Clinical Neurology and Neurosurgery 181 (2019) 98–103

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Prognosticating outcomes and survival for patients with lumbar spinal metastases: Results of a bayesian regression analysis

Andrew J. Schoenfeld[a,*], Marco L. Ferrone[a], Joseph H. Schwab[b], Justin A. Blucher[a], Lauren B. Barton[a], Mitchel B. Harris[b], James D. Kang[a]

[a] Department of Orthopaedic Surgery, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA, 02115, United States
[b] Department of Orthopaedic Surgery, Massachusetts General Hospital, 55 Fruit Street, Boston, MA, 02214, United States

ARTICLE INFO

Keywords:
Lumbar spinal metastases
Surgical intervention
Mortality
Ambulatory capacity
Prognosis
Principal component analysis
Bayes regression

ABSTRACT

Objectives: To assess the impact of surgical intervention on survival, ambulatory capacity, complications and readmissions following treatment for lumbar metastases.

Patients and Methods: We identified all adult patients treated for lumbar metastases between 2005 – 2017. To limit the potential for inherent bias to influence determinations, we used principal component analysis to identify confounders to be included in multivariable testing. Multivariable logistic regression was performed, followed by Bayesian analysis to generate conservative estimates of effect size and 95% confidence intervals (CI). In a sensitivity test, analyses were repeated in a population where patients who died before they could initiate treatment were excluded.

Results: In the period under study, we identified 571 patients who met inclusion criteria. Twenty-one percent of the cohort received a surgical intervention. Bayes regression indicated surgical intervention was independently associated with decreased mortality at 6-months (odds ratio [OR] 0.49; 95% CI 0.34, 0.68) and 1-year (OR 0.63; 95% CI 0.51, 0.76), along with lower odds of being non-ambulatory at 6-months following presentation (OR 0.29; 95% CI 0.18, 0.45). Surgery was also associated with increased odds of complications (OR 1.60; 95% CI 1.24, 2.06) and readmissions (OR 1.37; 95% CI 1.09, 1.72). Numerous clinical characteristics were found to be associated with the outcomes of interest including serum albumin, lung metastases and vertebral body collapse.

Conclusions: Given the favorable outcomes associated with the incorporation of surgery as a component of treatment, we believe that such interventions may be considered part of the treatment approach in patients with lumbar metastases.

1. Introduction

A variety of factors, including advances in chemotherapy, medical management and patient longevity, have culminated in an increase in the diagnosis of spinal metastases over the last decade. [1–4] Current estimates maintain that as many as 40% of cancer patients will develop metastasis to the spine [1,5,6], with between 20–45% involvement of the lumbar region in these situations [1,3,5,6]. There are several unique anatomic and biomechanical considerations with respect to metastases to the lumbar region that do not pertain to cervical or thoracic metastatic disease [1,5,6]. Foremost, except at the thoracolumbar junction, metastases to the lumbar region do not threaten the spinal cord, although cauda equina involvement remains a concern. At the same time, the lumbar nerve roots are responsible for sensory and motor function in the lower extremities and perineal region that ultimately impact ambulatory capacity and bowel and bladder control. The high weight-bearing demand borne by the lumbar vertebrae also appears to increase the risk for biomechanical instability [1,5,6], while the large size of the vertebral bodies, rich vascular supply and restricted access to the spinal column due to presence of the pelvic ring and major vessels heighten the potential for peri-operative morbidity in the event of surgery [1,2,5,6].

At present, there are a limited number of studies that consider treatment experience and outcomes specific to patients who present with lumbar metastases. [5,6] For the reasons outlined above, findings for individuals with cervical and thoracic metastatic involvement may not necessarily be translatable. Furthermore, the information presently available is largely limited to single center experience and select groups

* Corresponding author.
E-mail address: ajschoen@neomed.edu (A.J. Schoenfeld).

https://doi.org/10.1016/j.clineuro.2019.04.009
Received 25 January 2019; Received in revised form 19 March 2019; Accepted 11 April 2019
Available online 22 April 2019
0303-8467/

of patients with a high probability of indication bias. At the same time, there are no direct comparisons between patients treated operatively for lumbar spinal metastases and those receiving non-operative modalities. In the era of precision medicine, we believe it is necessary to develop best-available evidence that may be more specific to the care of patients with spinal metastases.

In this context, we sought to evaluate outcomes for individuals treated for lumbar metastatic disease over the last decade at one of two major academic medical centers. Specifically, we intended to consider the impact of surgical intervention on survival, ambulatory capacity, complications and readmissions following treatment using advanced statistical techniques that could control for confounding including secular trends in medical care. Based on prior publications [4,7–14], we hypothesized that patients who received surgery would have superior outcomes in terms of survival and ambulatory capacity while simultaneously experiencing higher rates of complications and readmissions.

2. Patients and methods

2.1. Data source

We queried the integrated clinical registry of Brigham and Women's Hospital and Massachusetts General Hospital to identify all patients treated for lumbar spinal metastases between January 1, 2005 and December 31, 2017. This electronic database has been successfully employed in the past for the purposes of studying aspects of health policy [15,16], orthopaedic [16], spine surgical [15,17] and oncology care [8,11,13]. Eligibility for inclusion in this study consisted of adults, aged 40–80, with lumbar metastases treated in the period under study at one of our two tertiary care centers. Individuals outside this age range, those with primary spine tumors, and patients who received only consultation or a second opinion, were excluded from consideration.

2.2. Data acquisition

The electronic health records of patients were used to determine age at presentation, year of presentation, biologic sex, race, medical comorbidities (classified using the Deyo-modified Charlson Index [CCI] [18], body mass index (BMI), primary cancer diagnosis (breast, lung, or other cancers including but not limited to colon, renal, prostate, thyroid, lymphoma/myeloma, head and neck sarcomas, hepatocellular, testicular, ovarian, melanoma and unknown primary) and location of metastases (including multi-level metastases involving the lumbar and other spinal regions) were recorded. Additional clinical data consisted of the presence of extra-spinal metastases at presentation, vertebral body collapse or pathologic fracture, spinal canal compromise, ambulatory status at presentation (independent, cane/walker, non-ambulatory) and symptoms at presentation, (axial pain/asymptomatic or neurologic symptoms [radiculopathy/myelopathy, paresis, paralysis, and/or cauda equina symptoms]). Laboratory values at presentation were also evaluated including albumin > 3.5 g/dL, white blood cell (WBC) count > 4.5 and platelet to lymphocyte ratio (PLR) > 180, a marker of elevated inflammatory state. [19,20].

The types of treatment received, including surgery or non-operative care, were determined and where applicable the approach of the surgical intervention (anterior, posterior, combined) and procedure (decompression alone, decompression and fusion, decompression and fusion with corpectomy) were also recorded. Non-operative treatments were categorized as chemotherapy/immunotherapy, radiation, or combinations thereof. Patients receiving stand-alone kyphoplasty and vertebroplasty without decompression, instrumentation or fusion were considered in the non-operative group.

Patients were classified in the surgical group if they received a surgical intervention as defined above and irrespective of other non-operative treatments administered before, or after, the intervention. Major complications, determined using a previously published algorithm that captures infectious events (superficial or deep), cardiovascular, cerebrovascular and venous thromboembolic events (deep venous thrombosis and/or pulmonary embolism), delirium, sepsis, shock, wound breakdown, pulmonary and urinary complications [12,21], and readmissions were assessed up to 90-days following the initiation of treatment. Survival was evaluated at 6-months and 1-year following presentation and post-treatment ambulatory function was determined at the 6-month time-point.

2.3. Variable definition

Survival at 6-months and 1-year following treatment were the primary outcomes, with 90-day complications and readmissions, as well as a non-ambulatory status at 6-months, considered secondary. Treatment received (surgery vs non-operative care) was the primary predictor variable. All other characteristics abstracted were eligible covariates.

2.4. Principle component analysis (PCA)

To limit the potential for inherent bias to influence our determinations and prevent the development of overfit statistical models, we used PCA [22] to identify important confounders to be included in multivariable testing [23]. A correlation matrix was employed to assess the associations of socio-demographic and clinical characteristics with a decision for surgery, followed by a scree plot and loading plot to assess clustering and the development of Eigen values. Factors that clustered with surgery on the loading plot and those with absolute Eigen vectors of ≥ 0.1 in PCA were included in multivariable testing to adjust for confounding. Year of treatment was forced into all multivariable models to account for secular trends, as were ambulatory status and vertebral body collapse at presentation given their influence on surgical intervention [1,5,10,12,24,25].

2.5. Statistical testing

Initial bivariate testing was performed using chi-squared tests for categorical variables and student's *t*-test with unequal variance or the Wilcoxon rank-sum test for non-parametric continuous data. Multivariable logistic regression was performed adjusting for clinical and socio-demographic characteristics, followed by Bayesian analysis using random-walk Metropolis-Hastings sampling to allow generation of conservative estimates of the effect size and 95% confidence intervals (CI). [23] Only those variables that demonstrated odds ratios (OR) and 95% CI with p-value < 0.05 following Bayesian regression were considered independent predictors of the outcomes of interest in this study. In a sensitivity test, the above analyses were repeated in a population where patients who died before they could initiate treatment were excluded from consideration to address immortal time bias [26]. All analyses were performed using STATA v15.0 (STATA Corp., College Station, TX). This study received institutional review board approval prior to commencement.

3. Results

In the period under study, we identified 571 patients who met inclusion criteria. The average age of the cohort as a whole was 57.7 (SD 9.6) and 83% of patients were White (Table 1). Lung (25%) and breast (24%) cancer were the most frequently encountered primary diagnoses. Thirty-seven percent of the cohort had spinal metastases exclusively in the lumbar region with the remainder exhibiting involvement in the lumbar and other locations within the spine. Fifty-five percent of patients also demonstrated additional extra-spinal osseous metastases with 27% and 17% found to have involvement of the liver and lungs, respectively. Seventy-three percent of the population was independently ambulatory at presentation, while 8% were non-ambulators, and 39% manifested neurologic symptoms of some degree.

Table 1
Demographic characteristics of patients treated for spinal metastases involving the lumbar spine (2005–2017).

Number of Cases (N)	571
Age (mean, SD)	57.7 (9.6)
Female Sex (%)	299 (52)
White (%)	475 (83)
Body Mass Index (mean, SD)	27.2 (5.9)
Number of Co-morbidities (%)	
1–2	343 (60)
3–4	228 (40)
Primary Cancer (%)	
Breast	139 (24)
Lung	140 (25)
Other	292 (51)
Location of Spinal Metastases	
Lumbar	213 (37)
Multiple Regions Including the Lumbar Spine	358 (63)
Albumin > 3.5 g/dL (%)	333 (58)
WBC Count > 4.5 (%)	444 (78)
Platelet to Lymphocyte Ratio > 180 (%)	300 (53)
Lung Metastases (%)	96 (17)
Liver Metastases (%)	153 (27)
Additional Bone Metastases (%)	313 (55)
Vertebral Body Collapse/Pathologic Fracture (%)	298 (52)
Spinal Canal Compromise (%)	236 (41)
Ambulatory Status at Presentation (%)	
Independent Ambulator	414 (73)
Ambulatory with Assistance	114 (20)
Non-ambulator	43 (8)
Symptoms at Presentation (%)	
Axial Pain/Asymptomatic	347 (61)
Neurologic Symptoms	224 (39)

Twenty-one percent of the cohort received a surgical intervention, with a posterior approach most common (101/122; 83%). Stand-alone anterior procedures were performed in 11 patients (9%). Among the posterior procedures, decompression-fusion procedures, including corpectomies, were most frequently performed (81/101; 80%). Ninety-one percent of surgical patients also received chemotherapy and/or radiation. Twenty-four percent of patients were treated with chemotherapy alone, 13% with radiation alone and 36% with chemotherapy and radiation. The mortality rate was 35% at 6-months and 48% at 1-year, with 11% of survivors non-ambulatory at the 6-month time-point (Appendix 1). Overall, readmissions were documented in 34% and complications occurred in 27%. The 6-month mortality rate for those treated surgically was 25% as compared to 37% among patients managed non-operatively ($p = 0.009$). At the 1-year time-point, mortality among surgical patients was 38%, while it was 51% for individuals receiving non-operative treatment ($p = 0.009$).

At baseline, however, there were several significant differences in socio-demographic and clinical characteristics between patients who were treated exclusively non-operatively and those who received a surgical intervention (Table 2) supporting the need for adjusted analyses. Of these, the results of PCA (Fig. 1) indicated that age, biologic sex, CCI, primary cancer diagnosis, serum albumin, WBC count and PLR at presentation, along with lung metastases and vertebral body collapse should be included in the adjusted models (Fig. 2).

Following adjusted analysis, including Bayes regression (Table 3), surgical intervention was found to be independently associated with decreased mortality at 6-months (OR 0.49; 95% CI 0.34, 0.68) and 1-year (OR 0.63; 95% CI 0.51, 0.76), along with lower odds of being non-ambulatory at 6-months following presentation (OR 0.29; 95% CI 0.18, 0.45). At the same time, surgery was associated with increased odds of complications (OR 1.60; 95% CI 1.24, 2.06) and readmissions (OR 1.37; 95% CI 1.09, 1.72).

Numerous clinical characteristics were found to be associated with the outcomes of interest following logistic (Appendix 2) and Bayesian regression (Table 4). Low serum albumin (≤3.5 g/dL), the presence of

Table 2
Demographic characteristics of patients treated for spinal metastases involving the lumbar spine with an operative or non-operative approach (2005–2017).

	Non-operative	**Operative**	**P-value**
Number of Cases (N)	449	122	–
Age (mean, SD)	57.4 (9.8)	58.8 (8.9)	0.15
Female Sex (%)	250 (56)	49 (40)	0.003
White (%)	377 (84)	98 (80)	0.19
Body Mass Index (mean, SD)	27.2 (6.1)	26.9 (5.0)	1.0
Number of Co-morbidities (%)			0.79
1-2	271 (60)	72 (59)	
≥3	178 (40)	50 (41)	
Primary Cancer (%)			< 0.001
Breast	119 (27)	20 (16)	
Lung	122 (27)	18 (15)	
Other	208 (46)	84 (69)	
Location of Spinal Metastases			< 0.001
Lumbar	139 (31)	74 (61)	
Multiple Regions Including the Lumbar Spine	310 (69)	48 (39)	
Albumin > 3.5 g/dL (%)	257 (57)	76 (62)	0.51
WBC Count > 4.5 (%)	339 (76)	105 (86)	0.04
Platelet to Lymphocyte Ratio > 180 (%)	234 (52)	66 (54)	0.69
Lung Metastases (%)	81 (18)	15 (12)	0.13
Liver Metastases (%)	136 (30)	17 (14)	< 0.001
Additional Bone Metastases (%)	266 (59)	47 (39)	< 0.001
Vertebral Body Collapse (%)	226 (50)	72 (59)	0.09
Spinal Canal Compromise (%)	141 (31)	95 (78)	< 0.001
Ambulatory Status at Presentation (%)			0.26
Independent Ambulator	319 (71)	95 (78)	
Ambulatory with Assistance	96 (21)	18 (15)	
Non-ambulator	34 (8)	9 (7)	
Symptoms at Presentation (%)			< 0.001
Axial Pain/Asymptomatic	310(69)	37 (30)	
Neurologic Symptoms	139 (31)	85 (70)	

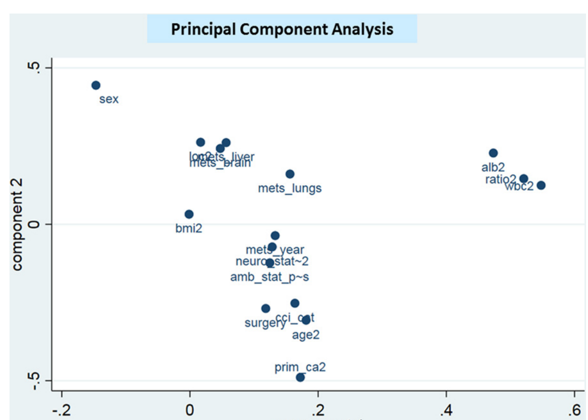

Fig. 1. Results of the principal component analysis loading plot demonstrating clustering of variables with surgery according to Eigen values. sex – biologic sex; loc – location of metastatic disease; mets_liver – liver metastases; mets_brian – brain metastases; mets_lung – lung metastases; bmi2 – body mass index; mets_year – year of treatment; neuro_stat˜2 – symptoms at presentation; amb_stat_p˜s – ambulatory status at presentation; cci_cat – Charlson comorbidity score; age2 – age of the patient at presentation; prim_ca2 – primary cancer diagnosis; alb2 – serum albumin at presentation; ratio2 – platelet to lymphocyte ratio at presentation; wbc2 – white blood cell count at presentation.

lung metastases and vertebral body collapse were the only clinical factors that were significant predictors of all the outcomes considered. CCI ≥ 3, PLR > 180 and requiring ambulatory assistance, or being non-ambulatory at presentation, were all significantly associated with higher mortality at both the 6-month and 1-year time-points (Table 4). Findings for our primary outcomes were preserved in sensitivity testing

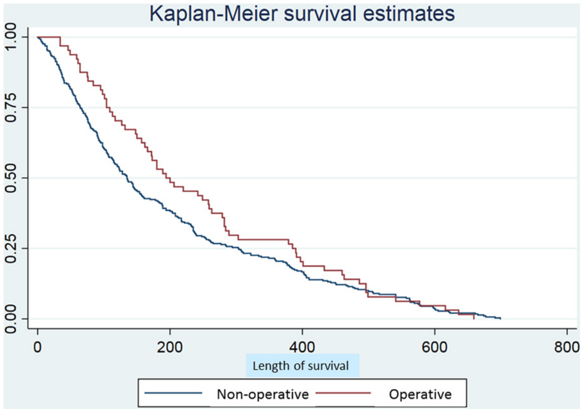

Fig. 2. Kaplan-Meier curves demonstrating survival among patients treated operatively (red line) and non-operatively (blue line) for spinal metastatic disease (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

as well (Appendix 3).

4. Discussion

The prevalence of spinal metastatic disease has increased over the course of the last decade, with as many as half of all patients developing this condition experiencing some degree of lumbar involvement. [1,3,5,6] The unique anatomic characteristics of the lumbar spine, including the morphology of the vertebrae and neurologic structures, as well as different technical considerations with respect to surgery [1,5,6], support the need to perform investigations focused on the treatment of metastatic disease in this region. In this era of modern healthcare metrics, it is vital to develop evidence-based treatment recommendations specific to individuals with metastatic disease involving the lumbar spine. We sought to achieve this goal using data from patients treated at two tertiary academic centers over the course of the last ten years.

We were able to include over 500 patients in this work, which represents one of the largest series of patients with lumbar metastases in the literature. The relatively narrow time period of study, sample size, duration of follow-up and the fact that we included operatively and non-operatively managed patients represent advantages over prior studies. The average age, clinical characteristics, primary cancer diagnoses, survival times and complication rates are also commensurate with other publications [2, 4–7, 9,12,14,24,25], which reinforces the potential for translation to regular clinical practice.

We found that a treatment strategy that included surgery was associated with a 51% reduction in the odds of 6-month mortality (95% CI 0.34, 0.68) and 37% reduction in the likelihood of 1-year mortality (95% CI 0.51, 0.76), as well as a 71% decrease in the odds of becoming non-ambulatory (95% CI 0.18, 0.45) 6-months into treatment. Perhaps not unexpectedly, surgical intervention was associated with an increased likelihood of complications and readmissions as compared to non-operative management. This represents an important trade-off that is a central component of decision making at the time of a patient's presentation with spinal metastases. Specifically, while surgical interventions are associated with improved survival and maintenance of ambulatory capacity, such anticipated benefits come at the cost of short-term limitations associated with undergoing surgery and an increased likelihood of morbidity and readmissions in the peri-operative period.

At the same time, we were also able to identify important clinical factors influential of outcomes irrespective of treatment including an increased number of co-morbidities, vertebral body collapse, lung metastases, low serum albumin, elevated PLR and compromised

Table 3
Estimates of the effect of surgery on outcomes among patients treated for spinal metastases involving the lumbar spine (2005–2017). Results are presented as odds ratio (OR) with 95% Confidence Interval (CI). ORs and 95% CI exclusive of 1.0 were considered significant (bold text).

Effect of Surgery	6-month MortalityOR (95% CI)	1-year MortalityOR (95% CI)	Non-Ambulatory at 6-months following presentation OR (95% CI)	Complications OR (95% CI)	Readmissions OR (95% CI)
Unadjusted	**0.55 (0.35, 0.87)**	**0.58 (0.39, 0.88)**	0.44 (0.16, 1.16)	1.43 (0.93, 2.21)	1.16 (0.77, 1.77)
Multivariable Logistic Regression	**0.49 (0.28, 0.83)**	**0.60 (0.37, 0.98)**	0.36 (0.12, 1.14)	1.61 (1.00, 2.60)	1.38 (0.87, 2.18)
Bayesian Logistic Regression	**0.49 (0.34, 0.68)**	**0.63 (0.51, 0.76)**	**0.29 (0.18, 0.45)**	**1.60 (1.24, 2.06)**	**1.37 (1.09, 1.72)**

Clinical Neurology and Neurosurgery 181 (2019) 98–103

Table 4
Estimates of the effect of clinical factors on outcomes among patients treated for spinal metastases involving the lumbar spine (2005–2017) following Bayesian logistic regression analysis that also adjusted for the performance of surgery, age, biologic sex and year of presentation. Results are presented as odds ratio (OR) with 95% Confidence Interval (CI). ORs and 95% CI exclusive of 1.0 were considered significant (bold text).

Variable	6-month MortalityOR (95% CI)	1-year MortalityOR (95% CI)	Non-Ambulatory at 6-months following presentationOR (95% CI)	ComplicationsOR (95% CI)	ReadmissionsOR (95% CI)
Number of Co-morbidities ≥3	**2.04 (1.45, 2.74)**	**1.61 (1.26, 2.08)**	1.40 (0.88, 2.12)	**1.51 (1.04, 2.02)**	**1.59 (1.26, 1.97)**
Albumin ≤3.5 g/dL	**3.59 (2.74, 4.62)**	**3.21 (2.38, 4.33)**	**4.85 (2.74, 8.10)**	**1.37 (1.04, 1.75)**	**1.41 (1.15, 1.71)**
Primary Cancer					
Lung	Reference	Reference	Reference	Reference	Reference
Breast	**0.31 (0.23, 0.40)**	**0.19 (0.13, 0.26)**	**0.33 (0.20, 0.50)**	**0.33 (0.19, 0.51)**	**0.20 (0.16, 0.26)**
Other	**0.65 (0.46, 0.84)**	**0.51 (0.34, 0.74)**	**0.41 (0.28, 0.61)**	**0.53 (0.35, 0.74)**	**0.43 (0.31, 0.57)**
WBC Count ≤4.5	**0.33 (0.26, 0.42)**	1.13 (0.85, 1.48)	0.76 (0.53, 1.07)	**1.78 (1.30, 2.38)**	**2.51 (2.01, 3.09)**
Platelet to Lymphocyte Ratio > 180	**1.87 (1.37, 2.45)**	**1.85 (1.32, 2.54)**	1.70 (0.81, 3.22)	0.92 (0.66, 1.24)	1.25 (0.91, 1.71)
Lung Metastases	**1.98 (1.44, 2.62)**	**4.16 (3.02, 5.50)**	**3.11 (1.94, 4.60)**	**2.21 (1.49, 3.15)**	**1.84 (1.36, 2.38)**
Vertebral Body Collapse	**1.75 (1.37, 2.25)**	**1.57 (1.27, 1.92)**	**3.54 (2.50, 5.14)**	**1.73 (1.51, 1.98)**	**1.64 (1.39, 1.93)**
Ambulatory Status at Presentation					
Independent Ambulator	Reference	Reference	Reference	Reference	Reference
Ambulatory with Assistance	**2.02 (1.70, 2.36)**	**2.23 (1.69, 2.93)**	**1.63 (1.08, 2.37)**	0.90 (0.67, 1.15)	0.86 (0.72, 1.03)
Non-ambulator	**5.63 (3.71, 8.12)**	**8.71 (4.81, 14.21)**	**19.23 (6.57, 49.57)**	1.17 (0.75, 1.84)	**0.69 (0.55, 0.86)**

ambulatory function at the time of presentation. Vertebral body collapse, lung metastases and impaired ambulatory function at presentation may herald a heightened disease burden that portends reduced survival and increased risk of complications. [3,7,8, 10–12, 24,25], Loss of ambulatory function also has been shown to be inimical to near-term survival in a number of prior works on skeletal metastatic disease [3, 9–13, 24,27]. Pre-treatment hypoalbuminemia, as a marker of impaired nutritional status, has been previously reported to be associated with inferior outcomes and increased risk for wound infection, in prior works on spine surgery in general [21] as well as efforts dedicated to metastatic disease [3,10,12,13]. The influence of albumin on wound healing, along with general physiologic function, could help explain the increased likelihood of inferior outcomes including survival, ambulatory capacity and complications observed in our study. Similar considerations pertain to elevations in PLR, which is indicative of elevated inflammatory states in patients with cancer [19,20]. Prior studies have reported that elevated PLR is associated with worse survival in patients with non-small cell lung cancer [19] and skeletal metastases from a variety of primary tumors [20].

The results of this analysis should be interpreted in light of limitations including the retrospective study design. We are limited to consider the variables captured within our dataset and cannot characterize the rationale behind treatment decisions, including selection of surgery or specific non-operative interventions. We realize that the potential remains for selection and/or indication bias to confound our results, as patients who received surgery may have been selected for this procedure given more favorable clinical characteristics. Radiographic imaging was not uniformly available and the types of imaging at presentation were not standardized across all patients. In light of the above facts, we were not able to utilize established scoring systems in this analysis such as the Tomita or Tokuhasi scales, or an instability score. It is important to realize, however, that recent work has not shown these grading schemes to be reliable in prognosticating clinical outcomes [14]. Furthermore, we maintain that our methodology, including a reliance on PCA analysis, Bayesian regression and sensitivity tests, adjusts for the impact of any inherent biases. Bayes regression, in particular, allows us to present estimates that are as conservative as possible. Nonetheless, we acknowledge the potential for bias to persist from unmeasured confounders. As the regression models were motivated by our primary outcomes related to survival, the capacity to detect differences and model calibration may differ across our secondary measures. Last, while likely translatable based on similar patient characteristics appreciated in other works, we acknowledge that our findings may not be universally generalizable, especially in populations whose socio-demographic or clinical characteristics are dramatically different from the cohort presented here.

5. Conclusion

We feel that our determinations have important meaning for patients with spinal metastatic disease as well as hospitals and providers. We were able to confirm our hypothesis that patients with lumbar metastases who received surgery experienced superior outcomes in terms of survival and ambulatory capacity. We have also identified clinical characteristics appropriate for risk adjustment and patient counseling at the time of presentation. In addition, our estimations may prove useful in prognosticating natural history and anticipated outcomes for patients and families. In this context, the adverse influence of poor nutritional status, increased tumor burden, elevated inflammatory states and compromised ambulatory status should be made clear at the outset. Furthermore, in light of the favorable outcomes associated with the incorporation of surgery as a component of treatment, we believe that such interventions may be part of the treatment approach, unless formally contraindicated by other factors, in patients with lumbar spinal metastases.

Author Contributions

AJS, MLF, JHS, MBH and JDK made significant contributions towards the conception and design of the study. AJS, MLF, JHS, JAB and LBB were responsible for data acquisition. AJS and JAB performed data analysis. AJS, MLF, JHS, MBH, JAB and LBB drafted the manuscript and AJS, MLF, JHS, MBH and JDK critically revised the manuscript for intellectual content. MLF, JAB and LBB provided administrative assistance and technical support. All authors approved the version of manuscript to be published and agreed to be accountable for all aspects of the study.

Funding and Disclosure

This research was funded by a National Institutes of Health (NIH-NIAMS) grant (K23-AR071464) to Dr. Schoenfeld. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the NIH or the Federal government.

Conflicts of interest

The authors have no other conflicts of interest to disclose.

Acknowledgement

This research was funded by a National Institutes of Health (NIH-NIAMS) grant (K23-AR071464) to Dr. Schoenfeld. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the NIH or the Federal government.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2019.04.009.

References

[1] P.S. Rose, J.M. Buchowski, Metastatic disease in the thoracic and lumbar spine: evaluation and management, J. Am. Acad. Orthop. Surg. 19 (2011) 37–48.

[2] J.J. Wise, J.S. Fischgrund, H.N. Herkowitz, D. Montgomery, L.T. Kurz, Complication, survival rates, and risk factors of surgery for metastatic disease of the spine, Spine 24 (1999) 1943–1951.

[3] A.J. Schoenfeld, D.A. Leonard, E. Saadat, C.M. Bono, M.B. Harris, M.L. Ferrone, Predictors of 30- and 90-day survival following surgical intervention for spinal metastases: a prognostic study conducted at four academic centers, Spine 41 (2016) E503–E509.

[4] F. Sailhan, S. Prost, F. Zairi, O. Gille, H. Pascal-Mousselard, S. Bennis, Y.P. Charles, B. Blondel, S. Fuentes, Retrospective multicenter study by the French Spine Society of surgical treatment for spinal metastasis in France, Orthop. Traumatol. Surg. Res. (July 30) (2018), https://doi.org/10.1016/j.otsr.2018.06.006 pii: S1877-0568(18)30183-X [Epub ahead of print].

[5] P.J. Holman, D. Suki, I. McCutcheon, J.P. Wolinsky, L.D. Rhines, Z.L. Gokaslan, Surgical management of metastatic disease of the lumbar spine: experience with 139 patients, J. Neurosurg. Spine 2 (2005) 550–563.

[6] J. Moliterno, C.A. Veselis, M.A. Hershey, E. Lis, I. Laufer, M.H. Bilsky, Improvement in pain after lumbar surgery in cancer patients with mechanical radiculopathy, Spine J. 14 (2014) 2434–2439.

[7] O. Barzilai, L. McLaughlin, M.K. Amato, A.S. Reiner, S.Q. Ogilvie, E. Lis, Y. Yamada, M.H. Bilsky, I. Laufer, Predictors of quality of life improvement after surgery for metastatic tumors of the spine: prospective cohort study, Spine J. 18 (2018) 1109–1115.

[8] N.R. Paulino Pereira, S.J. Janssen, E. van Dijk, M.B. Harris, F.J. Hornicek, M.L. Ferrone, J.H. Schwab, Development of a prognostic survival algorithm for patients with metastatic spine disease, J. Bone Joint Surg. Am. 98 (2016) 1767–1776.

[9] D. Choi, Z. Fox, T. Albert, M. Arts, L. Balabaud, C. Bunger, J.M. Buchowski, M.H. Coppes, B. Depreitere, M.G. Fehlings, J. Harrop, N. Kawahara, J.A. Martin-Benlloch, E.M. Massicotte, C. Mazel, F.C. Oner, W. Peul, N. Quraishi, Y. Tokuhashi, K. Tomita, J.J. Verlaan, M. Wang, H.A. Crockard, Prediction of quality of life and survival after surgery for symptomatic spinal metastases: a multicenter cohort study to determine suitability for surgical treatment, Neurosurgery 77 (2015) 698–708.

[10] A.K. Ghori, D.A. Leonard, A.J. Schoenfeld, E. Saadat, N. Scott, M.L. Ferrone, A.M. Pearson, M.B. Harris, Modeling 1-year survival after surgery on the metastatic spine, Spine J. 15 (2015) 2345–2350.

[11] A.V. Karhade, Thio QCBS, P.T. Ogink, C.M. Bono, M.L. Ferrone, K.S. Oh, P.J. Saylor, A.J. Schoenfeld, J.H. Shin, M.B. Harris, J.H. Schwab, Predicting 90-Day and 1-Year mortality in spinal metastatic disease: development and internal validation, Neurosurgery (March 14) (2019), https://doi.org/10.1093/neuros/nyz070 pii: nyz070 [Epub ahead of print].

[12] A.J. Schoenfeld, H.V. Le, Y. Marjoua, D.A. Leonard, P.J. Belmont, Jr, C.M. Bono, M.B. Harris, Assessing the utility of a clinical prediction.n score regarding 30-day morbidity and mortality following metastatic spine surgery: the New England Spinal Metastasis Score (NESMS), Spine J. 16 (2016) 482–490.

[13] D.D. Shi, Y.H. Chen, T.C. Lam, D. Leonard, T.A. Balboni, A. Schoenfeld, S. Skamene, D.N. Cagney, J.H. Chi, C.H. Cho, M. Harris, M.L. Ferrone, L.M. Hertan, Assessing the utility of a prognostication model to predict 1-year mortality in patients undergoing radiation therapy for spinal metastases, Spine J. 18 (2018) 935–940.

[14] A.K. Ahmed, C.R. Goodwin, A. Heravi, R. Kim, N. Abu-Bonsrah, E. Sankey, D. Kerekes, R. De la Garza Ramos, J. Schwab, D.M. Sciubba, Predicting survival for metastatic spine disease: a comparison of nine scoring systems, Spine J. (2018), https://doi.org/10.1016/j.spinee.2018.03.011 pii: S1529-9430(18)30100-1 [Epub ahead of print].

[15] G. Lonne, A.J. Schoenfeld, T.D. Cha, O.P. Nygaard, J.A.H. Zwart, T. Solberg, Variation in selection criteria and approaches to surgery for lumbar spinal stenosis among patients treated in Boston and Norway, Clin. Neurol. Neurosurg. 156 (2017) 77–82.

[16] A.J. Schoenfeld, D.G. Tobert, Leonard D.A. Le HV, A.L. Yau, P. Rajan, C.H. Cho, J.D. Kang, C.M. Bono, M.B. Harris, Utility of adding magnetic resonance imaging to computed tomography alone in the evaluation of cervical spine injury: a propensity matched analysis, Spine 43 (2018) 179–184.

[17] A.J. Schoenfeld, C.M. Bono, W.M. Reichmann, N. Warholic, K.B. Wood, E. Losina, J.N. Katz, M.B. Harris, Type II odontoid fractures of the cervical spine: Do treatment type and medical co-morbidities affect mortality in elderly patients? Spine 36 (2011) 879–885.

[18] R.A. Deyo, D.C. Cherkin, M.A. Ciol, Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases, J. Clin. Epidemiol. 45 (1992) 613–619.

[19] S. Diem, S. Schmid, M. Krapf, L. Flatz, D. Born, W. Jochum, A.J. Templeton, M. Früh, Neutrophil-to-Lymphocyte ratio (NLR) and Platelet-to-Lymphocyte ratio (PLR) as prognostic markers in patients with non-small cell lung cancer (NSCLC) treated with nivolumab, Lung Cancer. 111 (2017) 176–181.

[20] Q.C.B.S. Thio, W.A. Goudriaan, S.J. Janssen, N.R. Paulino Pereira, D.M. Sciubba, R.P. Rosovksy, J.H. Schwab, Prognostic role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients with bone metastases, Br. J. Cancer 119 (2018) 737–743.

[21] A.J. Schoenfeld, P.A. Carey, A.W. Cleveland 3rd, J.O. Bader, C.M. Bono, Patient factors, comorbidities, and surgical characteristics that increase mortality and complication risk after spinal arthrodesis: a prognostic study based on 5,887 patients, Spine J. 13 (2013) 1171–1179.

[22] A. Dinno, Implementing Horn's parallel analysis for principal component analysis and factor analysis, Stata J. 9 (2009) 291–298.

[23] J.S. Long, J. Freese, Regression Models for Categorical Dependent Variables Using STATA, 2nd edition, STATA Press, College Station, TX, 2006.

[24] R.J. Petteys, S.M. Spitz, C.R. Goodwin, N. Abu-Bonsrah, A. Bydon, T.F. Witham, J.P. Wolinsky, Z.L. Gokaslan, D.M. Sciubba, Factors associated with improved survival following surgery for renal cell carcinoma spinal metastases, Neurosurg. Focus 41 (2016) E13.

[25] Y. Tang, Q. Jintao, J. Qu, H. Liu, T. Chu, J. Xiao, Y. Zhou, Effect of surgery on quality of life of patients with spinal metastasis from non-small-cell lung cancer, J. Bone Joint Surg. Am. 98 (2016) 396–402.

[26] A. Gleiss, R. Oberbauer, G. Heinze, An unjustified benefit: immortal time bias in the analysis of time-dependent events, Transpl. Int. 31 (2018) 125–130.

[27] W.Y. Lo, S.H. Yang, Metastatic spinal cord compression (MSCC) treated with palliative decompression: surgical timing and survival rate, PLoS One 12 (2017) e0190342.