Outcomes and survival of spinal metastasis with epidural compression

ABSTRACT

Objective: The goal of the study was to retrospectively evaluate the demographics, clinical manifestation, outcomes, treatment result, and survival of patients with spinal metastasis with epidural metastasis who underwent surgical treatment.

Materials and Methods: A retrospective evaluation of 103 patients with spinal metastasis and epidural compression who underwent surgical treatment between 2009 and 2015 was performed. The recorded parameters selected for the study were general demographic data (gender, age, and educational level) and clinical data (primary tumor, performance status according to Karnofsky score, neurological status according to Frankel scale, pain, surgical treatment outcomes, and patient survival).

Results: The mean age of the patients was 55.28 ± 15.79 years, and spinal metastasis was more frequent in males (61.7%). The two most frequent tumors were malignant breast cancer (26.21%) and prostate cancer (22.33%). Preoperative pain was presented in 96 (94.12%) patients and improvement was observed in 44 (47.31%) patients. Symptoms of spinal cord compression were the initial clinical manifestation of the primary tumor in 35 (33.98%) patients. Neurological deficit was observed in 66 (64.07%) patients, and improvement was observed in 43 (41.74%) patients. Improvement of functional outcome and pain was observed in 34 (37.38%) patients. The mean survival was 12.26 months. Longer survival (mean 19.13 months) was observed in patients who showed improvement in their ability to walk or kept it preserved (Frankel D or E).

Conclusions: Surgical treatment of spinal metastasis can improve pain and functional activities. Longer survival was observed in patients that keep or recovery the walking ability.

Keywords: Neoplasm, neoplasm metastasis, operative procedures, spine

INTRODUCTION

The spine is a common site for bone metastases, and it is reported that 60%–70% of patients with systemic cancer develop spinal metastases, although only 10% are symptomatic.[1,2] Spinal cord compression (SCC) occurs in 5%–20% of patients with spinal metastases, and there is an increased risk for developing SCC if cancer has already spread to bones. It can lead to significant morbidity due to pain, spinal instability, and neurological deficits.[1,3] Certain cancers display bone tropism with more than one-half of patients developing spinal metastases, such as prostate and breast.[1,4] The thoracic spine is the most frequently affected segment, followed by lumbar and cervical spine.[5,6] Epidural or vertebral metastasis is presented in 94.48% of patients, and intradural extramedullary (5%–6%) or intramedullary metastases (0.5%) are rare.[1,5]

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The widespread availability of advanced imaging and the improvement of survival with the use of target therapies have contributed to increase the magnitude of the problem related to spinal metastasis.[1,3] The number of spine metastasis has shown considerable increase, and it is expected an increase in the number of survivors and patients who will undergo surgery.[6,7]

Surgical treatment of spinal metastasis received acceptance and began to be widely used after the report of a controlled trial by Patchell *et al.* showing that surgery followed by radiotherapy provided better outcomes compared to radiotherapy alone in patients with a life expectancy superior to 3 months.[8] The report of Patchell *et al.* influenced the indication for surgical treatment of spinal metastasis and adopted the threshold of life expectancy that has also influenced the decision for surgical indication.[8,9]

The goal of surgical treatment of spinal metastasis remains palliative for pain relief, restoration or preservation of the neurological function, stabilization of spinal segment, and improvement of health-related quality of life.[10,11] The prognosis of spinal metastasis is not very promising and difficult to predict as well as the therapeutic decision. The surgical treatment is palliative, but patients with spinal metastasis and good-to-moderate prognoses seem to benefit from surgical treatment.[11-13] The therapeutic decision of spinal metastases has considered the nature of the primary tumor, the patient's overall clinical condition, neurological status, and survival scales.[1,7,14-16] However, it is very difficult to predict the prognosis of a patient with spinal metastasis and choose the best treatment option.

Our facility is a reference center for oncology, and the number of referred patients with spinal metastasis is growing. The motivation of the study was to perform a critical retrospective evaluation of patients who underwent surgical treatment of spinal metastasis with epidural compression.

MATERIALS AND METHODS

The study has been approved by the institutional ethical committee (IEC/6513/2015). A retrospective review and data collection of all patients with spinal metastasis and epidural compression who underwent surgical treatment between March 2009 and August 2015 in the Department of Orthopedics and Anesthesiology of the Faculty of Medicine of Ribeirao Preto - São Paulo University - Brazil - were performed. The inclusion criteria were patients older than 18 years with a diagnosis of spinal metastasis and epidural metastasis of solid malignant tumor who underwent surgical treatment. The exclusion criteria were patients who previously had a

surgical approach to spinal decompression and with diagnosis of hematological malignancy. One hundred and three patients who met the inclusion criteria were enrolled in the study.

Posterior decompression and stabilization using pedicle screw were the mainstay treatment in all 103 patients. Posterior reconstruction of the anterior column using methacrylate and cages was additionally performed in 25 patients and a combined approach in seven patients.

The recorded parameters selected for the study were general demographics data (gender, age, and educational level) and clinical data (primary tumor, performance status according to Karnofsky score,[17] location, neurological status according to Frankel scale,[18] pain, surgical treatment outcomes, and patient survival).

Statistical analysis

The clinical data were described through absolute and percentage frequencies (qualitative variables) and through measures such as mean, standard deviation, minimum, median, and maximum (quantitative variables). ANOVA followed by Tukey's test was used to compare the difference between time elapsed between the onset of symptoms and the performance of imaging for diagnosis. McNemar test was used to verify the effect of intervention in relation to qualitative variables (pain and classification according to Frankel scale in the pre- and post-operative period). The cumulative survival curve was generated by Kaplan–Meyer method and the log-rank test to evaluate curve differences. The level of significance (P) was set at 0.05.

RESULTS

Data of 103 patients were collected. Sixty-three (61.7%) were male. The mean age of the patients was 5.28 ± 15.79 years. The two most frequent tumors were malignant breast cancer (26.21%) and prostate cancer (22.33%). The primary tumor site was unable to be identified in 7 patients (6.8%) [Table 1]. The most common location of spinal metastasis was in thoracic spine (62 patients - 60.19%), followed by cervical spine (24 patients - 23.30%) and lumbar spine (17 patients - 16.50%).

A statistical difference was observed between educational levels in relation to the time elapsed between the onset of symptoms and the performance of imaging tests for diagnosis (ANOVA/Tukey's test - P 0.05). The longest period between symptoms and imaging tests for diagnosis was observed in patients with a low level of education [Table 2].

The patient performance scale according to Karnofsky performance status (KPS) was 50 in 9 *patient*s (8.91%), 60 in 33 *(32.67%)*, 70 in 34 *(33.66%)*, 80 in 21 *(20.79%)*, 90 in 3 *(2.97%)*, and 100 in 1 *(0.99%)* patient.

Preoperative pain was observed in 96 (94.12%) patients; however, 5 (5.88%) patients did not report pain despite spinal canal compression symptoms. Pain improvement was observed in 44 patients (47.31%), and there was statistical improvement of postoperative pain (McNemar test – $P < 0.05$), although 49 (52.69%) patients still had postoperative pain despite the stabilization and decompression of the affected vertebral segment.

The symptoms of spinal compression were the initial manifestation of the primary tumor in 35 (33.98%) patients. These patients were unaware of the presence of the primary tumor that was diagnosed after the treatment of spinal metastasis. Pre- and post-operative neurological deficit according to the Frankel scale is illustrated in Table 3. Preoperative neurological deficit was presented in 66 (64.07%) of patients and reduced to 43 (41.74%) after surgery. Ten patients were excluded from analysis because there was no reliable information. There was a statistical improvement of neurological deficit according to the Frankel scale in 38.73% of patients (McNemar test – $P < 0.01$). Worsening of the neurological deficit was observed in 3 (3.23%) patients [Table 3].

Functional improvement was considered as a change of Frankel A, B, or C to Frankel D or E [Table 4]. The patient who had improvement or kept Frankel D or E grade had a statistical longer survival (19.13 months) compared to patients who did not show functional improvement (7.89 months) (log-rank test [$P < 0.01$]) [Figure 1]. Considering the outcomes of functional improvement and pain, it was observed that 34 (37.38%) patients improved both and 19 (21.11%) patients did not improve both.

The mean patient survival of all patients was 12.26 months [Figure 1]. The patient survival varied according to the type of primary tumor, and it was higher in patients with prostate (average 17.46 months) and breast tumors (average 15.90 months). The survival of the six most frequent types of tumor is illustrated in Table 5.

The patient survival was statistically higher in patients that functional improvement (average 16.05 months) compared with patients without functional improvement (average 6.82 months) ($P = 0.05$).

The survival of patients who presented symptoms of spinal cord compression before de-diagnosis of the primary tumor (18.35 months) showed a statistical difference compared to the group of patients who already had a diagnosis of the primary tumor (11.57 months).

DISCUSSION

The sample of patients studied has confirmed the reports indicating the spine as a common site for bone metastasis that can produce epidural compression with high morbidity and

Table 1: Distribution of primary tumors

Primary tumor	Sex		Total, n (%)
	Male, *n* (%)	Female, *n* (%)	
Adrenal	1 (1.59)	0	1 (0.97)
Bladder	2 (3.17)	0	2 (1.94)
Oral cavity	3 (4.76)	1 (2.50)	4 (3.88)
Cervix	0	2 (5.00)	2 (1.94)
Colon	2 (3.17)	1 (2.50)	3 (2.91)
Esophagus	1 (1.59)	0	1 (0.97)
Small intestine	1 (1.59)	0	1 (0.97)
Breast	0	27 (67.50)	27 (26.21)
Choroid plexus melanoma	1 (1.59)	0	1 (0.97)
Nasopharynx	1 (1.59)	0	1 (0.97)
Oropharynx	1 (1.59)	0	1 (0.97)
Prostate	23 (36.51)	0	23 (22.33)
Lung	4 (6.35)	1 (2.50)	5 (4.85)
Rectum	3 (4.76)	2 (5.00)	5 (4.85)
Kidney	3 (4.76)	0	3 (2.91)
Sarcoma	7 (11.11)	1 (2.50)	8 (7.77)
Maxillary sinus	1 (1.59)	0 (0.00)	1 (0.97)
Unknown primary tumors	5 (7.94)	2 (5.00)	7 (6.80)
Testicle	2 (3.17)	0	2 (1.94)
Thyroid	2 (3.17)	2 (5.00)	4 (3.88)
Gallbladder	0	1 (2.50)	1 (0.97)
Total	63 (100.00)	40 (100.00)	103 (100.00)

Table 2: Time interval (days) of symptoms onset and imaging tests for diagnosis according to patient educational level

Educational level	n	Average (days)	SD	Minimum (days)	Median (days)	Maximum (days)	Tukey's test *P*<0.05
Illiterate	4	85	54.92	7	99	135	*
Incomplete 1ˢᵗ grade	14	300.79	554.62	1	90	2118	
1ˢᵗ complete elementary degree	58	65.97	71.58	1	52.5	365	*
2ⁿᵈ degree complete	19	81.89	57.05	17	69	198	*
University education	7	24	18.53	1	30	45	

*Statistical difference at the 5% level of significance. ANOVA followed by Tukey's test *P*<0.05. SD - Standard deviation

reduced quality of life.[1,2,4] The thoracic spine was the most frequent location, and breast and prostate spinal metastases were the most frequently observed primary tumor in our patients and other reports of the same country.[10,11,13,15,16,19] Contrary to what was reported in other countries, metastases of primary lung tumor were less frequent in our patients as well as in local reports.[10,13,15,19,20] This finding may be related to the lack of target therapies in our country, which has increased the survival of these patients. It was not possible to identify the primary tumor in 7 (6.8%) patients. Metastases of unknown primary tumor site are found in about 4% of all cancers and 13% of spinal metastases.[14,21] Unknown primary tumors are aggressive, and patient survival is shorter.[14,21,22] Spinal metastasis can occur in any age group; they are most

Figure 1: The Kaplan–Meier survival curve of the overall group of patients

Table 3: Pre- and post-operative neurological deficit according to Frankel scale

	Sex		Total, *n* (%)
	Male, *n* (%)	Female, *n* (%)	
Preoperative Frankel			
A	10 (15.87)	5 (12.50)	15 (14.56)
B	8 (12.70)	5 (12.50)	13 (12.62)
C	15 (23.81)	6 (15.00)	21 (20.39)
D	12 (19.05)	5 (12.50)	17 (16.50)
E	18 (28.57)	19 (47.50)	37 (35.92)
Postoperative Frankel			
Missing information	7	3	10
A	5 (8.93)	5 (13.51)	10 (10.75)
B	8 (14.29)	1 (2.7)	9 (9.68)
C	7 (12.50)	3 (8.11)	10 (10.75)
D	11 (19.64)	3 (8.11)	14 (15.05)
E	25 (44.64)	25 (67.57)	50 (53.76)
Total	63 (100.00)	40 (100.00)	103 (100.00)

commonly observed between 40 and 70 years and most frequent in males.[23,24] The mean age of our patients and the higher frequency in males were according to the reported literature.[1,2,5]

It has been suggested that the incidence of spinal metastasis would be higher in males than females because of higher incidence of prostate cancer relative to breast cancer.[1,23] However, in our patients, spinal metastasis was more frequent in males although breast was more frequent than prostate cancer in the overall group.

Education level has not been considered in the reports of spine metastasis. In our patients, the longest period between symptoms and imaging test for diagnosis was observed in patients with low level of education. A statistical difference was observed between educational levels in relation to the time elapsed between the onset of symptoms and the performance of imaging tests for diagnosis.

Pain is the most common manifestation in patients with spinal metastasis (80%–95%) followed by neurologic dysfunction (35%–75%),[1,25-27] and the findings of our patients are according to the literature. However, the first clinical manifestation in 33.98% of our patients was symptoms of spinal compression, and they were unaware of the presence of primary tumor. This clinical finding was similar in both sexes, and it has not been evidenced in the relevant literature.[1,23,25]

In our group of patients, we observed a statistical improvement in pain and neurological symptoms after surgical treatment (68% of patients were able to walk after surgery). A meta-analysis of nonrandomized cohorts showed that surgery was 1.3 times more likely to maintain ambulation and twice as likely to restore ambulation.[3,28,29] We did not take into account the modality of surgical treatment or the location of metastasis, but only the performance of decompression of the vertebral canal and surgical stabilization. Metastasis location, surgical approach, or method of reconstruction of the affected vertebral body was not considered.

The lack of patient-reported outcome instruments specifically designed for spinal oncologic disease and the retrospective collected data were a limitation to evaluate the improvement of health-related quality of life. We established the functional improvement criteria, including pain and neurological improvement (Frankel D and E). According to our established criteria, 37.38% of patients showed functional criteria improvement, and the survival of these patients was higher compared to patients that did not show functional
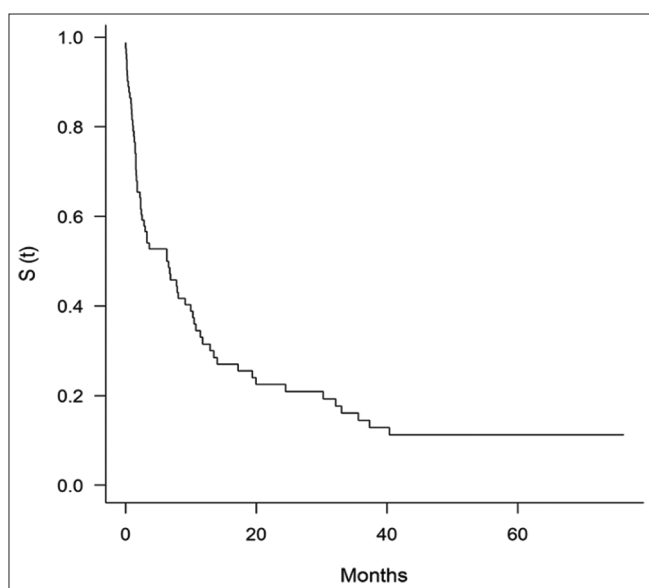
Table 4: Average survival (months) according to postoperative functional improvement

Frankel	Total	Deaths	Censored (%)	Average survival (95% CI)	P
		Time to death (months)			
Improvement or kept functionality preserved	64	50	14 (21.88)	19.13 (14.45–23.80)	<0.01
Worsen functionality	29	26	3 (10.34)	7.89 (4.58–11.20)	
Total	93	76	17 (18.28)		

*Log-rank test. CI - Confidence interval

Table 5: Average patient survival in months among the most frequent tumors

Primary tumor	Total	Deaths	Censored (%)	Average survival	95% CI for mean survival
		Time to death (months)			
Breast	27	22	5 (18.52)	15.90	10.27–21.53
Prostate	23	21	2 (8.7)	17.46	11.32–23.6
Lung	5	5	0	7.30	0–16.3
Rectum	5	5	0	5.00	0.1–9.9
Sarcoma	8	7	1 (12.5)	3.29	1.87–4.71
Unknown primary tumors	7	7	0	3.16	0–6.6

CI - Confidence interval

improvement. The surgical treatment was worth to perform on this group of patients. However, the identification of these groups of patient is still a challenge.

Although scales have been devised for survival of patients with spinal metastasis, there is the dearth of evidence related to predictors of neurologic, functional, and quality of life outcomes for patients with spinal metastasis.[7] Expected survival of at least 3 months has been presented as an essential prerequisite for surgical treatment.[8,25] However, these assumptions are not evidence-based, and it was reported that quality of life 6 weeks after surgery for spinal metastasis is independent of survival.[9] Considering the presence of epidural metastases in our patients, the surgical indication was related to its association with gross instability, pain, and/or neurological deficit that are classical indications for surgical treatment of spinal metastases provided that clinical conditions and other mentioned parameters were suitable to tolerate the surgical procedure.[11,26]

The overall general patient condition (KPS) has an important role in our surgical indication treatment. There was no patient with less than 50% according to KPS in our group of patients who underwent surgical treatment. KPS has been shown to be one of the strongest prognostic indicators for survival, and a significant association has been reported between KPS and duration of survival.[1,23,26] Prognostic factors for survival varied substantially according to the primary tumor combined with negative factor [Figure 2].[7,11,12]

Reported median overall survival of the patients with spinal metastasis and spinal cord compression ranges from 3–7 months, with a 36% probability of survival, to 12 months.[1] The mean survival of our patients was 12.26 months and statistically difference was observed among specific tumor type, functional improvement, walkability, and symptoms of spinal cord compression as the first tumor manifestation, according to similar reports.[30] Overall survival depends on the type of primary tumor, patient general condition, risk factors, and a multidisciplinary approach. Surgical treatment is only part of the therapeutic approach, and its association with other therapies has demonstrated positive outcomes.[1,2,5,11,25] Surgery should be reserved for patients with moderate or good prognosis, and it should be avoided for patients with poor prognosis.[12,25]

The surgical technique used in our patients followed the classical concept of stabilization and decompression of vertebral segment. Spinal stereotactic radiotherapy was not available in our facilities at the time. The reports of separation surgery and less invasive surgery associated with stereotactic radiotherapy can provide the reported results of surgery associated with radiotherapy with less morbidity and complications.[28,29] Unfortunately, we cannot afford reported drugs that are effective in treating spinal metastasis conservatively or associated with surgery.

The retrospective analysis of the results of patients with spinal metastasis and epidural compression, although with some drawbacks of the study design, allowed some conclusions that will contribute to improve the care of these groups of patients.

Surgery together with a multidisciplinary approach (pain management, radiotherapy, chemotherapy, surgery, and
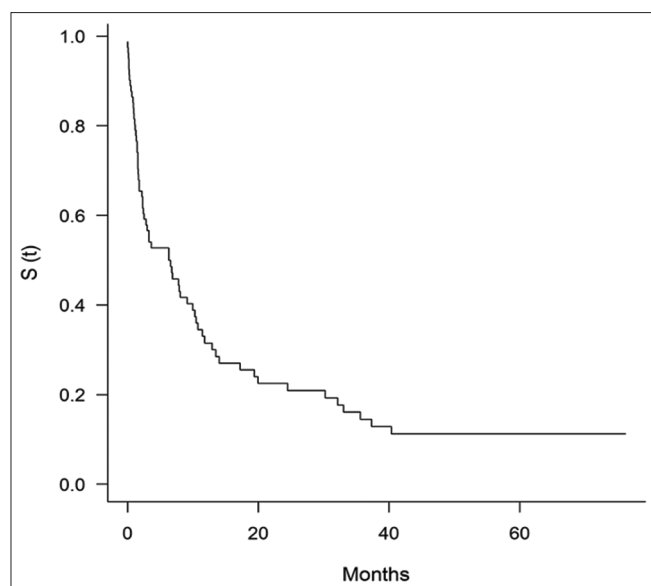
Figure 2: The Kaplan–Meier survival curve according to functional improvement. Red line represents Frankel A, B, and C patients. Black line represents Frankel D and E patients (functional improvement)

rehabilitation) has an important role in surgical treatment of spinal metastasis, and improvement in pain, neurological deficit, and function can be achieved. Less invasive surgery and new implant technologies associated with stereotactic radiosurgery or stereotactic body radiotherapy could offer less surgical morbidity and the advantages of the traditional surgical treatment for the selected group of patients.[28,29]

CONCLUSIONS

Surgical treatment of spinal metastasis with epidural compression should be considered in selected patients. Surgical treatment can improve pain, neurological deficit, and functional activities. Surgical treatment together with a multidisciplinary approach should be considered in selected patients.

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Conflicts of interest
There are no conflicts of interest.

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