade E
Survival group	28	Before surgery	0 (0.0)	0 (0.0)	2 (7.1)	5 (17.9)	21 (75.0)
		1 mo after surgery	0 (0.0)	0 (0.0)	0 (0.0)	6 (21.4)	22 (78.6)
Death group	81	Before surgery	0 (0.0)	3 (3.7)[a]	11 (13.6)[a]	21 (5.9)[a]	46 (56.8)[a]
		1 mo after surgery	15 (18.5)[b]	14 (17.3)[b]	8 (9.9)[b]	23 (28.4)	21 (25.9)[b]

[a]$P < 0.05$ *vs* the survival group before the surgery;
[b]$P < 0.05$ *vs* the survival group at 1 mo after the surgery.

Table 3 Comparison of spinal instability neoplastic score between the survival group and the death group, *n* (%)

Groups	*n*	SINS score, points		
		1 to 6	7 to 12	13 to 18
Survival group	28	12 (42.8)	13 (46.4)	3 (10.7)
Death group	81	11 (13.6)	61 (75.3)	9 (11.1)
χ^2 value		8.125	13.098	0.542
P value		0.015	0.009	0.761

SINS: Spinal instability neoplastic score.

After comparing the revised Tokuhashi score in patients with metastatic spinal tumors who had different survival outcomes, it discovered that the proportion of patients who reported 0 to 8 points for revised Tokuhashi score was higher in the death group than in the survival group, and the proportion of patients who reported 12 to 15 points was lower in the death group than in the survival group (all $P < 0.05$, Table 4).

Evaluation of indices for the prediction of outcomes in patients with metastatic spinal tumors indicated that scores of Frankel spinal cord injury functional classification scale, MSCC, SINS and revised Tokuhashi scale were important factors influencing the pattens of surgery (all $P < 0.05$).

DISCUSSION

Due to the development of society and economy and advances in cancer screening technology, the incidence of metastatic spinal cancer has increased markedly. Unfortunately, when cancer spreads to the spinal column, it means the cancer is mostly at the advanced stage with poor outcomes. Therefore, it is important to discuss the prognostic factors and indices for the prediction of prognosis in patients with metastasis to the spinal column[17,18].

The results suggested that older age, complications of metastases from elsewhere, subtotal corpectomy, fixation and decompression, high number of spinal tumors, hostile attitude to tumors and low Karnofsky performance score have a negative effect on the prognosis in patients with metastatic spinal tumors. Weak immune function and other possible system disorders in older patients may lead to poorer outcomes than in younger patients[19]. Patients with complications of metastases from elsewhere, low Karnofsky performance score and high number of spinal tumors had poor general condition and primary tumor Node Metastasis stage. The use of subtotal corpectomy, fixation and decompression may be based on the poor physical performance in patients who were not eligible for minimally invasive percutaneous surgery. With the growth of metastatic spinal tumors and the increase in the number of affected spinal body, various complications frequently occurred, including injuries to spinal body and spinal nerve roots, injuries to spine strength caused by tumor,

Table 4 Differences in the revised Tokuhashi score between the survival group and the death group, *n* (%)

Groups	*n*	Revised Tokuhashi score, points		
		0 to 8	9 to 11	12 to 15
Survival group	28	6 (21.4)	10 (35.7)	12 (42.8)
Death group	81	34 (42.0)	36 (44.4)	11 (13.6)
χ^2 value		11.153	5.327	16.542
P value		0.001	0.041	0.001

pathological fractures, compression of nerve root caused by tumor, severe local pain and even paralysis, which may seriously affect the treatment and quality of life[20]. Patient inactive attitude to tumors may result in poor compliance with treatment. Especially, anxiety and depression may have serious effect on the outcomes[21-23]. Most metastatic spinal tumors were derived from lung cancer, indicating the incidence of lung cancer is high compared with other types of cancer. Strategies such as early detection, diagnosis and treatment as well as tobacco control for all are urgently needed to promote reduction in the incidence of metastatic spinal tumors.

Frankel spinal cord injury functional classification scale is constantly used for rough assessment of spinal cord injuries showing a certain significance. The occurrence of MSCC in patients with metastatic spinal tumors may have serious effect on quality of life, and the mortality is high. SINS score can be used to assess spinal stability. The revised Tokuhashi score is usually used preoperatively to evaluate the outcomes and to give guidance to the clinicians to select the appropriate treatment approaches for individuals. The present study results demonstrated that Frankel spinal cord injury functional classification scale score, MSCC, SINS and revised Tokuhashi score were important factors influencing the treatment selection.

CONCLUSION

All in all, patients with older age, complications of metastases from elsewhere, subtotal corpectomy, fixation and decompression, high number of spinal tumors, hostile attitude to tumors and low Karnofsky performance score have poor prognosis. Frankel spinal cord injury functional classification scale score, MSCC, SINS and revised Tokuhashi score were important factors influencing the treatment of metastatic spinal tumors.

ARTICLE HIGHLIGHTS

Research background

Spinal metastasis is common in patients with cancer. The optimal treatment for metastatic spine tumors should be selected based on prognostic predictions.

Research motivation

In order to find influential factors that guide treatment decision making, the study examined spinal cord injury function, the incidence of metastatic spinal cord compression (MSCC), spinal instability neoplastic score (SINS), survival and factors associated with prognosis in patients with metastatic spinal cancer.

Research objectives

To examine the factors for predicting the prognoses and its predictive value in patients with metastatic spinal cancer.

Research methods

A study was performed involving 109 patients with metastatic spinal cancer. Clinical, sociodemographic and prognostic data were extracted. They were classified into two groups: Patients with survival of 3 years or over 3 years were enrolled in a survival group and those with survival under 3 years were enrolled in a death group. The incidence of MSCC and SINS and Frankel spinal cord injury functional classification

scale score and revised Tokuhashi score were compared between the two groups. The prognostic significance of factors influencing the prognosis of patients with metastatic spinal cancer was analyzed including general information, Frankel spinal cord injury functional classification scale score, SINS score and revised Tokuhashi score.

Research results

There were significant differences in outcomes of patients with metastatic spinal cancer of different age, treatment methods, number of spinal tumors, Karnofsky performance score, Frankel spinal cord injury functional classification scale score, SINS score and revised Tokuhashi score, indicating that these factors have significant effects on the prognosis of patients with metastatic spinal cancer.

Research conclusions

The detection of the above important factors may be useful for aiding the selection of appropriate treatment modalities for metastatic spinal cancer.

Research perspectives

The subjects of the current study were restricted to patients with some cancer types and patients undergoing surgical treatment. Additional clinical studies with larger sample sizes investigating extra novel factors are required to validate further these findings.

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