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Original Article

Minimally invasive posterior percutaneous pedicle screw fixation for instability of spinal metastases

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Abstract: Objective: This study aimed to evaluate the efficacy of percutaneous pedicle screw fixation (PPSF) for instability of spinal metastases. Methods: This is a retrospective study of patients with spinal metastases from January 2013 to March 2016. PPSF was performed for twenty-five patients. Thirty-one patients were treated by radiotherapy alone. Visual analog scale (VAS) score was used to assess pain status. The activities of daily living (ADL) scale was used to evaluate functional ability of patients. Results: There were significant differences in the VAS score before and after operation. Multiple linear regression analysis showed that postoperative VAS score was concerned with the treatment method. Surgery was significantly superior to radiation in pain relief and postoperative ADL evaluation was related to the treatment method and pre-operative ADL evaluation. The results show that good post-operative life quality is related to surgery and good pre-operative life quality. Conclusion: For some patients with spinal metastases, PPSF is a good option for alleviating pain and improving quality of life.

Keywords: Spinal metastases, percutaneous, pedicle screw, minimally invasive technology, surgery, radiotherapy

Introduction

Spinal metastasis is one of the most common complications of advanced cancer. The life expectancy of most patients is usually short. Therefore, the main goal of treatment is to improve the quality of remaining life such as pain relief and maintaining ambulatory function. In the past, radiotherapy (RT) was the primary treatment for spinal metastases. Later, studies have confirmed that surgery combined with RT was superior to RT alone in the aspects of ambulatory function and survival outcome [1-3]. At present, for spinal metastases without spinal instability, radiation therapy is still preferred but patients with symptomatic spinal cord compression and spinal instability should be treated with surgery as early as possible [4]. Because of poor prognosis, surgery for spinal metastases should be carried out as minimally invasive as possible. Vertebroplasty and kyphoplasty are less invasive operations for spinal stabilization. However, these operations may not be indicated if there is posterior vertebral wall destruction or pathologic burst fracture. Open decompression and stabilization are optional for spinal cord compression. More aggressive surgery is not suitable for most patients with spinal metastases as their expected life is less than one year. Risks and benefits of surgery must be weighed according to the life expectancy and functional outcome of the patients [5]. For patients with severe pain or vertebral instability of spinal metastases, percutaneous vertebroplasty (PVP) is the optimal choice. Polymethyl methacrylate (PMMA) cement is injected into affected vertebral bodies to improve the stabilization of vertebral bodies. Unfortunately, these procedures may not be indicated when patients have posterior vertebral wall destruction [6]. Studies have shown that the amount of injected PMMA correlated with cement leakage [7]. An insufficient amount of PMMA may be injected to avoid cement leakage or tumor retropulsion. Consequently, there remains a group of patients needing restoration of spinal mechanical stability for whom neither PVP nor open surgery is appropriate. Percu-

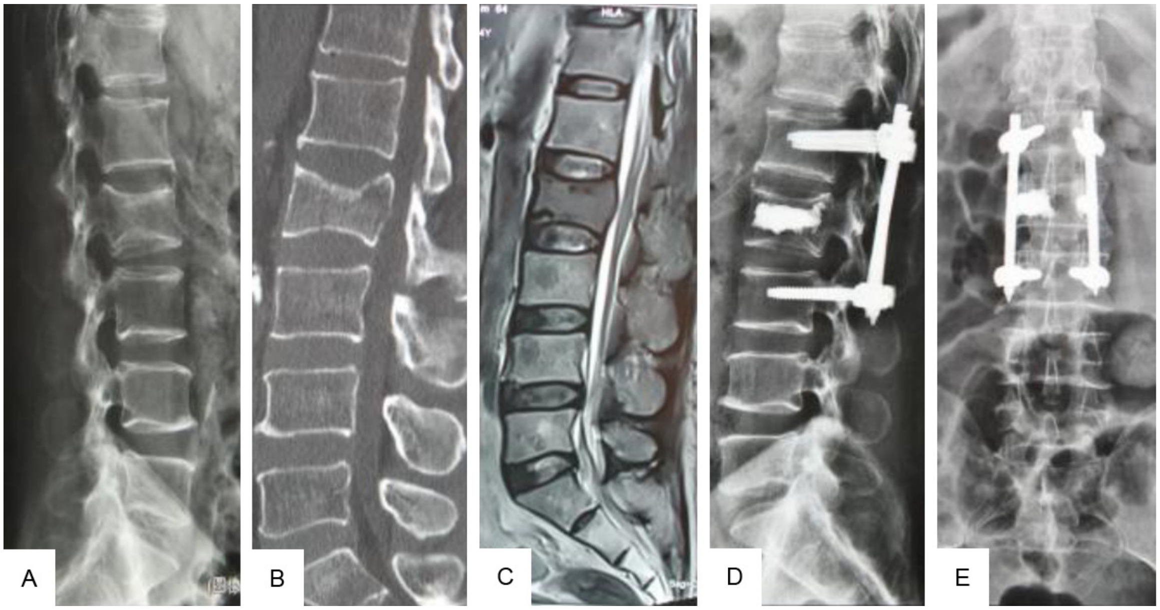

Figure 1. X-ray shows compression fractures of L2 (A). Computed tomography (CT) and T2-weighted magnetic resonance imaging (MRI) shows L2 vertebral body was collapsed and posterior wall was complete (B and C). PPSF and PVP were performed at L1, L3 and L2, respectively. Volume of PMMA was 4 mL. Postoperative imaging shows increased height of the L2 vertebral body (D and E).

taneous pedicle screw fixation (PPSF) may be an option to fill the gap between PVP and open surgery [8-10].

Materials and methods

Patients

Fifty-six patients with thoracic and lumbar spinal metastases from January 2013 to March 2016 were enrolled in this retrospective study, approved by the Medical Research Ethics Board of the 307 Hospital of the Chinese People's Liberation Army. Data were collected from patients, their family members, and patient files. Twenty-five consecutive patients were treated with PPSF (with/without PVP) and postoperative chemotherapy/RT. The primary indications of PPSF were severe local pain due to mechanical instability and a high risk of cement leakage. Thirty-one patients were treated with RT alone. Spinal cord compression and severe neurological deficits were excluded. Minimally invasive surgery was determined by radiologist, oncologist, and spine surgeons.

Surgical procedures

After general anesthesia, patient was placed in the prone position. Vertebrae were located by fluoroscopy, including fractured vertebral bodies and the near upper and lower unaffected vertebral bodies. An incision was then placed on the skin beside vertebral spines. The trochar was passed through soft tissues down to the bony surface. Once trochar was confirmed on the lateral border of the pedicle, trochar could be penetrated into vertebral body under fluoroscopic guidance. Pedicle screws were then inserted. After pedicle screws and screw extensions were placed, rods were passed into the screw heads through channels in the extensions (**Figure 1**). PVP was then performed in 7 patients. The bone needle was inserted into the vertebral body. PMMA cement was then injected to brace the collapsed vertebral body (4.5 ± 1.4 ml). The mean operation time was 73 ± 16 minutes (range, 55-115 minutes) and intra-operative blood loss was less than 150 mL. Post-operative adjuvant radiotherapy was performed for 21 patients one week later.

Statistical analysis

Visual analog scale (VAS) score was used to assess pain status. The activities of daily living (ADL) scale was used to evaluate the functional ability of patients. SPSS 18.0 software (SPSS Institute, Chicago, USA) was used for statistical analyses. Continuous quantitative variables are described as mean ± standard deviation. Comparison between the two groups was analyzed by multiple regression analysis. Overall

Table 1. Clinical characteristics and outcomes of patients undergoing surgery

No	Gender	Age	Primary tumor	Site	VAS score									ADL score			Survival Time (m)
					Preop	24 h	1 w	2 w	1 m	2 m	3 m	6 m	12 m	Preop	Postop 1 m	Postop 3 m	
1	M	64	Lung	L2	6	3	2	3	2	2	-	-	-	49	68	-	4.4
2	M	60	Prostate	T12	6	3	2	2	2	1	1	1	-	57	74	76	9.6
3	M	57	Renal	T10	6	4	3	4	3	2	1	1	1	56	78	82	14.8
4	M	53	Prostate	T12	5	3	1	1	2	1	1	1	1	66	93	94	24.3
5	F	67	Lung	T6/8	5	3	3	3	2	2	2	2	-	46	79	79	8.5
6	F	60	Breast	T11	8	2	2	2	2	2	2	2	-	50	71	70	8.7
7	M	71	Lung	T8	6	2	2	2	2	2	1	-	-	46	70	58	5.3
8	F	61	Lung	T12/L3	8	3	1	1	1	1	1	0	-	51	75	76	9.6
9	M	55	Renal	L2/3	5	4	3	4	3	2	1	1	-	44	81	81	10.5
10	M	51	Stomach	T11/12	7	2	2	2	2	2	2	1	-	40	76	75	6.6
11	F	61	Lung	T6	6	3	2	2	2	1	1	1	-	50	77	73	7.8
12	M	54	Renal	L3/4	7	3	1	1	1	0	0	0	1	69	83	87	15.4
13	F	56	Breast	T12	6	4	2	2	3	2	1	2	2	56	78	80	13.3
14	M	60	Lung	T9	4	2	2	2	2	1	1	1	2	60	82	87	12.6
15	M	57	Prostate	T10	7	3	3	3	2	2	2	3	3	55	91	90	17
16	F	54	Breast	T8	6	4	2	4	3	1	1	1	3	54	85	87	13.5
17	M	60	Lung	L4	5	3	2	2	2	2	2	2	2	50	82	80	14
18	M	63	Renal	L3	8	3	3	3	2	2	1	1	1	58	87	88	15.2
19	F	57	Breast	T9	7	4	2	2	2	1	1	1	2	66	89	83	14.2
20	F	60	Breast	T11	7	3	3	3	2	2	1	1	1	52	86	90	11.5
21	F	65	Lung	L3/4	5	3	2	2	2	1	1	1	2	64	85	88	15.8
22	M	62	Renal	T10	7	4	3	4	3	2	2	2	2	62	83	83	13.2
23	F	53	Breast	L3	6	3	3	3	2	2	2	2	2	71	94	96	21.1
24	M	61	Prostate	T9/11	7	3	2	3	2	1	1	0	1	75	90	94	22.4
25	M	52	Lung	L2	6	3	3	3	3	2	2	2	2	58	83	85	12.2

survival was analyzed by using Kaplan-Meier method and log-rank test. In all analyses, a value of $P < 0.05$ was considered to be statistically significant.

Results

Patient characteristics

Fifty-six patients were enrolled in this retrospective study including 21 females and 35 males. The mean age of surgery group (**Table 1**. n = 25) and RT group (**Table 2**. n = 31) were 59 ± 6.3 years and 61 ± 7.6 years ($P > 0.1$), respectively. The primary tumors included lung cancer (24 cases), breast cancer (13 cases), renal cancer (7 cases), prostate cancer (8 cases), and stomach cancer (4 cases). In the surgery group, 31 vertebrae were invaded. T6 (2x), T8 (3x), T9 (3x), T10 (3x), T11 (4x), T12 (4x), L2 (3x), L3 (6x), and L4 (3x). PPSF combined with PVP was performed for 7 patients. Fifteen patients accepted the targeted therapy. Post-operative RT was performed for 21 patients one week later. In the RT group, forty-three vertebrae were invaded as follows, T2 (2x), T3 (1x), T5 (2x), T6 (4x), T7 (2x), T8 (3x), T9 (2x), T10 (4x), T11 (5x), T12 (4x), L1 (2x), L2 (4x), L3 (4x), L4 (3x), and L5 (1x). RT was performed in a cumulative dose of 30 Gy with 10 fractions (16 cases), 45 Gy with 15 fractions (11 cases), and 30 Gy with 5 fractions (4 cases). None of the patients had radiation myelopathy.

One patient with asymptomatic para-vertebral cement leakage and none with internal fixation loosening were observed. Vertebral compression fractures after RT were observed in 4 patients. The number of patients available for VAS evaluation at each follow up interval were 56 (100%) at 24 hours to 2 months, 53 (95%) at 3 months, 46 (82%) at 6 months, and 31 (55%) at 12 months.

VAS scores of the surgery group were decreased from 6.24 ± 1.05 to 3.08 ± 0.64 at the 24-hour

Table 2. Clinical characteristics and outcomes of patients undergoing RT

NO	Gender	Age	Primary tumor	Site	VAS score									ADL score			Survival Time (m)
					Pre-RT	24 h	1 w	2 w	1 m	2 m	3 m	6 m	12 m	Pre-RT	Post-RT 1 m	Post-RT 3 m	
1	M	66	Stomach	T9	6	6	6	4	4	4	3	3	-	67	74	78	10.4
2	M	73	Lung	T12	4	4	5	4	3	3	-	-	-	42	44	-	3.8
3	F	52	Breast	T2	5	5	5	3	4	4	2	2	3	66	78	83	16.6
4	M	64	Lung	T11	3	3	4	4	3	3	3	3	-	58	66	69	9
5	F	65	Stomach	T5/6/7	7	7	6	4	4	4	3	-	-	52	58	52	4.9
6	M	63	Renal	L4	6	6	5	4	3	3	3	2	2	75	82	84	15.8
7	F	59	Lung	T2/3	8	8	7	6	5	5	4	-	-	48	48	53	5.2
8	M	65	Lung	T11	6	6	6	6	4	4	2	3	3	73	77	85	18.2
9	M	54	Prostate	L2/3	5	5	5	4	3	3	2	4	4	80	85	88	21.4
10	M	62	Lung	T10	6	6	6	6	5	4	3	4	-	53	58	65	6.8
11	F	58	Breast	T11	7	7	6	4	4	4	2	2	-	57	60	64	8.9
12	M	66	Lung	T6	6	6	6	6	4	4	3	-	-	45	52	41	4.6
13	F	62	Lung	T9	6	6	6	6	5	5	3	3	-	67	70	69	10.1
14	M	63	Lung	L1/2	6	6	6	4	3	3	-	-	-	44	48	-	3.1
15	M	68	Prostate	T10/L4	4	4	5	4	3	3	3	3	-	62	64	66	10.5
16	F	60	Breast	T11/12	5	5	5	5	5	5	4	3	2	63	61	68	13
17	M	61	Lung	T5	6	6	6	6	4	4	3	3	-	61	65	67	11.3
18	F	56	Renal	L3	7	7	7	6	5	5	4	3	3	58	66	69	12.3
19	M	67	Lung	T8/L1	5	5	5	5	4	4	3	3	4	69	71	80	17.6
20	F	60	Breast	T10/11	4	4	4	3	3	3	1	3	4	70	76	76	15.4
21	M	54	Lung	T10	6	6	5	3	4	4	3	-	-	46	50	46	4.3
22	F	68	Breast	T6/7	5	5	5	4	4	4	3	3	4	69	75	78	15.3
23	M	73	Lung	L2	6	6	6	5	4	4	3	-	-	44	46	49	4.9
24	M	57	Lung	T12	7	7	7	6	5	5	3	3	4	68	72	79	16.8
25	M	58	Prostate	L3	4	4	4	4	3	3	3	4	5	73	79	81	17.2
26	M	62	Stomach	T8	5	5	4	4	3	3	2	2	2	64	75	78	12.6
27	M	56	Prostate	L3/4/5	7	7	6	4	3	3	3	2	3	69	72	87	18.5
28	M	65	Lung	T6	4	4	4	3	3	2	2	-	-	52	58	59	5.6
29	F	54	Breast	T12	7	7	7	5	4	4	3	3	2	72	77	84	20.8
30	M	53	Lung	L2	8	8	7	4	3	3	2	2	3	78	83	88	22
31	F	57	Breast	T8	6	6	5	5	4	4	2	2	-	53	57	62	7.2

postoperative time point ($P < 0.001$) and was 2.25 ± 0.92 at 1 week ($P < 0.001$), 2.52 ± 0.82 at 2 weeks ($P < 0.001$), 2.18 ± 0.68 at 1 month ($P < 0.001$), 1.56 ± 0.57 at 2 months ($P < 0.001$), 1.28 ± 0.54 at 3 months ($P < 0.001$), 1.24 ± 0.78 at 6 months ($P < 0.001$), and 1.76 ± 0.42 at 12 months ($P < 0.001$). However, VAS scores of the RT group were significantly decreased at 2 weeks after treatment. VAS score was 4.55 ± 1.03 at 2 weeks ($P < 0.001$), 3.82 ± 0.83 at 1 month ($P < 0.001$), 3.73 ± 0.76 at 2 months ($P < 0.001$), 2.77 ± 0.84 at 3 months ($P < 0.001$), 2.81 ± 0.94 at 6 months ($P < 0.001$), and 3.17 ± 0.56 at 12 months ($P < 0.001$, **Figure 2**). We used multiple linear regression analysis to avoid confounding bias on postoperative VAS scores (Y1). Age (X1), primary tumor types (X2), number of involved vertebrae (X3), treatment method (X4), preoperative ADL evaluation (X5), and preoperative VAS score (X6) were considered. Age (X1), primary tumor types (X2), number of involved vertebrae (X3), preoperative ADL evaluation (X5), and preoperative VAS score (X6) were removed by regression model. Multiple linear regression equation ($Y1 = 0.514 + 0.78X4$) showed that postoperative VAS score (Y1) was concerned with treatment method (X4). However, surgery was significantly superior to radiation in regards to pain relief. VAS scores of the surgery group and RT group at 1 month after treatment were improved by an average of 4.08 ± 1.32 and 1.9

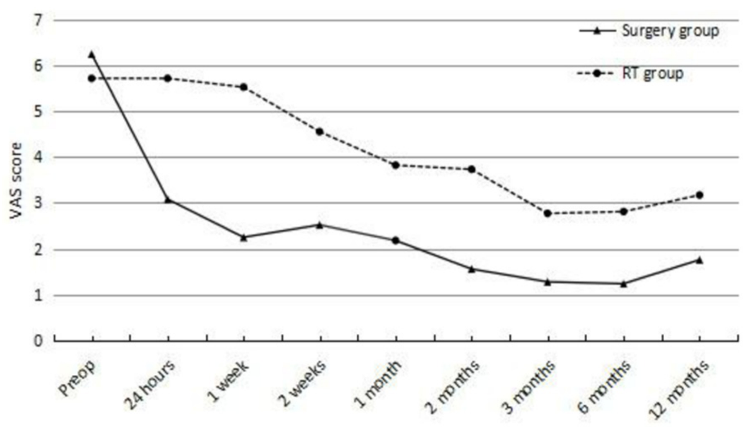

Figure 2. Pre-operative and post-operative VAS scores of surgery and RT groups.

Table 3. The ADL scores at pre- and postoperative 1 month and 3 months

Group	Pre-operative (N = 56)	Post-operative 1 month (N = 56)	Post-operative 3 months (N = 53)
Surgery	56.2 ± 8.9	81.6 ± 7.5*	84.6 ± 7.5*
RT	61.2 ± 10.3	61.3 ± 9.8	70.6 ± 12.3*
P-value	0.07	< 0.001#	< 0.001#

Notes: ADL, activities of daily living; RT, radiotherapy; N, number of patients; ns, not significant; *, $P < 0.05$ in comparison to preoperative ADL scores; #, compared with difference of postoperative and preoperative ADL scores

± 1.11, respectively (P < 0.001). VAS scores of the surgery group at 6 months after treatment were improved by an average of 5.0 ± 1.41, significantly better than that of the RT group (P < 0.001).

ADL scores were increased from pre-operative 56.2 ± 8.9 to post-operative 81.6 ± 7.5 (P < 0.05, **Table 3**). Multiple linear regression analysis showed that postoperative ADL evaluation (Y2) was related to the treatment method (X4) and pre-operative ADL evaluation (X5). Regression equation (Y2 = 52.31-0.793X4 + 0.715X5) showed that good postoperative life quality was related to surgery and good pre-operative life quality.

The overall median survival times were 12.6 months and 6 months and 12 month survival rates were 82% and 54%, respectively. The median survival time of surgery and RT groups were 14 months and 11.3 months, respectively. There was no significant difference in survival between the two groups (P = 0.662, **Figure 3**).

Discussion

Bone is the third most common site for metastases following lung and liver. The spine is the most common site of bone metastases. Incidence of spine metastases increases as patients with advanced cancer live longer. In the past, invasive surgical operation has not been recommended for spinal metastases. Radiotherapy was the primary treatment for spinal metastases. In 2005, a prospective randomized trial showed that decompressive surgery followed by radiotherapy was superior to radiotherapy alone. Subsequently, more and more surgical techniques have been used in the treatment of spinal metastases such as total spondylectomy, circumferential decompression, or posterior laminectomy decompression with stabilization, PVP, and PPSF. Selecting the appropriate surgery is an important part of individualized and multidisciplinary treatment due to the short life expectancy of most spinal metastases. The goal of treatment for metastatic spinal tumors is most often palliative rather than curative. The purposes of surgery are to relieve pain, maintain or improve neurological deficit, and improve the quality of remaining life. At present, surgery is an essential method of spinal cord decompression and spinal stability. Decompression surgery would be recommended for symptomatic spinal cord compression. For patients with severe mechanical pain such as compression fracture, minimally invasive surgery is preferred with shorter operation time, less bleeding, and quicker recovery. Therefore, chemotherapy and radiotherapy would not be delayed [11]. Moreover, it is also suitable for patients with poor general conditions that have surgical indications such as mechanical pain and ambulatory dysfunction caused by spinal instability. Many studies have confirmed that minimally invasive surgery is safe and effective for relieving mechanical pain and restoring spinal stability [9, 10, 12]. Metastatic lesion local control depends on post-operative radiotherapy or systemic chemotherapy.

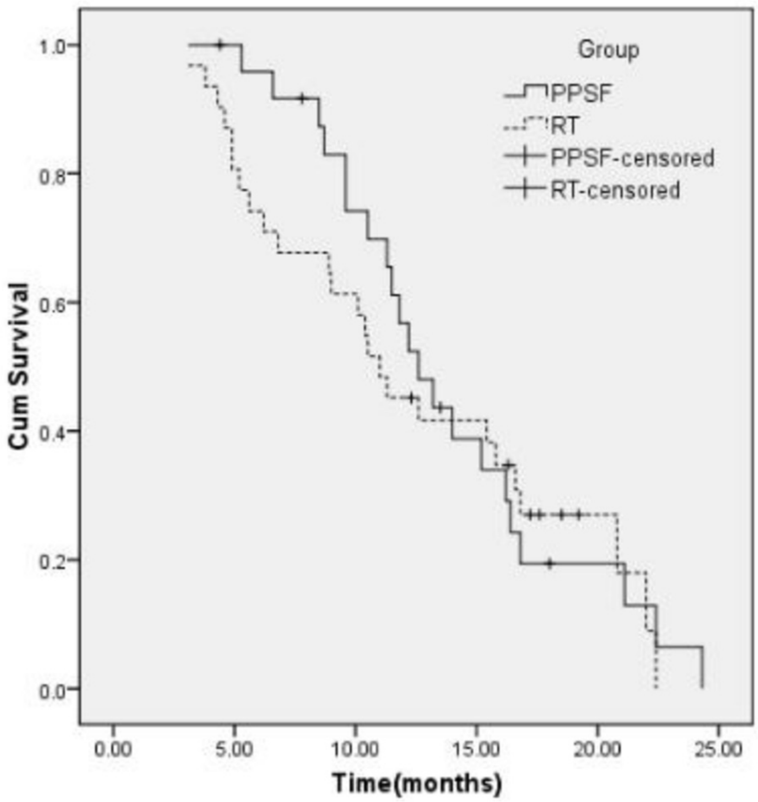

Figure 3. Survival curves of the two groups. The median survival time of surgery and RT groups were 14 months and 11.3 months, respectively (P = 0.662).

Normally, the vertebral body supports 80% axial load [13]. Unfortunately, 60-70% spinal metastases invade the vertebral body [14]. Affected vertebrae are at high risk of pathological fracture. Studies have shown that PVP can effectively relieve pain and improve spinal stability. Post-operative radiotherapy, chemotherapy, or molecular targeting treatment can reduce the local recurrence [2, 3, 15, 16]. However, PVP is associated with cement leakage in 10-40% patients [17, 18]. Stiffness and strength of affected vertebral body are associated with the volume of injected bone cement because the amount of injected PMMA has been correlated with cement leakage [19]. A sufficient amount of PMMA to restore spinal stability cannot be injected in all cases, to avoid cement leakage or tumor retropulsion. Therefore, the amount of PMMA should be individualized. Patients with an incomplete back wall of vertebra are unfavorable to PVP. Thus, PPSF may be a good choice for some patients who need to restore spinal stability but for whom PVP or kyphoplasty is unsuitable.

From single to multiple segments, PPSF can provide stabilization to fractured bodies with the help of upper and lower vertebral bodies. Studies have shown that long-segment fixation is better than short-segment due to dispersed stress [20]. In this study, PPSF was performed for 25 patients with mechanical pain. During the follow up, screws loosening or rods fracturing was not observed. The mean VAS decreased from preoperative 6.24 ± 1.05 to 3.08 ± 0.64 at the 24-hour postoperative time point ($P < 0.001$). However, VAS score of RT group at time points before postoperative 2 weeks was not a significant statistical difference from the preoperative baseline score. The two groups achieved long-term relief of mechanical pain. The pain status of surgery group was superior to RT group at each postoperative time point ($P < 0.05$). Meanwhile, ADL evaluation of surgery group was superior to RT group at postoperative 1 month and 3 month time points. We consider that PPSF followed by radiotherapy to be superior to radiotherapy alone in pain relief and improvement of quality of life. Four patients (13%) appeared with radiation-related compression fractures after radiotherapy, similar to other studies [21-23].

PPSF is a safe technique to stable vertebrae due to the use of intraoperative imaging technology. Our research has demonstrated that PPSF can be safely performed. There were no intervention-related complications and instrumentation failures in these patients through the last follow up. Moussazadeh et al. conducted a retrospective study showing that the proportion of patients with severe pain decreased from 86% preoperatively to 0% and 65% of patients reporting no referable instability pain postoperatively [9]. Recently, a study focused on complications of PPSF showed that PPSF for unstable spinal metastases had fewer complications, compared to open surgical procedures, and limited blood loss and high early ambulation rate [24].

Conclusion

In conclusion, treatment for spinal metastases should be individualized and employ a multidisciplinary strategy. Our preliminary results demonstrate that PPSF can be safely performed for spinal metastases. For some patients with spinal metastases, PPSF is a good option for alleviating pain and improving quality of life.

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Disclosure of conflict of interest

None.

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