



ORIGINAL PAPER

Wound-related complications in the surgical treatment of vertebral metastatic disease – A case series analysis



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KEYWORDS

Vertebral metastatic disease;
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Abstract

Introduction and objectives: Spinal metastases (SM) account for 5–30% of patients with cancer, causing pain, deformity and/or neurological deficit. Postoperative complications are a concerning subject and wound-related complications (WRC) may delay adjuvant treatment. The objective of this study was to analyze the incidence of WRC in patients with SM that underwent surgical treatment as well as possible risk factors related to the occurrence of complications. **Materials and methods:** Patients with SM operated between 2011 and 2021 were analyzed. Demographics characteristics, primary tumor, general and neurological status, Tokuhashi score, type of surgical treatment, surgical length, preoperative serum albumin and hemoglobin, pre and postoperative adjuvant treatment were analyzed. The incidence and risk factors of WRC – surgical site infection, hematoma, and/or dehiscence – at 90 days was evaluated. Patients were classified in two groups according to the absence/presence of WRC.

Results: 198 patients (121 males and 77 females) with an average age of 65 years (range 54–73 years) were analyzed. WRC were observed in 44 patients (22%). On multivariable analysis, significant predictors for developing WRC were low Tokuhashi score (OR=7.89, 95% CI=1.37–45.35, $p=0.021$), prostate cancer as primary tumor (6.73, 1.14–39.65, $p=0.035$), and preoperative serum albumin level ≤ 3.5 g/dL (2.31, 1.02–5.22, $p=0.044$). There was no difference between groups on 90 days survival rate ($p=0.714$).

Conclusions: In our series, the incidence of WRC was 22%, main risk factors for complications were low Tokuhashi score, lower preoperative serum albumin, and prostate cancer. Finally, short-term survival rate was not affected by the occurrence of WRC.

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PALABRAS CLAVE

Enfermedad metastásica vertebral; Complicación de la herida; Infección del sitio quirúrgico

Complicaciones relacionadas con la herida en el tratamiento quirúrgico de la enfermedad metastásica vertebral: análisis de una serie de casos

Resumen

Introducción y objetivos: Las metástasis espinales (MV) pueden ocurrir en el 5-30% de los pacientes con cáncer, provocando dolor, deformidad y/o déficit neurológico. Las complicaciones postoperatorias son un motivo de preocupación y las complicaciones relacionadas con la herida (CRH) pueden retrasar el inicio del tratamiento adyuvante. El objetivo de este estudio fue analizar la incidencia de CRH en pacientes con MV sometidos a tratamiento quirúrgico y evaluar los posibles factores de riesgo relacionados con estas complicaciones.

Materiales y métodos: Se analizaron pacientes operados por MV entre 2011 y 2021. Se analizaron características demográficas, tumor primario, estado general y neurológico, score de Tokuhashi, tipo de tratamiento quirúrgico, duración de la cirugía, albúmina sérica y hemoglobina preoperatorias, tratamiento adyuvante pre- y postoperatorio. Se evaluó la incidencia y los factores de riesgo de la CRH (infección del sitio quirúrgico, hematoma y/o dehiscencia) a los 90 días. Los pacientes se clasificaron en dos grupos según la ausencia/presencia de CRH.

Resultados: Se analizaron 198 pacientes (121 hombres y 77 mujeres) con una edad promedio de 65 años (rango 54-73 años). Se observaron CRH en 44 pacientes (22%). En el análisis multivariado, los predictores significativos para el desarrollo de CRH fueron un score de Tokuhashi bajo (OR=7,89; IC del 95%=1,37-45,35; $p=0,021$), cáncer de próstata como tumor primario (OR=6,73; IC del 95%=1,14-39,65; $p=0,035$) y albúmina sérica preoperatoria $\leq 3,5$ g/dL (OR=2.31; IC del 95%=1,02-5,22; $p=0,044$). No hubo diferencias entre los grupos en la supervivencia a los 90 días ($p=0,714$).

Conclusiones: En nuestra serie, la incidencia de CRH fue del 22%, los principales factores de riesgo para su aparición fueron el score de Tokuhashi bajo, la albúmina sérica preoperatoria más baja y el cáncer de próstata. Finalmente, la tasa de supervivencia a corto plazo no se vio afectada por la ocurrencia de CRH.

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Introduction

Spinal metastases are present in 5–30% of patients with cancer at the time of diagnosis, being a common cause of back pain, deformity, and weakness in this selected group of patients.¹ Nowadays, an increased survival rate has been observed in different oncologic subgroups, probably related to early diagnosis as well as medical and surgical treatment improvements. An increase in the prevalence of oncologic conditions and associated comorbidities requiring surgical treatment is expected along with growing life expectancy and population aging.^{2,3} Despite surgical innovations, undesirable adverse events continue to occur in highly vulnerable patients.^{4,5}

Surgical treatment of patients with SM can be associated with higher risk of local complications such as surgical site infection and wound dehiscence,^{6,7} those events are related to the high prevalence of associated comorbidities, poor nutritional status, and use of adjuvant therapies.⁸ While intense efforts have been made to analyze postoperative mortality rates, little emphasis has been put on immediate postoperative morbidity rates.^{9,10}

Wound-related complications are associated with longer hospital length of stay, higher re-operation rates and delay in starting the adjuvant therapy. The aim of this study is to report the incidence of wound-related postoperative complications in patients with metastatic spinal disease and

analyze related risk factors as well as their impact on the short-term survival rate.

Material and methods**Study design and data collection**

After the approval of the Institutional Review Board (Protocol number 5989, IRB00010193), a retrospective reviewed study of patients with metastatic vertebral disease who underwent surgical treatment in a single institution between January 2011 and February 2021 was conducted. Patients with lymphoproliferative lesions ($n=22$) and primary tumors ($n=13$) were excluded. Data analysis included: baseline patient's demographics parameters, type of primary tumor, neurological status measured by Frankel classification (classified as neurological compromise Frankel A–D and no neurological compromise Frankel E), Tokuhashi score (classified in three groups: Tokuhashi group 1: score 0–8, Tokuhashi group 2: score 9–11 and Tokuhashi group 3: score 12–15), type of surgical treatment: patients were classified as decompression alone versus instrumentation with/without decompression, length of surgery (minutes), pre and postoperative adjuvant treatment – radiotherapy and/or chemotherapy. Additionally, preoperative analytics,

Table 1 Demographic characteristics of the patient population according to the groups.

Variable	NWRC	WRC	<i>p</i> value
Number of patients	154	44	–
Men/Women (%)	88 (57%)/66 (43%)	33 (75%)/11 (25%)	0.289
Age > 62 years	81 (52.6)	19 (43.2)	0.549
Lung (%)	26 (16.8)	16 (36.4)	0.825
Kidney (%)	30 (19.4)	8 (18.2)	0.455
Breast (%)	25 (16.2)	2 (4.5)	0.472
Prostate (%)	15 (9.7)	10 (24.4)	0.011
Thyroid (%)	14 (9.1)	3 (6.8)	0.944
Colon (%)	13 (8.4)	2 (4.5)	0.945
Skin (%)	9 (5.8)	1 (2.3)	0.559
Others (%)	15 (9.7)	7 (15.9)	0.442

Abbreviations: NWRC, not wound-related complications; WRC, wound-related complications.

such as serum albumin levels (g/dL), hematocrit (%) and hemoglobin (g/dL) were studied.

Wound-related complications

Wound related complications were defined as a deviation of the postoperative wound evolution that required surgical intervention, including wound hematoma requiring drainage, dehiscence and deep surgical site infection needing closure and/or surgical debridement within the first 90 postoperative days. Non-surgically treated superficial wound infections were excluded. Patients were classified in two cohorts according to the absence – not wound related-complications cohort (NWRC) – or the presence of wound-related complications cohort (WRC). The postoperative mortality rate within the first 90 days was compared between cohorts.

Statistical analysis

For each continuous variable, the Shapiro–Wilk test was performed to analyze the normal distribution of quantitative variables. Among the variables of interest, age and hematocrit were found to have a normal distribution and therefore, were dichotomized using the media as the cutoff value – e.g., with 62 years for age (≤ 62 or > 62), and with 35% for hematocrit (≤ 35 or > 35); preoperative hemoglobin, preoperative serum albumin level, and length of surgery were found to have a non-normal distribution and therefore, were dichotomized using the median as the cutoff value – e.g., with 12 g/dL for hemoglobin (≤ 12 or > 12), with 3.5 g/dL for albumin (≤ 3.5 or > 3.5), and with 180 min for length of surgery (≤ 180 or > 180). For inter-group comparisons of categorical variables, Pearson χ^2 analysis and Fisher's Exact test were employed, as appropriate based upon cell numbers. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated for each variable, in terms of its impact upon the presence of WRC (yes/no). Multivariable analysis was performed by binary logistic regression analysis. For each model, independent variables were introduced into the model by forward entry and retained in the final model when $p < 0.1$. The analysis of survival was performed using Kaplan–Meier method and comparison between groups using

the log-rank test. The statistical software program SPSS version 25 for Mac (IBM, Armonk, NY) was employed. Any two-tailed p value < 0.05 was considered statistically significant.

Results

198 patients (121 males and 77 females) were included with an average age of 62.1 ± 13.01 years. 44 patients (22.2%) were enrolled in the WRC cohort (Table 1). The most common primary tumors were Lung (20%), kidney (18.6%) and Breast (13%).

Wound-related complication cohort (WRCG)

From 44 patients, 27 suffered deep infection (61.3%), followed by 9 wound dehiscence (20.4%) and 8 wound hematomas (18.2%). Patients in the wound-related complication cohort had significantly lower Tokuhashi score of 7.34 ± 2.5 ($p < 0.01$), higher prevalence of prostate cancer and lower preoperative albumin (Table 2). Regarding postoperative characteristics, the prevalence of postoperative Frankel E neurological status was significantly lower in the WRC group (Table 3).

The comparison between serum albumin level ≤ 3.5 versus > 3.5 g/dL to the time of the WRC showed a significant rise of occurrence at 20th postoperative day in the group ≤ 3.5 g/dL ($p = 0.06$) (Fig. 1).

Multivariate analysis

Regarding risk factors related to the occurrence of wound related complications, multivariate analysis showed that lower Tokuhashi Score (< 8) OR: 7.88 (95% CI 1.3–45.3) ($p = 0.0021$), primary prostate cancer OR 6.72 (95% CI 1.14–39.65) ($p = 0.03$) and hypoalbuminemia (< 3.5 mg/dL) OR: 2.31 (95% CI 1.02–5.22) ($p = 0.044$) were statistically significant, Table 4.

Table 2 Clinical Characteristics and preoperative variables.

Variable	NWRC N (%)	WRC N (%)	p value
Tokuhashi score 0–8	62 (40.3)	28 (63.6)	0.02
Tokuhashi score 9–11	61 (39.6)	14 (31.8)	0.848
Tokuhashi score 12–15	31 (20.1)	2 (4.5)	0.469
ASA III	117 (75.9)	38 (86.4)	0.34
Preoperative neurologic Status (Frankel E)	80 (51.9)	15 (34.1)	0.09
Preoperative Radiotherapy	31 (20.1)	14 (31.8)	0.78
Hemoglobin ≤ 12 g/dL	55 (35.7)	19 (46.3)	0.183
Hematocrit ≤ 35 (%)	80 (51.9)	20 (48.8)	0.804
Albumin ≤ 3.5 g/dL	72 (46.7)	25 (61.0)	0.085

Table 3 Operative and postoperative variables.

Variable	NWRC (n = 154)	WRC (n = 44)	p value
Type of surgery (need of any instrumentation)	129 (83.8)	36 (81.8)	0.93
Unprogrammed surgery	61 (39.6)	14 (31.8)	0.848
Length of surgery > 180 min	73 (47.4)	20 (45.4)	0.794
Postoperative neurological status Frankel E	98 (63.6)	16 (36.3)	0.02
Adjuvant chemotherapy	61 (39.6)	14 (31.8)	0.848
Mortality at 90 days	22 (14.2)	10 (22.7)	0.714

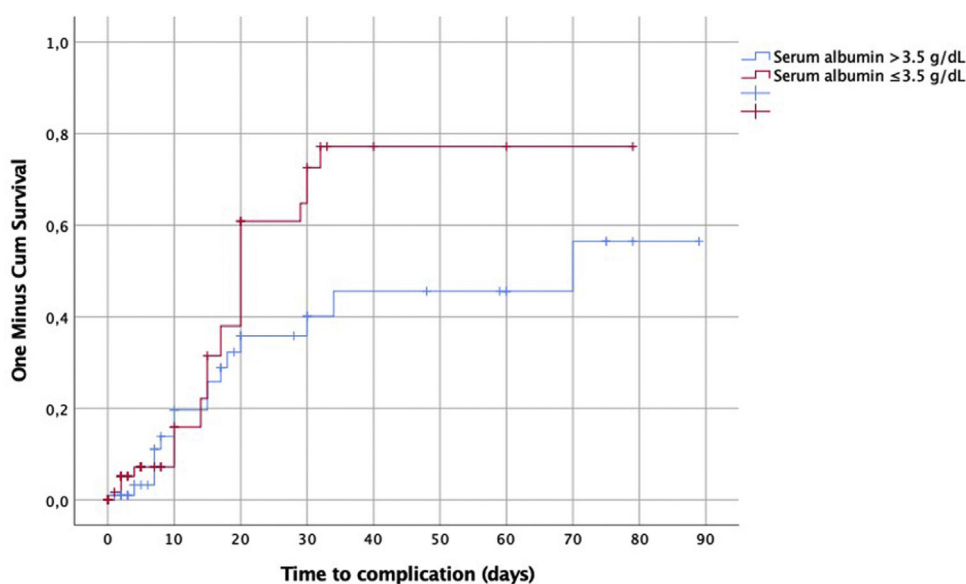


Figure 1 Accumulative incidence in time of wound-related complications according to preoperative serum albumin level.

Survival analysis

Survival rates at 90 days of follow-up between did not show a statistically significant difference between the groups ($p=0.714$) (Fig. 2).

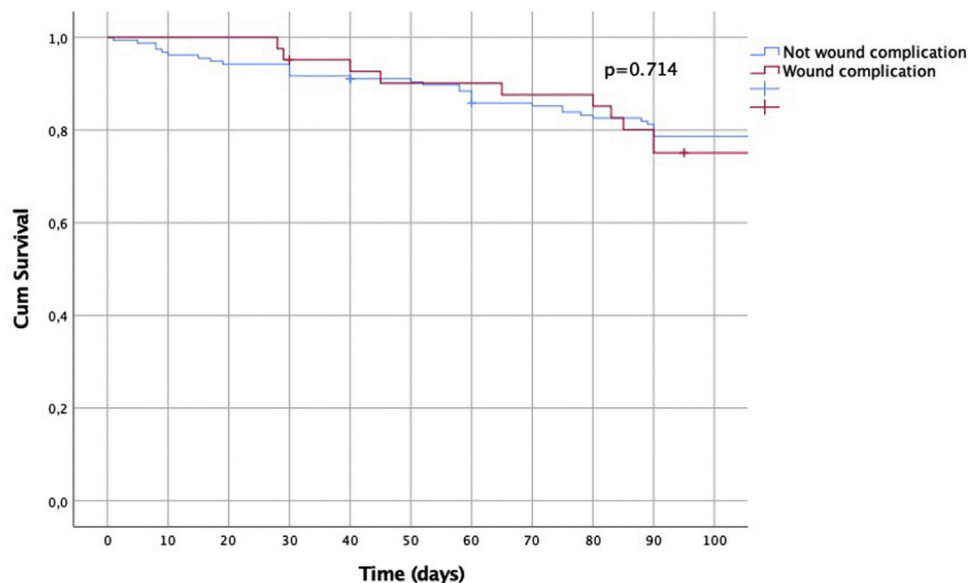
Discussion

Postoperative wound-related complications in patients with spinal metastasis are associated with higher morbidity,

hospital length of stay and may delay postoperative oncologic treatment affecting quality of life and mortality rate.^{11,12} In our study, we found that 22% of patients with spinal metastasis who underwent spinal surgery suffered a wound-related complication that required re-operation (dehiscence, hematoma or surgical site infection). Moreover, patients with lower survival rate (based on Tokuhashi score), lower preoperative albumin level and prostate cancer were more likely to develop wound-related complications.

Table 4 Multivariate analysis for developing wound-related complications.

Variable	Odds ratio	95% CI	p value
Age ≤ 62 years	0.493	0.19–1.22	0.49
Women	1.022	0.38–2.77	0.96
Tokuhashi 0–8	7.888	1.37–45.32	0.02
Tokuhashi 9–11	3.840	0.72–20.50	0.11
Lung cancer	1.574	0.34–7.39	0.825
Kidney cancer	2.120	0.39–11.56	0.455
Prostate	6.726	1.14–39.65	0.03
ASA	1.567	0.51–4.86	0.164
Unprogrammed surgery	1.579	0.55–4.53	0.39
Postoperative neurologic status Frankel E	0.779	0.28–2.16	0.63
Type of surgery (need of any instrumentation)	0.856	0.25–2.97	0.30
Neoadjuvant chemotherapy	0.501	0.21–1.21	0.10
Preoperative radiotherapy	0.771	0.32–1.84	0.783
Hemoglobin ≤ 12 g/dL	3.284	0.96–11.26	0.183
Hematocrit $\leq 35\%$	1.552	0.48–4.99	0.804
Albumin ≤ 3.5 g/dL	2.313	1.02–5.22	0.04
Length of surgery > 180 min	1.636	0.66–4.07	0.28

**Figure 2** Kaplan–Meier method analyzing the survival rate according to the presence or not of wound-related complications.

Hypoalbuminemia is a known independent risk factor for developing spinal wound complications, increased hospital length of stay and readmission,^{13–15} this is probably associated with poor nutritional status, comorbidities and inflammation that affect normal wound healing mechanisms.¹⁶ He et al.¹⁷ showed significant association between lower albumin levels and wound dehiscence in 554 patients that underwent single-level posterior lumbar fusion surgery. In patients with spinal metastasis, the role of albumin levels appears to be also related to higher mortality.¹⁸ In our study, we observed that lower preoperative albumin levels were associated with higher incidence of wound-related complications. We observed a substantial increment of wound-related complications in patients with lower albumin by the end of the third week, this finding has been highlighted in other studies.^{3,19–21}

The role of Tokuhashi score in predicting survival has been extensively studied in the literature^{2,22–24} with an overall acceptable survival prediction. This study analyzes the role of Tokuhashi score in predicting wound related complication, showing that a significantly higher complication rate was related to those patients with a score of 0–8 (survival rate of less than 6 months). Contrasting the available evidence,^{25,26} this study found that prostate cancer, as primary tumor, was associated with higher WRC regardless the history of preoperative radiotherapy.

Even though the presence of these type of complications can eventually lead to a sepsis and death,^{27,28} the occurrence of wound-related complication and subsequent reoperation was not associated with higher mortality at 90 days in our series. This data demonstrate that short-term

mortality rate is not affected by these complications and the need of further procedures.

Our study has some limitations. First, this is a retrospective case series analysis level IV evidence study. Nevertheless, we consider this series interesting due to the number of patients included and the short follow-up related to the primary outcome that could influence the lower loss of patients during the 90-days period making our results more reliable. Another limitation is related to the amount of radiotherapy and/or type of chemotherapy in our series which were considered as a binary variable (presence/absence) without specification regarding time, dose and type of treatments, these variables are known factors that can affect wound healing.²⁶ Regardless this matter, this study showed no significant influence on the occurrence of WRC, perhaps related to a type II error (false negative error), this probably could be addressed with a large series or multicenter analysis.

Conclusions

The incidence of wound-related complications after surgical treatment of spinal metastasis was 22%. The main risk factors to develop wound-related complications in our study were low Tokuhashi score, prostate cancer as primary tumor and low preoperative serum albumin level. The occurrence of WRC was not associated with a lower survival rate. These factors should be considered at the time of surgical decision-making.

Level of evidence

Level of evidence IV.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Right to privacy and informed consent

The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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