EFFECTIVENESS OF THE SURGICAL INTERVENTION IN THE QUALITY OF LIFE AND SURVIVAL OF PATIENTS WITH METASTATIC LESIONS IN THE SPINE

EFETIVIDADE DA INTERVENÇÃO CIRÚRGICA NA QUALIDADE DE VIDA E NA SOBREVIDA DOS PACIENTES COM LESÕES METASTÁTICAS NA COLUNA VERTEBRAL

EFECTIVIDAD DE LA INTERVENCIÓN QUIRÚRGICA EN LA CALIDAD DE VIDA Y EN LA SOBREVIDA DE LOS PACIENTES CON LESIONES METASTÁSICAS EN LA COLUMNA VERTEBRAL

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ABSTRACT

Objective: To evaluate the impact of surgical treatment of metastatic epidural spinal lesions on the quality of life of patients, pain relief and survival. Methods: Patients with single or double spinal lesions, in good clinical conditions to undergo surgery, were included. Staging and prognostic evaluation were performed, based on imaging studies, according to the criteria of Enneking and Tokuhashi, and neurological status (Frankel), pain (visual analogue scale, VAS) and quality of life index (Oswestry) were also assessed. Survival was calculated. Results: The study included 67 patients, 34 men and 33 women, aged 13-88 years (mean: 53). Most had the breast (23 cases) as the primary site of the tumor and metastasis in the lumbar region, especially in L2 and L3. Pathologic fractures were diagnosed in 45 patients. The mean VAS score was initially 9 (5-10) reducing in the second day after surgery to 2 (1-7) and to 1 (0-6) in the first and sixth months. Following 6 months, 18 deaths were observed (one intraoperatively, five in the first month and 12 at 6 months). The neurological status was correlated with survival: patients who were Frankel E before surgery showed increased survival. Conclusion: The surgery does not influence patient survival, except for patients with neurological deficits, who have a worse prognosis. Treatment of metastatic lesions is often palliative, but patients present improved neurological and pain relief and few complications after surgery, justifying surgical intervention.

Keywords: Neoplasm metastasis; General surgery; Quality of life; Spine; Therapeutics; Prognosis.

RESUMO

Objetivo: Avaliar o impacto do tratamento cirúrgico de lesões metastáticas epidurais na coluna vertebral sobre a qualidade de vida dos pacientes, a melhora da dor e a sobrevida. Métodos: Pacientes com lesão única ou dupla na coluna vertebral, em condições de serem submetidos à cirurgia, foram incluídos. Foram realizados estadiamento e avaliação prognóstica a partir de exames de imagem, pelos critérios de Enneking e Tokuhashi, avaliação neurológica (Frankel), da dor (escala visual analógica, EVA) e da qualidade de vida (índice de Oswestry). Foi calculada a sobrevida. Resultados: Foram incluídos no estudo 67 pacientes, 34 homens e 33 mulheres, com idade de 13 a 88 anos (média: 53). A maioria tinha a mama (23 casos) como sítio primário do tumor e metástase na região lombar, principalmente em L2 e L3. Fratura patológica foi diagnosticada em 45 pacientes. O escore médio na escala EVA foi inicialmente 9 (5-10), reduzindo-se, no segundo dia após a cirurgia, para 2 (1-7) e para 1 (0-6) no primeiro e sexto meses. No seguimento aos 6 meses, foram observados 18 óbitos (um intraoperatório, cinco no primeiro mês e 12 aos 6 meses). A situação neurológica correlacionou-se com a sobrevida: os pacientes que no momento da cirurgia estavam em Frankel E apresentaram sobrevida maior. Conclusão: A cirurgia não influencia na sobrevida do paciente, exceto nos pacientes com déficit neurológico, que apresentam pior prognóstico. O tratamento da lesão metastática é muitas vezes paliativo, mas os pacientes apresentam melhora neurológica e alívio da dor e poucas complicações, justificando a intervenção cirúrgica.

Descritores: Metástase neoplásica; Cirurgia geral; Qualidade de vida; Coluna vertebral; Terapêutica; Prognóstico.

RESUMEN

Objetivo: Evaluar el impacto del tratamiento quirúrgico de lesiones metastásicas epidurales en la columna vertebral sobre la calidad de vida de los pacientes, la mejoría del dolor y la sobrevida. Métodos: Se incluyeron pacientes con lesión única o doble en la columna vertebral, en condiciones de ser sometidos a cirugía. Se realizaron estadiamiento y evaluación pronóstica, a partir de exámenes de imagen, según los criterios de Enneking y Tokuhashi, evaluación neurológica (Frankel) y del dolor (escala visual analógica, EVA), y de la calidad de vida (índice de Oswestry). Se calculó la sobrevida. Resultados: Se incluyeron en el estudio 67 pacientes, 34 hombres y 33 mujeres, de edades de 13 a 88 años (promedio: 53). La mayoría tenía la mama (23 casos) como sitio primario del tumor y metástasis en la región lumbar, principalmente en L2 y L3. Fractura patológica fue diagnosticada en 45 pacientes. La puntuación promedio en la escala EVA fue, inicialmente, 9 (5-10), reduciéndose, en el segundo día después de la cirugía, para 2 (1-7) y para 1 (0-6) en el primero y sexto meses. En el seguimiento, a los 6 meses, se observaron 18 óbitos (uno intraoperatorio, cinco en el primer mes y 12 a los 6 meses). La situación neurológica se correlacionó con la sobrevida: los pacientes, quienes a la fecha de la cirugía estaban en Frankel E, presentaron sobrevida más prolongada. Conclusión: La cirugía no tiene influencia en la sobrevida del paciente, excepto para los pacientes con déficit neurológico, que presentan pronóstico peor. Muchas veces, el tratamiento de la lesión metastásica es un paliativo, pero los pacientes presentan mejoría neurológica y alivio del dolor, y pocas complicaciones, justificando la intervención quirúrgica.

Descriptores: Metástasis neoplásica; Cirugía general; Calidad de vida; Columna vertebral; Terapéutica; Pronóstico.

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INTRODUCTION

An estimated 1.47 million cases of cancer are diagnosed annually in the United States.[1] The skeletal system is the third most common site of metastatic implantation.[2,3] With improvements in the adjuvant treatments of tumors, the life expectancy of patients has increased, and with it, the incidence of associated lesions.[4] Thus, 50% of these patients will develop bone metastases,[5] and the spinal column is the most commonly affected location of the musculoskeletal system.[6,7]

The metastatic involvement of the spine can be manifested in various ways, and pain is the main symptom, present in virtually all cases, often intensively, and leads the patient to a decrease of their activities, and, in many cases, to a restriction of ambulation.[8] The presence of bony destruction very often leads to fracture, instability, and deformity. It progresses to the more severe presentation, which is neural compression, either by a pathologic fracture or tumoral invasion.[9,10]

Surgical intervention plays an important role in the treatment of patients with epidural lesions with or without compressed neural tissue. Other treatments include radiation, chemotherapy, the use of orthotics, pain management, and radiosurgery. Surgical treatment has provided the patient with pain relief, protection of neural tissue, and the possibility of walking. It thereby improves the quality of life, because it allows for relative independence and the decreased use of analgesics.[11,12]

The objective of this study is to evaluate the results of the surgical treatment of epidural metastatic lesions of the spine, evaluating the impact of surgery on the patients' quality of life, pain relief, and correlating with primary focus, sex, and survival.

PATIENTS AND METHODS

Prospective observational study beginning in July 2006 and ending in January 2010, including all consecutive patients with metastatic spinal lesions who presented the conditions for undergoing surgery at the Department of Orthopedics and Traumatology, Hospital Santa Marcelina, São Paulo, Brazil.

Inclusion criteria: single or double lesions in the spine in patients meeting clinical conditions to undergo surgical intervention based on the evaluation of the American Society of Anesthesiologists (ASA),[13] including ASA patients I, II, and III.

Exclusion criteria: severe systemic involvement, previous radiotherapy in the affected vertebral segment, disseminated systemic disease, and previous spinal cancer surgery.

After diagnosis, all patients underwent staging, which was conducted starting with computed tomography (CT) of the chest, abdomen, pelvis, and the vertebral segment involved; magnetic resonance imaging (MRI) of the affected segment and bone scintigraphy, according to the criteria of Enneking *et al*.[14] If other segments of the spine showed uptake on scintigraphy, the segments were included in the imaging study.

The patients were operated with posterior instrumentation (pedicle screws) or an anterior and posterior approach in the lumbar spine. All patients underwent radiotherapy after surgery, at a dose of 3000 cGy fractionated into 10 sessions.

Neurological status was assessed by the scale of Frankel *et al*.[15] The preoperative assessment was made based on the criteria of Tokuhashi *et al*.[16] Pain was assessed using the visual analogue scale (VAS) preoperatively, immediately postoperatively, and in the first and sixth month.

Survival was recorded as the number of patients alive at the 12-month follow-up.

Quality of life was assessed indirectly by the Oswestry functional assessment questionnaire (ODI, Oswestry Disability Index).[17,18]

Statistical analysis included chi-square test, Fisher's exact test, Student's t-test, Mann- Whitney test, Spearman correlation, and analysis of variance (ANOVA), and was performed using the Statistical Package for Social Sciences (SPSS) software.

RESULTS

During the study period, 67 patients were included, 34 men and 33 women. The age ranged from 13 to 88 years with a mean of 53 years. (Figure 1)

The region that was primarily affected by cancer was the breast in 23 cases, the prostate in 11 cases, the gastrointestinal system in seven cases, the lung in six cases, the kidney in five cases, the thyroid in three cases, the uterus in three cases, and the tumor was hematopoietic in four cases. The primary site could not be located in four cases. There was one case of osteosarcoma.

The most affected topography was the lumbar spine, specifically L2 and L3, responsible for 23 of the diagnosed cases. Two patients with a tumor in two non-contiguous vertebrae were included because of their clinical condition, one patient with a lesion in T11 and L2 and the other with involvement in T6 and L3, both with primary breast cancer showing a good response to adjuvant treatment. Pathologic fracture was observed in 45 patients.

The most commonly performed surgery was that of posterior instrumentation with pedicle screws, performed in 62 patients, cervical corpectomy in three cases, and anterior and posterior approach was performed in the lumbar spine in two patients. (Figure 2)

Regarding the evaluation of neurological status by the Frankel *et al*.[15] scale, 49 patients presented Frankel E, 11 Frankel D, six Frankel C, and one Frankel A. No patient was observed with Frankel B. (Figure 3)

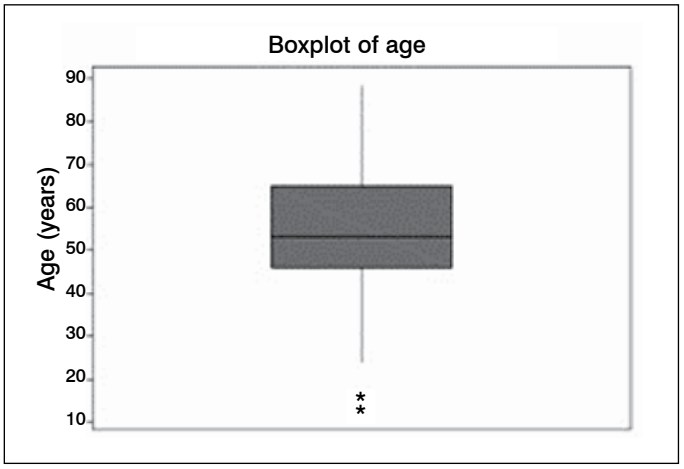

Figure 1. Mean age of the patients with metastatic lesions in the spine.

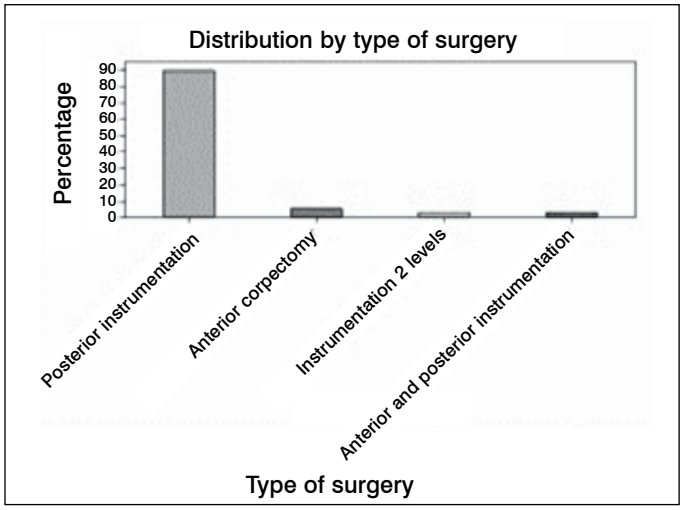

Figure 2. The surgery with posterior instrumentation is a significant majority (chi-square test with $p < 0.001$). There are no significant differences in the proportion of other surgeries (chi-square test with $p = 0.867$).

We noted that SIIb staging was predominant. In the evaluation of prognostic criteria, the lowest Tokuhashi score was seven, but this patient was admitted to the emergency room with cauda equina syndrome requiring emergency decompression, and the highest score was 14, with a mean of 10.

The initial mean VAS score was 9 (5-10). In the immediate postoperative period, collected on the second day after surgery, it was 2 (1-7). On the first and sixth month, it was 1 (0-4), with no changes. Using ANOVA for repeated measures calculation, a significant decrease was observed from the preoperative to the immediate postoperative period and in the first and sixth month, but no difference was present between the last two ($p < 0.001$) (Figure 4).

Through the Oswestry questionnaire (ODI), it was possible to evaluate the patients' limitations preoperatively, and in the first and sixth month (we did not use it in the immediate postoperative period since a more complete evaluation of patients was not possible). The average before surgery was 54%, ranging from 31 to 81%. At one month, the average was 29% (12-53%), and at six months, the average was 16% (4-42%). We observed a significant decrease in the evaluation among patients in the postoperative follow-up ($p < 0.001$). (Figure 5)

The mean survival was 10 months (0-24), with a standard deviation of 8.3. In the six-month follow-up, we recorded a total of 18 deaths, one during surgery, five in the first month, and 12 in the six-month follow-up. The intraoperative death was due to thromboembolic complications.

We observed that the mean age for males was higher than females, 57 years for men and 50 years for women, but this was of no significance from a statistical standpoint. (Figure 6)

When comparing the affected site in relation to sex, we found significant differences only in L2, with a higher proportion of males (Fisher's exact test, $p = 0.003$).

There was no significant difference regarding sex and postoperative pain. Pain relief was observed in both sexes, with a significant improvement in the VAS score (group $p = 0.6150$; intragroup $p < 0.001$). (Figure 7)

When comparing the Tokuhashi criteria and the sex of the patients, we observed no significant difference in mean between the sexes according to the Student's t-test ($p = 0.175$).

When we analyze the quality of life in relation to sex, we observed that there is no difference between the sexes. There was difference in the ODI in both sexes, with a significant improvement in all (intergroup $p = 0, 361$; intragroup $p < 0.001$). (Figure 8)

We found a widely varying average of age among the tumors. Lymphoma showed an average of only 14 years, whereas multiple myeloma was 72 years, and a young average for gynecological tumors of only 33 years. (Figure 9)

We compared age with pain and previous fractures and no significant differences were observed for the distribution of age and presence of fracture (Mann-Whitney test, $p = 0.466$).

By calculating the Spearman correlation between age and pain at the various moments, we found no significant correlation

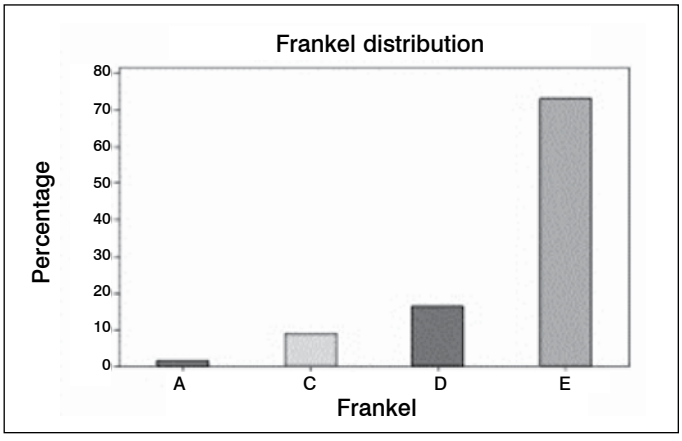

Figure 3. There are significant differences in the proportions of Frankel (chi–square test with $p < 0.001$). Searching for which proportion of Frankel type differs from the others, we found that Frankel type E is the significant majority (chi–square test with $p < 0.001$).

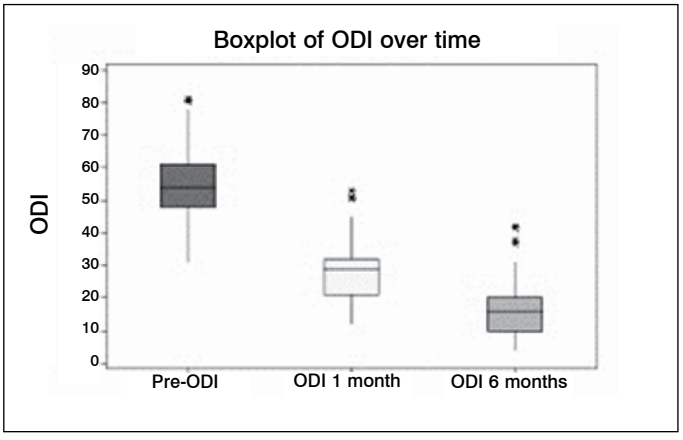

Figure 5. Comparing ODI by repeated measures ANOVA, we found significant differences over time ($p < 0.001$). All times differ significantly between them (all $p < 0.001$).

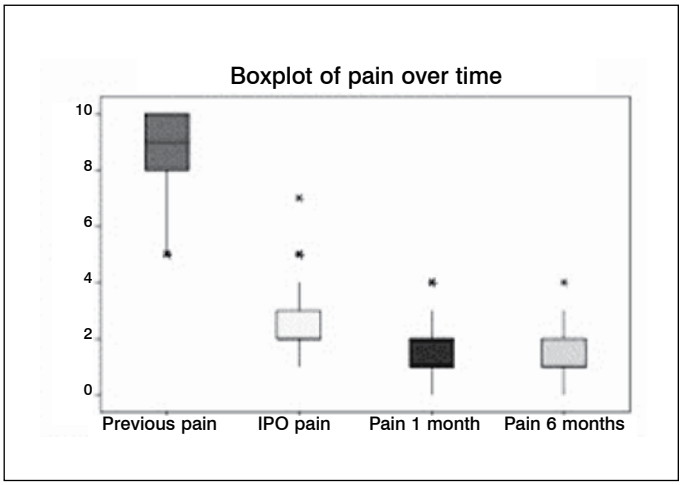

Figure 4. Comparing pain over time by repeated measures ANOVA, we found that there are significant differences over time ($p < 0.001$).

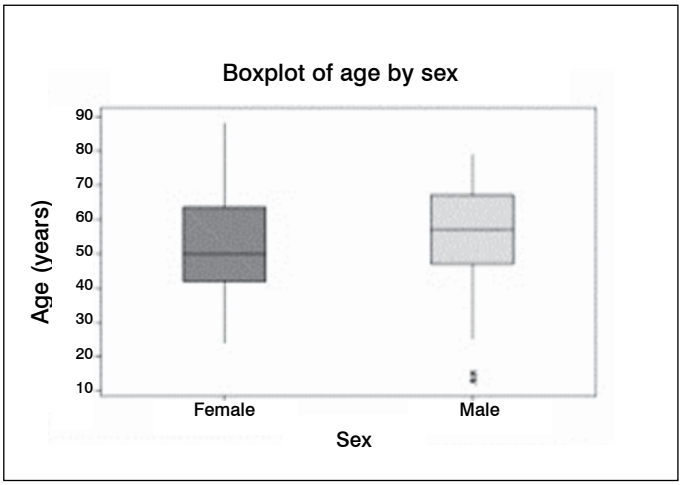

Figure 6. Comparing the mean age between the sexes by the Student's t-test, we found no significant differences between them ($p = 0.397$).

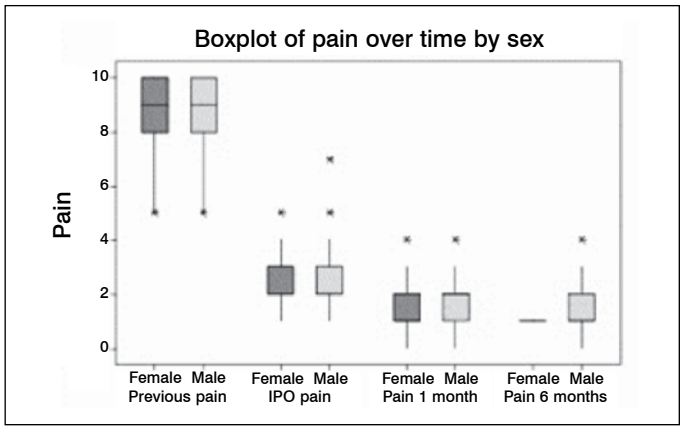

Figure 7. Using repeated measures ANOVA, we found no significant differences in the behavior of pain over time between sexes (interaction p = 0.360). Between the sexes, we found no significant differences at any time (intergroup p = 0.615). Over time, we found significant changes in pain in both sexes (intragroup p < 0.001). That is, except for between one month and six months (p = 0.797), all other time points differed between them in pain (p < 0.001).

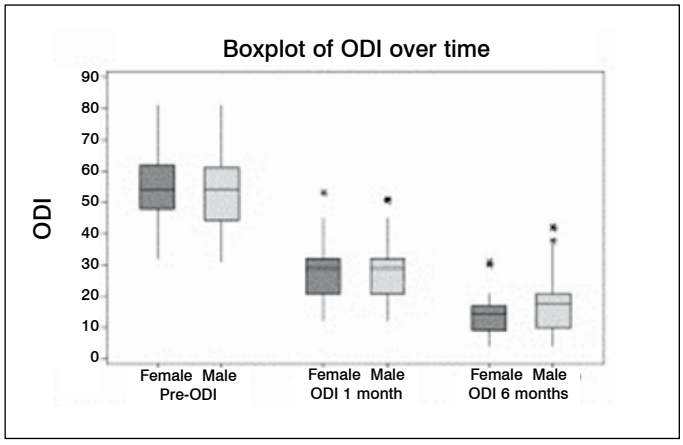

Figure 8. Using repeated measures ANOVA, we found no significant differences in ODI behavior over time between sexes (interaction p = 0.412). Between the sexes, we found no significant differences at any time (intergroup p = 0.361). Over time, we found significant changes in pain in both sexes (intragroup p < 0.001). All time points differed between them (p < 0.001).

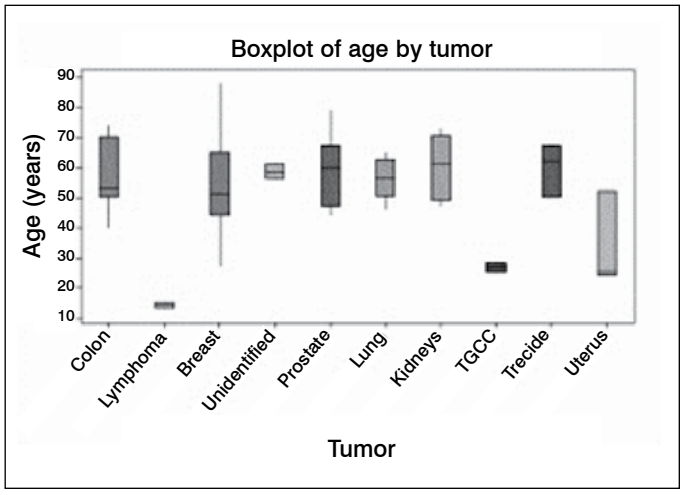

Figure 9. Comparison of mean age by ANOVA among tumors, we found significant differences between the different types in relation to primary site (p <0.001).

between age and pain at any time. By relating tumor type and pain with previous fracture, we found no significant difference between those who had a previous fracture for the various tumor types (chi-square test, p = 0.695). Using a repeated measures ANOVA, we found no significant differences at any time (intergroup p = 0.177). Over time, we found significant changes in pain for all tumors (intragroup p < 0.001).

In the analysis of staging based on the Enneking criteria related to fracture, we found significant differences in the proportions of those who had a previous fracture between the Enneking stages (chi-square test with p < 0.001). The type with greatest number of previous fractures was the SIB (p = 0.006).

We found no significant relationship between the presence of pain and previous fractures, noting that pain did not differentiate those who have to those who do not have fractures (intergroup p = 0.776). We observed significant pain improvement in both groups, regardless of the presence of fracture (p = 0.001). (Figure 10) We also observed that the presence or absence of fracture did not interfere in the quality of life of patients. We verified that the limitation measured by the ODI was similar for those who did and those who did not have a fracture, and that improvements in daily limitations occurred in both patients, regardless of the associated fracture. (Figure 11)

In calculating the Spearman correlation between pain and the Tokuhashi score, survival, and ODI, previous pain had a correlation only to the Tokuhashi score (r = -0.391 with p = 0.001), meaning that the higher the prior pain, the smaller the Tokuhashi value, and the pre-ODI (r = 0.282 with p = 0.021), meaning that the higher the prior pain, the greater the ODI.

Comparing the neurological status and survival, we found that Frankel E patients at surgery had a higher survival than other patients (ANOVA with p < 0.001). (Figure 12)

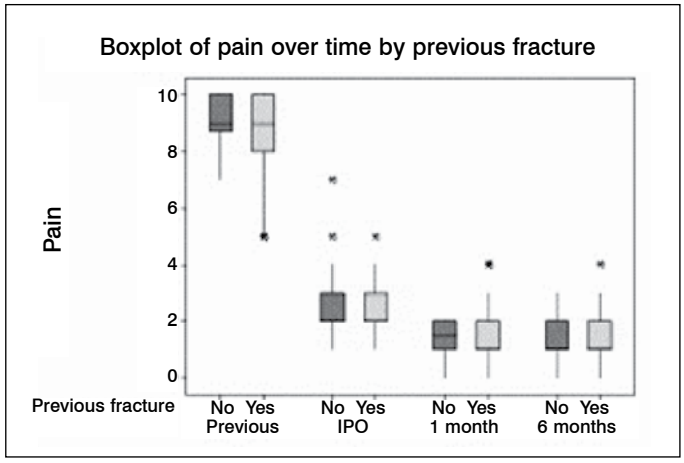

Figure 10. Using repeated measures ANOVA, we found no significant differences in the behavior of pain over time among those who did or did not have a fracture (interaction p = 0.230). Among those who did or did not have a previous fracture, we found no significant differences at any time (intergroup p = 0.776). Over time, we noticed significant changes in pain for those who had and those who did not have a previous fracture (intragroup p < 0.001). Seeking the time point that differed from the others, we found that only one month did not differ significantly from six months, with the remaining moments being significantly different between them (p < 0.001).

DISCUSSION

Life expectancy and quality of life, especially the latter, are important factors to be assessed prior to lumbar spine surgery, for it is a major surgery with significant risks. North *et al*.[19] reported that the appropriate choice of the patient may bring greater benefits; neural protection is always based on values or factors. North *et al*. revised some prognostic factors, such as the primary tumor, noting that

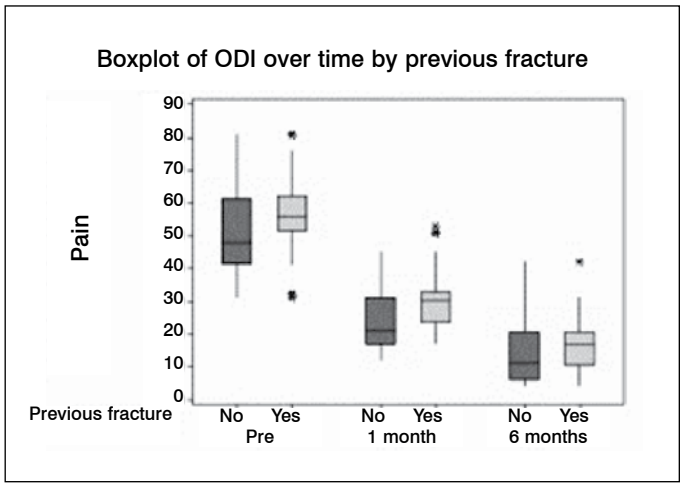

Figure 11. Using repeated measures ANOVA, we found no significant differences in the behavior of ODI over time among those who did or did not have a fracture (interaction p = 0.157). Over time, we noticed significant changes in ODI for those who did and who did not have a previous fracture (intragroup p <0.001). We found significant differences between all time points.

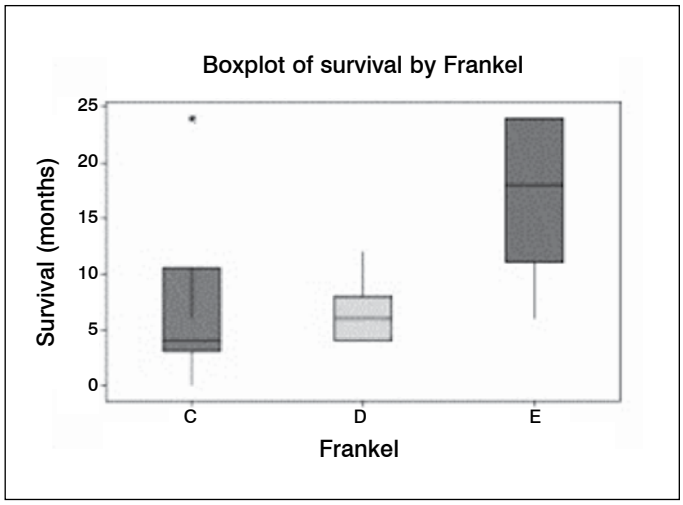

Figure 12. We found significant differences in mean survival between the Frankel types (ANOVA with p < 0.001). Patients with Frankel E present an average survival significantly higher than the others.

lung or gastrointestinal tumors had a worse outcome, and as did we, based on the Tokuhashi criteria, also using the type of tumor as a criterion. We observed that more aggressive tumors showed greater limitations and more intense pain, with greater restrictions.

The same authors observed that a neurological deficit worsened the prognosis of the patient, a fact confirmed by us: patients who had a worse loss of strength and were restricted to the bed evolved poorly, including an intraoperative death in one patient, who had been confined to a wheelchair due to loss of strength.

Soares[20] performed a very interesting survey evaluating the mechanisms of metastatic implantation, explaining why some diseases prefer the spine to other sites, assessing not only the vasculature, but also the ratio of stimulatory and inhibitory tumor growth factors and their relation to tumor growth, in addition to the tissue predisposition to cancer cells implantation.

Vrionis *et al*.[21] performed an analysis of en bloc resections of patients with spinal metastases, but reported that the outcome is uncertain, and that there is a decrease in local recurrence, but that it is unrelated to improved survival in patients. We performed corpectomy in only two cases, obtaining good results in one, but the other, who at the time of surgery showed only focal uptake in the lumbar spine, developed distant metastasis and local recurrence, progressing to death seven months after surgery.

The evaluation based on the criteria of Panjabi *et al*.[22] has not been well established for tumor lesions, generating questions, and sometimes did not make clear how mildly unstable changes could evolve into a neurological deficit or intractable pain. Some authors have suggested new classifications for better assessment.[23-25] This author used the Kostuik criteria as a base for better assessment of instability. In our study, there was a high prevalence of pain without a direct correlation with the presence of fracture, but there was a correlation with the presence of tumor tissue in the affected vertebral body.[26]

Vrionis and Small[21] show a difference between acute and chronic instability, correlating them with clinical and radiological changes. We had difficulty with this type of classification, for in reporting, we had a high incidence of pain when based on the VAS, but we did not find fractures in all patients, which leads us to wonder whether there is a correlation of fracture or deformity linked to instability, or if tumor invasion alone is the cause of isolated pain.

In their review, Jacobs and Perrin[27] summarized their results and obtained data that were similar to ours. They reported reduced pain in 90% of patients and maintenance of the neurological condition, with worse prognosis or shorter survival for those with partial or total deficit, on bedrest, or confined to a wheelchair. Steinmetz *et al*.[28] emphasize the importance of the study of spinal cancer surgery, reporting the need for understanding the pathophysiology and biology of the tumor, as there has been significant progress in the area of adjuvant treatments, and excellent results with surgical treatment associated with clinical improvement of the patient, emphasizing surgery before chemotherapy or radiotherapy, a procedure performed by us in all cases, since prior radiotherapy in the spine was considered a contraindication for surgery by us due to the postoperative risks and complications observed in operated patients, such as infection and surgical wound dehiscence.

In a review of the treatment of pathological fractures, Defino *et al*.[29] obtained results similar to ours, such as improvement in pain, justifying the intervention even in situations with a short life expectancy. Our patients are always evaluated by a multidisciplinary team, involving oncologists, radiation therapists, clinicians, orthopedists, and spine surgeons, intending to offer the best treatment for patients, according to Khan and Donthineni,[30] who evaluated the need for an approach with multiple specialists and the need for surgery in selected patients in order to achieve an improved quality of life and the prevention of clinical complications.

The understanding of the spinal tumor is important, and its study is key to the development of new algorithms. Gasbarrini *et al*.[31] described a new protocol for the clinical treatment, partial surgery and radical surgery with spondylectomy in selected cases. The authors report the need for urgent intervention in patients with acute neurological deficit, regardless of the prognosis, corroborating our study, where one patient without indication for surgery by the Tokuhashi criteria, but presenting the cauda equina syndrome, underwent urgent decompression, with neurological improvement and return of bladder and bowel functions, in addition to the ability to walk, despite death occurring three months later due to clinical complications.

Falicov *et al*.[32] conducted a study that evaluates the impact of surgery on the quality of life of patients. Although the authors used different tools from those used by us, the results were similar, with improvements in pain, quality of life, and a low complication rate.

CONCLUSION

The early diagnosis of spinal metastases requires a multidisciplinary team. Pain is most often the main symptom, and must be appreciated, especially when associated with other symptoms, such as weight loss, or progressive worsening of its intensity.

The improvement in the quality of life of patients was detected clinically, with decreased pain and maintenance of the neurological status. Surgical intervention is an optimal approach depending on the clinical conditions, the degree of instability and tumor location.

The surgery does not influence the patient's survival, except for patients with neurological deficits, who have a worse prognosis. Treatment of a metastatic lesion is often palliative, but during this time, patients show improvement in pain, neural protection, and few complications, justifying surgical intervention.

All authors declare no potential conflict of interest concerning this article.

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