Original Article

Is there a correlation between the spinal instability neoplastic score and mechanical pain in patients with metastatic spinal cord compression? A prospective cohort study

ABSTRACT

Introduction: The decision for selecting patients for surgical treatment of metastatic spinal cord compression (MSCC) is challenging even for experienced surgeons. Recently, the spinal instability neoplastic score (SINS) has been proposed to help surgeons in the evaluation of spinal stability in the setting of spinal metastases. This study aimed to evaluate the correlation between SINS and preoperative visual analog scale (VAS), as well as the pre- and post-operative association of the VAS and neurological function.

Methods: A prospective cohort study was conducted in a tertiary referral cancer center. Seventy-nine patients with MSCC were surgically treated from June 2012 to March 2015. Pain status before and after surgery was assessed using VAS score, and neurological status was evaluated using the American Spine Injury Association Impairment Scale (AIS) before and after surgery. Pain was classified as VAS (0–4) none or mild pain; VAS (5–8) moderate pain; and VAS (9–10) as severe pain. Neurological function was scored as AIS A: Complete deficits, AIS B–D: Incomplete deficits, AIS E: Neurologically intact. SINS degrees were classified as 0–6-stable; 7–12 potentially unstable, and 13–18-unstable. Spearman's correlation coefficient test was utilized for correlation between pain and SINS; Chi-square association test was utilized for evaluating pre- and post-operative pain and AIS, as well as the association between SINS and tumor types.

Results: A higher SINS correlates with severe mechanical pain preoperatively ($\rho = 0.38$, $P = 0.001$); surgical procedure improved neurological function ($P = 0.0001$), and decrease pain ($P = 0.84$). Finally, a higher SINS was also associated with osteolytic tumors ($P = 0.03$).

Conclusions: The SINS correlates with mechanical pain. Surgery provides a significant improvement in pain and neurological status, especially in patients who presented higher SINS scores and some degree of preoperative neurological function.

Keywords: Mechanical pain, metastatic spinal cord compression, spinal instability neoplastic score, spinal metastases

INTRODUCTION

The spine is the third most common site affected by metastases after the liver and lungs.[1] When bone metastases occur, a variety of skeletal related events (SREs) can take place, such as pain, hypercalcemia, pathological fractures, and neurological dysfunction secondary to metastatic spinal cord compression (MSCC).[2] The occurrence of these events are associated with significant decrease in patient's quality of life, specially MSCC, which is believed to occur in up to 10% of patients who develop spinal metastasis, furthermore, MSCC portends advanced disease and a shorter overall survival.[3-5]

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Recent advances and development of new treatments options have increased the survival of patients harboring malignant disease, and there is an actual trend toward a growing number of occurrence of such SREs in the past few decades.[6,7]

A randomized prospective trial demonstrated the superiority of surgery plus radiotherapy in comparison to radiotherapy alone in the management of MSCC in terms of maintenance and recovery of ambulation and sphincter function, functional status, and pain level reduction.[8] However, how to select patients for surgical treatment is still under debate. In this context, over the last decades, several scoring systems[5,9-12] have been proposed to predict survival of patients being treated with spinal metastasis, however they do not keep up with the incorporation of new treatment modalities, such as new chemotherapy agents, and especially the development of stereotactic spinal radiosurgery.[13] Laufer *et al*. proposed a decision-making algorithm to select patients to the appropriate oncologic treatment known as the NOMS framework considering these new treatment modalities.[14] In this context, the Spine Oncology Study Group published the score known as spinal instability neoplastic score (SINS).[15] This new score is used to assess the stability of the spine in patients with MSSC, even though with sparse clinical evidence about its real efficacy.[16,17]

Our study aims to evaluate the correlation between preoperative SINS and visual analogue scale (VAS for pain evaluation); and the pre- and post-operative association of the VAS and American Spine Injury Association Impairment Scale (AIS); SINS score and primary tumor association.

METHODS

A prospective analysis of data collected in 105 patients who presented with MSSC was performed. All patients underwent surgery aiming circumferential spinal cord decompression and stabilization between June 2012 and March 2015 in a tertiary cancer hospital in Goiania, Brazil. This study was approved by our Institutional Ethics Committee.

Inclusion criteria for surgical treatment were spinal instability according to the SINS, significant mechanical pain, symptomatic spinal cord compression for spinal metastases, life expectancy >3 months according to the clinical oncology evaluation and reasonable clinical status to underwent a surgical procedure. Patients with complete neurological deficits for >72 h did not undergo surgical treatment, as well as those with poor clinical status.

We excluded 16 patients who presented spinal cord compression by hematological disease (lymphoma or multiple myeloma) and 10 patients in which postoperative data was missing. Thus, 79 patients were followed in this cohort study.

Pre- and post-operative assessment tools

Pain and functional scores were obtained before and 3 months after surgery. The pain was evaluated using the VAS score as follow: VAS (0–4): mild pain; VAS (5–8): moderate pain; VAS (9–10): severe pain. Using the AIS assessed the neurological function. Spinal instability was graded in the preoperative computed tomography and magnetic resonance imaging scans according to the SINS [Table 1]. The patients were followed in the clinical outpatient care until the patient's death.

Statistical analysis

Spearman's correlation coefficient test was utilized for correlation between preoperative VAS and SINS. The Chi-square association test was utilized for evaluating the association between pre- and post-operative VAS and American Spine Injury Association; SINS and specific tumor types. The log-rank testing was utilized to evaluate the effect of the occurrence of visceral metastases and overall survival. The survival rate was analyzed according to the Kaplan–Meier method. The SPSS version 18.0 (PASW, Chicago, IL, USA) program was utilized for all calculations. $P < 0.05$ was considered statistically significant.

RESULTS

Pre- and post-operative demographic data and associations

This cohort consisted of 41 men and 38 women with a mean age of 57.9 years (range 20–85 years). The most frequent primary tumor sites were prostate ($n = 23$, 29.1%), breast ($n = 18$, 22.8%), lung ($n = 8$, 10.1%), digestive system ($n = 6$, 7.6%), and others ($n = 24$, 30.4%). The thoracic spine was the most commonly affected site ($n = 40$ patients, 52.5%), followed by the lumbar region ($n = 23$, 28.8%), the cervical spine ($n = 14$, 17.7%), and the cervicothoracic region (C7-T1) ($n = 2$, 2.5%).

The majority of our patients presented with preoperative neurological dysfunction, graded as AIS A ($n = 7$, 8.9%); AIS B ($n = 7$, 8.9%); AIS C ($n = 12$, 15.2%); and AIS D ($n = 28$, 35.4%). Normal preoperative function, AIS E, was observed in 25 (31.6%) patients. The preoperative VAS score was 9–10 in 68 (86.1%) patients; 5–8 in 9 (11.4%) patients; and 0–4 in 2 (2.5%) patients.

The majority of patients presented with spinal instability as defined by a SINS of 13–18 points ($n = 48$ patients, 60.8%). A total of 28 (35.4%) patients had a potentially unstable spine

Table 1: Demographics and clinical characteristics for study subjects

Characteristic	*n* (%)
Gender	
Men	41 (51.9)
Women	38 (48.1)
Total	79 (100.0)
Tumor main histology origin	
Breast	18 (22.8)
Prostate	23 (29.1)
Lung	8 (10.1)
Gastrointestinal	6 (7.6)
Other	24 (30.4)
Total	79 (100.0)
Metastases location	
Cervical	14 (17.7)
Thoracic	40 (52.5)
Lumbar	23 (28.8)
Cervicothoracic	2 (2.5)
Total	79 (100.0)
AIS preoperatively	
A	7 (8.9)
B–D	47 (59.5)
E	25 (31.6)
Total	79 (100.0)
AIS postoperatively	
A	4 (5.1)
B–D	22 (27.8)
E	53 (67.1)
Total	79 (100.0)
VAS preoperatively	
0-4	2 (2.5)
5-8	9 (11.4)
9-10	68 (86.1)
Total	79 (100.0)
VAS postoperatively	
0-4	77 (97.5)
5-8	2 (2.5)
Total	79 (100.0)
Radiological characteristic of the lesion	
Osteolytic	63 (80.0)
Mixed	8 (10.0)
Osteoblastic	8 (10.0)
SINS preoperatively	
0-6 (stable)	3 (3.8)
7-12 (potentially unstable)	28 (35.4)
13-18 (unstable)	48 (60.8)
Total	79 (100.0)
Status	
Death	49 (62.0)
Survival	30 (38.0)
Total	79 (100.0)

AIS - American Spine Injury Association Impairment Scale; SINS - Spinal instability neoplastic score; VAS - Visual analog scale

with SINS of 7–12 points. Only 3 (3.8%) patients had a stable spine with SINS of 0–6 points [Table 1].

Neurological improvement

A total of 47 (59.5%) patients were rated as AIS B-D before surgery, and this number was significantly reduced to 22 (27.8%) patients after surgical treatment ($P < 0.001$; Chi-square test). This improvement was maintained 3 months after surgery. A total of seven patients presented with complete paraplegia (AIS A), of those, five individuals (71.43%) who were operated within 72 h of installment of the dysfunction presented clinical improvement, being able to walk with assistance at the moment of hospital discharge (AIS D).

At presentation, pain was severe and intractable ($n = 68$), moderate ($n = 9$), and mild ($n = 2$). At 1 month, 79 patients (100%) had less pain. Of patients who presented with moderate to severe pain ($n = 77$), (97.46%) demonstrated improvement in pain level, with 75 (95%) improving to mild or no pain. At the last follow-up, 50 patients (63.2%) who were still alive continued to show an improved pain level compared to that at presentation. Overall, at last, follow-up 50 (63.2%) had either no pain or mild pain requiring intermittent analgesic use. The cases which presented worsening of pain or lack of improvement was always due to tumor recurrence, instrument failure, or new distant spine or bone metastases.

We observed a significant association between higher SINS and the following tumor types: breast, lung, and digestive tract cancer ($P = 0.03$). Prostate cancer was associated with intermediate SINS ($P = 0.03$; Chi-square test) [Table 2].

A statistically significant correlation was found between severe preoperative pain (VAS 9–10) and higher SINS (13–18), which occurred in 46 (67.6%) of patients ($\rho = 0.38$, $P = 0.001$) [Table 3].

Survival

The median survival was 6 months (95% confidence interval [CI]: 3.12–8.61 months), with a total of 26 (33%) patients alive at 12 months after surgery [Figure 1]. The mortality rates were 10%, 36%, and 67% at 30 days, 3 months, and 12 months, respectively. Patients who presented with visceral metastasis had median survival of 5.3 months 95% CI (3.4–7.2) months, significantly lower than (17.8 months), 95% CI [12.52–23.1] observed in patients who had disease restricted to the spine ($P = 0.039$-Log-rank Mantel–Cox) [Figure 2]. At 13 months, 25% of patients with visceral metastases were alive as compared with 66% of patients without visceral metastases.

Complications

We observed a total of 21 patients (26.58%) complications within 30 days after surgery. Wound infection and wound breakdown occurred in nine patients (11.4%) and six

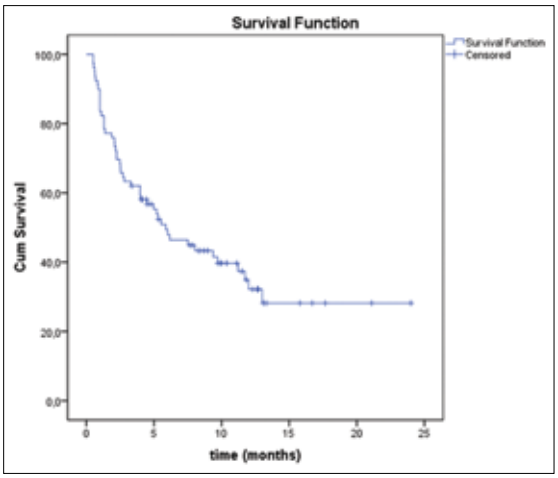

Figure 1: Mean global survival function - Kaplan–Meier plot

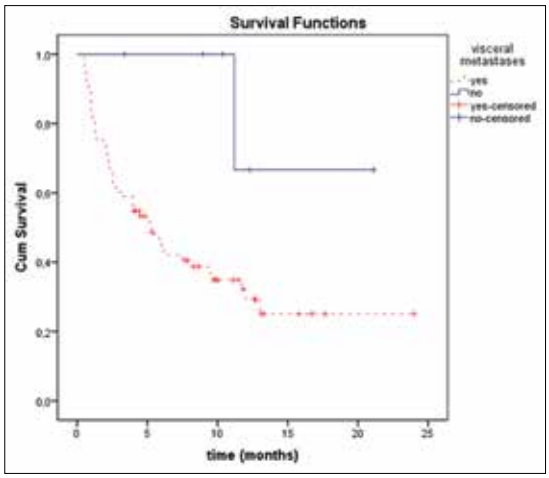

Figure 2: Mean survival function considering the presence of visceral metastases - Kaplan–Meier plot

Table 2: Associations between pre- and post-operative American Spine Injury Association, pre- and post-operative visual analog scale, spinal instability neoplastic score and tumor types

Preoperative ASIA	**Postoperative ASIA, *n* (%)**			***P***
	E	**B–D**	**A**	
E	25 (100.00)	0	0	<0.001
B–D	28 (59.57)	17 (36.17)	2 (4.26)	
A	0	5 (71.43)	2 (28.57)	
Preoperative VAS	**Postoperative VAS, *n* (%)**			***P***
	0-4	**5-8**	**9-10**	
0-4	2 (100.00)	0	0	0.84
5-8	9 (100.00)	0	0	
9-10	66 (97.10)	2 (2.90)	0	
Tumor type	**SINS, *n* (%)**			***P***
	0-6	**7-12**	**13-18**	
Breast	1 (5.26)	3 (15.79)	14 (73.68)	0.03
Prostate	2 (8.70)	14 (60.87)	7 (30.43)	
Lung	0	2 (28.57)	6 (85.71)	
Gastrointestinal	0	1 (14.29)	5 (71.43)	
Other	0	8 (33.33)	16 (66.67)	

AIS - American Spine Injury Association Impairment Scale; SINS - Spinal instability neoplastic score; VAS - Visual analog scale

Table 3: Correlation between spinal instability neoplastic score and preoperative visual analogue scale

Preoperative VAS	**SINS, *n* (%)**			**ρ**	***P***
	0-6	**7-12**	**13-18**		
0-4	0	2 (100.0)	0	0.38	0.001
5-8	2 (22.2)	5 (55.6)	2 (22.2)		
9-10	1 (1.5)	21 (30.9)	46 (67.6)		

ρ - Spearman's rank correlation coefficient; AIS - American Spine Injury Association Impairment Scale; SINS - Spinal instability neoplastic score; VAS - Visual analog scale

patients (7.6%), respectively. One patient presented with a cerebrospinal fluid leak (1.26%), two patients (2.5%) had pneumonia, one patient (1.26%) had a pulmonary embolism; finally, two patients (2.5%) presented neurological worsening after surgery.

We observed a significant increase in wound infection rates in patients who underwent preoperative radiotherapy ($P < 0.0001$, relative risk [RR]: 38.76) [Table 4].

DISCUSSION

Surgery for MSCC is considered a palliative treatment, usually reserved for patients with life expectancy >3 months, although this cutoff is fairly arbitrary.[18] The palliative advantages of surgical decompression and stabilization includes pain relief, maintenance and recovery of neurological function, improvement in local control and quality of life.[3,8,19-22] Several retrospective and prospective studies reported improvement in quality of life, overall survival, and neurological function after surgical treatment of MSCC.[8,11-13,23-30] Our results corroborate with this results. We analyzed three main factors used for decision-making in the surgical indication for MSCC: preoperative SINS, AIS, and VAS.

The most common tumor histology in the present study was prostate, breast, lung, and digestive tract, respectively. We were unable to identify differences in survival related to tumor histology in our cohort, however, other authors have reported better life expectancy for prostate and breast, compared with lung and digestive tract metastatic lesions.[13,29]

The majority of our cases presented with advanced disease where 74 patients (93.67%) had nonremovable visceral metastases. We observed a significantly longer overall survival at 13 months in the three patients (3.8%) without visceral metastases when compared to the 19 patients (24%) who were suffering from metastatic visceral disease ($P = 0.039$).

An analysis of the SINS in our patient's population demonstrated that up to 96.2% of our cases presented with

Table 4: Relative risk between wound infection and preoperative radiotherapy

Preoperative radiotherapy	Wound infection, *n* (%)		*P*	95% CI
	Yes	No		
Yes	9 (40.9)	13 (59.1)	<0.0001	38.76 (4.50-333.59)
No	1 (1.8)	56 (98.2)		

CI - Confidence interval

some evidence of mechanical failure, where 60.8% were classified as unstable and 35.4% as potentially unstable. Interesting, we also observed a significant correlation between higher SINS (13–18), and higher preoperative VAS (9–10) ($P < 0.001$ and $\rho = 0.38$).

Specific tumor types, such as breast, lung, and digestive tract metastatic lesions were significantly associated with higher SINS ($P = 0.03$). This finding may be explained by the osteolytic nature of these tumors, which are commonly associated with fractures and mechanical instability.

Surgery followed by radiation has higher chances to improve neurological function when compared to radiation alone.[8,22] We observed a significant functional improvement in 28 (60%) patients, which changed from incomplete neurological deficits to normal neurological function after surgery ($P < 0.001$). Surgical treatment allowed faster and sustained neurological recovery when decompression and stabilization was performed within 72 h of the installment of deficits. From the seven patients who had been admitted to the emergency surgery <72 h earlier, 5 (71.43%) had improved in their neurological function, with four out of five being able to walk with assistance.

The vast majority of our patients (97.46%) presented with moderate or severe mechanical pain. It is well known that such pain related with spinal instability is refractory to conservative management. In accordance to the experience of other authors, we observed significant clinical benefit with surgery, where 66 out of 68 patients who initially had a VAS score of 9–10, reporting a postoperative VAS score of 0–4.[2,3,13,19]

The occurrence of surgical complications in cases of MSCC is estimated to be as high as 20%–30%, with wound infection occurring in up to 30%.[13,19,31,32] We observed a complication rate of 27% in our cases, of those, wound infection occurred in 11.4%, with 6.6% of such patients requiring reoperation. We observed a very strong association between preoperative radiotherapy and wound infection (RR = 38) ($P = 0,0001$), which has been previously reported in other series, potentially attributed to radiation-induced skin changes, such as fibrosis and decreasing blood irrigation.[8,33,34]

The median overall survival of our cohort was 6 months [Figure 1]. This result is comparable with previous studies, in which a median survival varies between 5 and 14 months.[5,12,35]

We observed a mortality rate after 1, 3, and 12 months of 10%, 36%, and 67% respectively, which similar to the mortality rate reported in a prospective study conducted by Fehlings *et al*.[27] Furthermore, our 30-day mortality rate was 10%, which was also similar to the experience of other authors ranging from 4 to 22%.[13,31,32,36] Our study is limited to the relative small size and the heterogeneity of tumor types. However, we reported the relationship among the SINS, VAS, and neurological status, which may help spine surgeons to choose the best management of treat their patients with MSCC.

CONCLUSIONS

Our results go along with the notion that surgery MSCC improves neurological function and pain level of the great majority of the patients. We found a significant correlation with improvement in VAS score and functional outcome. Finally, surgery provided a significant improvement in pain and quality of life, especially in patients who presented higher SINS scores and preoperative neurological dysfunction.

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Conflicts of interest
There are no conflicts of interest.

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