Independent predictors of complication following surgery for spinal metastasis

Darryl Lau · Matthew R. Leach · Khoi D. Than ·
John Ziewacz · Frank La Marca · Paul Park

Received: 30 October 2012 / Accepted: 30 January 2013 / Published online: 8 February 2013
© Springer-Verlag Berlin Heidelberg 2013

Abstract

Purpose Surgery for spinal metastasis is often associated with significant morbidity. Despite a number of preoperative scoring systems/scales and identified variables that have been reported to predict complication risk, clinical studies that directly evaluate this issue using multivariate analysis are scarce. The goal of our study was to assess independent predictors of complication after surgery for spinal metastasis.

Methods We queried electronic medical records to identify a consecutive population of adult patients who underwent surgery for spinal metastasis for the period June 2005 through June 2011. Utilizing multivariate logistic regression, we assessed independent predictors of perioperative and postoperative adverse events.

Results A total of 106 patients were included in the final analysis. Overall complication rate was 21.7 %. Independent predictors for higher rates of complication were age greater than 40 years [40–65 years had odds ratio (OR) 1.91, 95 % confidence interval (CI) 1.02–16.78 and >65 years had OR 5.17, 95 % CI 1.54–29.81] and metastatic lesions involving three or more contiguous levels of the spine (OR 2.76, 95 % CI 1.09–9.61).

Conclusions Patients older than 40 years or patients who have metastatic lesions involving three or more contiguous vertebral levels appear to be at higher risk for complication. Patients older than 65 years have the greatest likelihood of complication.

Keywords Complication · Spinal metastasis · Spine · Surgery

Introduction

Surgical management of spinal metastasis is widely considered a palliative intervention for symptomatic improvement, as prognosis remains poor with survival times commonly less than a year after surgery [1–3]. Unfortunately, morbidity can be relatively high, with reported complication rates ranging from 25 to 34 % in patients undergoing surgery for spinal metastasis [1, 4–7]. While there are suggested preoperative scoring systems/scales and identified variables that have been reported to predict complication risk, additional studies are needed as there are few large clinical studies that directly evaluate this issue using multivariate analysis [2, 6–10]. In this study, we evaluate a cohort of patients who underwent surgery for spinal metastasis to identify independent predictors of complications.

Methods

This study was reviewed and approved by the Medical Sciences Institutional Review Board of the University of Michigan.

Patient data

Electronic medical records (including patient records and intraoperative anesthesia records) at the University of Michigan Health System were queried to identify all adult patients that underwent surgical intervention for spinal

D. Lau · M. R. Leach
University of Michigan Medical School, Ann Arbor, MI, USA

K. D. Than · J. Ziewacz · F. La Marca · P. Park (✉)
Department of Neurosurgery, University of Michigan Health System, 1500 E. Medical Center Drive, Room 3552 TC, Ann Arbor, MI 48109-5338, USA
e-mail: ppark@umich.edu

metastasis from June 2005 through June 2011. Indications for surgery included radiologic imaging consistent with spinal metastasis causing neurologic deficit and/or pain as well as concern for instability. Surgical intervention consisted of maximal tumor resection when feasible, combined with instrumented fusion when indicated for stability. Dependent on location of the metastasis and surgeon preference, an anterior, posterior, or combined/staged approach was performed. Of the 117 patients identified in the initial inquiry, 11 were excluded from the study due to incomplete data. All patients included in the study had a diagnosis of metastasis confirmed via examination of the pathology. Each metastasis was categorized based on primary site of origin/cell type: breast, gastrointestinal (cholangiocarcinoma, hepatocellular carcinoma, colon cancer, and gastric cancer), hematological (multiple myeloma/plasmacytoma, lymphoma, and leukemia), lung, melanoma, muscle (leiomyosarcoma), prostate, renal cell carcinoma, thyroid, or 'other.' A metastasis categorized as 'other' included cancers of unknown origin as well as those in which categorization would not allow a meaningful statistical analysis (squamous cell carcinoma of skin and bladder cancer).

Demographic and baseline clinical variables of interest included: age at time of surgery, sex, body mass index (BMI; kg/(height in meters)²), prior diagnosis of diabetes mellitus, coronary artery disease, or hypertension. Serum creatinine was also noted, and patients were categorized using a binary method (≤ 1.4 or >1.4) in order to assess for baseline renal injury/failure. Baseline functional status was measured via use of Karnofsky Performance Score (KPS) and preoperative ability to ambulate. Ambulation was defined as the ability to walk independently with or without an assistive device (i.e., cane or walker). Presenting symptoms were reviewed and categorized as pain only, neurological dysfunction only, or both.

The region of the spine (cervical, thoracic, lumbar, or sacral) occupied by the metastatic lesion as seen on magnetic resonance imaging was recorded. If lesions involved multiple regions of the spine, the patient was stratified into the region with the greatest involvement. Extensiveness of the cancer was recorded using multiple variables: number of contiguous vertebrae involved (categorized as 1, 2, and 3 or more), intradural involvement, and presence of extraspinal metastasis [no extraspinal site, 1–2 sites, or 3 or more sites (excluding primary origin of the cancer as an extraspinal site)].

The outcome of interest in this study was complication, defined as any intraoperative or postoperative event that required additional medical or surgical attention/treatment within 30 days of surgery. Mortality was analyzed and recorded both independently and as a result of complication.

Analysis of complications

First, descriptive statistics were used to describe the cohort of patients identified. Next, we employed Chi square tests to identify significant associations between covariates of interest and categorical outcomes (complications). Finally, multivariable logistic regression models of likelihood for complication were fit and adjusted for potential confounders. We adjusted for covariates found to be associated with postoperative outcomes in bivariate Chi square tests with a threshold *P* value of 0.200.

Results with *P* values <0.050 were considered statistically significant on final analysis. All statistical analyses were run using SAS software, version 9.2 (SAS Institute, Cary, NC).

Results

Of the 106 patients who underwent surgery for spinal metastasis, 13 (12.3 %) patients had breast cancer, 8 (7.5 %) had gastrointestinal cancer, 14 (13.2 %) had hematological cancer, 8 (7.5 %) had lung cancer, 10 (9.4 %) had melanoma, 8 (7.5 %) had leiomyosarcoma, 9 (8.5 %) had prostate cancer, 14 (13.2 %) had renal cell carcinoma, 4 (3.8 %) had thyroid cancer, and 18 (17.0 %) had cancers categorized as 'other.'

Complication rate and independent risk factors

Table 1 shows the results of descriptive statistics for covariates and complications. Of 106 patients, 23 had complications (an overall complication rate of 21.7 %). There was 1 death, for an overall mortality rate of 0.9 %. There was a noticeable trend toward higher complication rates with increasing age. Patients less than 40 years old had a complication rate of 7.7 %; this was significantly lower than for those patients aged 40–65 (18.3 %) and older than 65 years (40.9 %) ($P = 0.034$). Patients with diabetes had a significantly higher rate of complications than those without the disease (42.9 vs. 18.5 %, respectively) ($P = 0.039$). In addition, there was a trend toward a higher complication rate when more vertebrae were involved. Involvement of one vertebra resulted in a 15.1 % complication rate, two vertebrae resulted in a 25.0 % complication rate, and three or more vertebrae resulted in a 33.3 % complication rate, but this was not significant ($P = 0.198$). Specific complications included: wound infection and/or dehiscence (4), durotomy (3), malpositioned hardware requiring repositioning (2), urinary tract infection (2), deep vein thrombosis and thrombocytopenia (1), pulmonary embolus (1), intraoperative cardiac arrest

Table 1 Covariates and risk factors associated with complications in patients undergoing surgery for spinal metastasis

Patient descriptives	N	%	Complications		
			n	%	P value
Total	106	—	23	21.7	
Age					0.034
<40 years	13	12.3	1	7.7	
40–65 years	71	67.0	13	18.3	
>65 years	22	20.8	9	40.9	
Sex					0.423
Male	63	59.4	12	19.0	
Female	43	40.6	11	25.6	
Body mass index					0.832
<20	25	23.6	5	20.0	
20–25	25	23.6	7	28.0	
25–30	28	26.4	5	17.9	
>30	28	26.4	6	21.4	
Diabetes mellitus					0.039
Yes	14	13.2	6	42.9	
No	92	86.8	17	18.5	
Coronary artery disease					0.908
Yes	9	8.5	2	22.2	
No	97	91.5	21	21.6	
Hypertension					0.414
Yes	40	37.7	7	17.5	
No	66	62.3	16	24.2	
Serum creatinine (mg/dL)					0.623
≤1.4	99	93.4	22	22.2	
>1.4	7	6.6	1	14.3	
Ambulatory					0.814
Yes	81	76.4	18	22.2	
No	25	23.6	5	20.0	
Karnofsky performance score					0.289
10–40	21	19.8	7	33.3	
50–70	26	24.5	6	23.1	
80–100	59	55.7	10	16.9	
Primary tumor location					0.443
Breast	13	12.3	2	15.4	
Gastrointestinal	8	7.5	1	12.5	
Hematological	14	13.2	1	7.1	
Lung	8	7.5	3	37.5	
Melanoma	10	9.4	2	20.0	
Muscle	8	7.5	0	0.0	
Prostate	9	8.5	2	22.2	
Renal	14	13.2	5	35.7	
Thyroid	4	3.8	1	25.0	
Other	18	17.0	6	33.3	
Presentation					0.231
Pain	43	40.6	8	18.6	
Neurological deficit	27	25.5	9	33.3	

Table 1 continued

Patient descriptives	N	%	Complications		
			n	%	P value
Both	36	34.0	6	16.7	
Levels					0.777
Cervical	15	14.2	3	20.0	
Thoracic	65	61.3	14	21.5	
Lumbar	21	19.8	4	19.0	
Sacral	5	4.7	2	40.0	
Number of levels involved					0.198
1	53	50.0	8	15.1	
2	32	30.2	8	25.0	
3 or more	21	19.8	7	33.3	
Intradural					0.333
Yes	16	15.1	2	12.5	
No	90	84.9	21	23.3	
Metastasis to other sites					0.237
No extraspinal sites	40	37.7	11	27.5	
1–2 sites	44	41.5	10	22.7	
3 or more sites	22	20.8	2	9.1	
Chemotherapy					0.247
Yes	79	74.5	15	19.0	
No	27	25.5	8	29.6	
Radiotherapy					0.429
Yes	81	76.4	19	23.5	
No	25	23.6	4	16.0	
Surgical approach					0.987
Anterior	14	13.2	3	21.4	
Posterior	88	83.0	19	21.6	
Combined anterior-posterior	4	3.8	1	25.0	

(1), pseudomeningocele (1), CSF leak, anemia, and coagulopathy (1), weakness and loss of proprioception in lower extremities (1), spinal epidural hematoma (1), pneumonia (1), hoarseness and swallowing difficulties (1), hardware failure requiring removal (1), humerus fracture during positioning (patient with metastasis in right arm prior to surgery) (1), and wound dehiscence requiring operative repair and cardiopulmonary arrest/death secondary to pulmonary embolus (1).

Table 2 highlights the covariates that are independent risk factors and predictors of complication, adjusted for the single potential confounder identified (number of levels of involvement). Relative to patients younger than 40 years of age, there was a significant increase in odds for complication in the group of patients aged 40–65 [odds ratio (OR) 1.91, 95 % confidence interval (CI) 1.02–16.78; $P = 0.046$] and even greater odds in patients older than 65 years of age (OR 5.17, 95 % CI 1.54–29.81; $P = 0.016$). In addition, compared to patients with only one vertebra involved, the odds of

Table 2 Independent risk factors for complications in patients undergoing surgery for spinal metastasis

Patient descriptives	Complications		
	OR	95 % CI	P value
Age			
<40 years	ref	ref	ref
40–65 years	1.91	1.02–16.78	0.046
>65 years	5.17	1.54–29.81	0.016
Diabetes mellitus			
Yes	2.39	0.68–8.50	0.176
No	ref	ref	ref
Number of levels involved			
1	ref	ref	ref
2	1.60	0.51–5.07	0.421
3 or more	2.76	1.09–9.61	0.011

CI confidence interval, OR odds ratio, *ref* reference

complication among patients harboring metastatic lesions involving three or more contiguous vertebrae was 2.76 (95 % CI 1.09–9.61; $P = 0.011$).

Table 3 stratifies specific complication by age group (<40 years, 40–65 years, and >65 years) and Table 4 displays complications by number of contiguous vertebral levels (1 level, 2 levels, and 3 or more levels).

Discussion

When assessing patients with symptomatic spinal metastasis, knowledge of potential risk factors for increased complication is highly valuable in terms of counseling patients

on expectations and weighing the benefits of surgery. In this study, we assessed independent predictors of potential complications following surgery for spinal metastases. Our findings suggest that age older than 40 years or metastatic involvement in three or more contiguous vertebral levels are both independent predictors associated with higher risk of complication.

Spine surgery for metastatic disease is considered palliative and is typically undertaken to treat symptoms of refractory pain and/or neurologic deficit as well as instability. Morbidity from metastatic spine surgery is relatively common, with reported rates ranging from 25 to 34 % [1, 4–7]. In our cohort of patients, we observed a complication rate of 21.7 %, with the most common complications being wound infections and deep vein thrombosis/pulmonary embolus. Independent predictors of complications following surgery for spinal metastases reported in the current literature include the Charlson Comorbidity Index [8], Harrington Classification demonstrating significant neurological deficits [7], preoperative radiation [7, 9], greater than five levels of instrumentation [10], and age >65 years [6].

In our study, we also found older age to be an independent risk factor for higher rates of complication. The phenomena of “older” age being associated with greater rates of complication has been described in many surgical subspecialties including general surgery [11], orthopedics [12], and neurosurgery (spine surgery [13] and cranial surgery [14]). Although the OR of increased complication was highest in patients older than 65 years, what is interesting about our findings is the increase in complication rates starting at 40 years, a relatively young age. Most surgeons do not readily identify patients in their 40s as higher risk candidates based on age alone. However, it is important to keep in mind the nature of the cancer patient

Table 3 Specific complications stratified by age groups

	<40 Years (1/13 patients)	40–65 Years (13/71 patients)	>65 Years (9/23 patients)
Intraoperative complications	None	Durotomy (3) Intraoperative cardiac arrest (1)	Humerus fracture during repositioning (1)
Postoperative complications	Pneumonia (1)	Wound dehiscence/infection (2) Urinary tract infection (2) Hoarseness of voice and swallowing difficulties (1) Epidural hematoma (1) Malpositioned hardware requiring repositioning (1) CSF leak and coagulopathy (1) Wound dehiscence requiring wound repair, cardiopulmonary arrest due to pulmonary embolus, and death (1)	Wound dehiscence/infection (2) Weakness and loss of proprioception in lower extremity bilaterally (1) Hardware failure requiring removal (1) Malpositioned hardware requiring repositioning (1) Pulmonary embolus (1) Pseudomeningocele (1) Deep vein thrombosis and thrombocytopenia (1)

Table 4 Specific complications stratified by number of contiguous vertebral levels

	1 Level (8/53 patients)	2 Levels (8/32 patients)	3 or More levels (7/21 patients)
Intraoperative complications	Intraoperative cardiac arrest (1)	Durotomy (1)	Durotomy (2)
Postoperative complications	Wound dehiscence/infection (3)	Pseudomeningocele (1)	Humerus fracture during repositioning (1) Epidural hematoma (1)
	Pneumonia (1)	Malpositioned hardware requiring repositioning (1)	Malpositioned hardware requiring repositioning (1)
	Urinary tract infection (1)	Urinary tract infection (1)	CSF leak and coagulopathy (1)
	Hardware failure requiring removal (1)	Hoarseness and swallowing difficulties (1)	Wound dehiscence requiring wound repair, cardiopulmonary arrest due to pulmonary embolus, and death (1)
	Weakness and loss of proprioception in lower extremity bilaterally (1)	Pulmonary embolus (1) Wound dehiscence/infection (1) Deep vein thrombosis and thrombocytopenia (1)	

population; often patients with metastases are likely in the later stages of their disease. These patients may be debilitated, frail, and immune-compromised as a result of both physiological factors and treatment-related side-effects from chemo- and radiotherapy [3, 7]. In addition, it has been suggested that cancer patients have poor wound-healing ability, leading to greater susceptibility to infection and other complications [15, 16]. These factors potentially explain why wound infection/dehiscence was the most common complication in our study and in other cohorts [7]. Deep vein thrombosis and pulmonary embolus were also one of the most common complications experienced in our cohort and a cause of death in one patient. It is well known that patients with cancer are intrinsically hypercoagulable, and even more so following surgery [17]. As deep vein thrombosis and pulmonary embolus are highly morbid and can lead to mortality, in addition to low molecular weight heparin prophylaxis, it is highly recommended that patients be mobilized as soon as it is deemed safe [4].

In addition to age, metastasis involving three or more contiguous vertebral levels was a significant predictor of complication. While to our knowledge there are no studies that have specifically identified multiple metastatic vertebra involvement as a risk factor for complication, there are studies in the current literature reporting that patients who undergo surgery on multiple spinal levels have higher rates of complication. Shehadi et al. [10] examined 87 patients that underwent surgery for metastatic spinal disease from breast cancer and showed higher complication rates when 5 or more levels were instrumented. In addition, direct comparisons of single-level versus multi-level spine surgery for non-cancer related indications have also shown higher rates

of complication in multi-level surgery [18, 19]. This makes intuitive sense, as more involved surgical procedures are typically performed on patients with more extensive disease, and more aggressive procedures are usually associated with longer operative times, greater blood loss, and longer recovery times, which can translate into greater risk for intraoperative and postoperative complications [20, 21].

We recognize that there are limitations to this study. Our study was retrospective and, therefore, it is plausible that the associations observed may have been confounded by underlying factors not explicitly studied. One such factor is that we could not fully account for the type of surgical intervention performed, which has potential implications on complication rates. Although the approach was classified and evaluated, the type of surgical intervention performed was difficult to categorize because a wide spectrum of surgical procedures were performed and could not be sufficiently categorized without a very large cohort or case-controlled study for meaningful statistical analysis. However, the goal of our study was to identify preoperative factors associated with complication, despite the type of surgical procedure performed.

Despite these limitations, the results of our study have important implications for clinical management, as well as future research. Other articles have demonstrated that surgery for metastatic spinal disease is a valuable modality for improving function, relieving symptoms, and improving overall quality of life, especially in younger patients [22, 23]. The independent predictors of complication observed in our study might further enhance the ability of surgeons to objectively assess the potential morbidity and benefits of surgery for spinal metastasis.

Conclusions

Knowledge of potential predictors of complication is highly valuable for counseling patients and weighing the risks of surgical intervention. In this study, age greater than 65 years predicted the highest likelihood for complication. Interestingly, age greater than 40 years was also found to be a predictor of complication, as was metastasis involving three or more contiguous vertebral levels.

Conflict of interest Dr. Park is a consultant for Globus Medical and DePuy Spine and has received an honorarium from Medtronic in the past year. Dr. La Marca is a consultant for Globus Medical, Biomet, Lanx, and Stryker. None of the authors report a conflict of interest associated with the contents of this study.

References

- Finkelstein JA, Zaveri G, Wai E, Vidmar M, Kreder H, Chow E (2003) A population-based study of surgery for spinal metastases. Survival rates and complications. *J Bone Jt Surg Br* 85: 1045–1050
- Onimus M, Papin P, Gangloff S (1996) Results of surgical treatment of spinal thoracic and lumbar metastases. *Eur Spine J* 5:407–411
- Wibmer C, Leithner A, Hofmann G, Clar H, Kapitan M, Berg-hold A, Windhager R (2011) Survival analysis of 254 patients after manifestation of spinal metastases: evaluation of seven preoperative scoring systems. *Spine (Phila Pa 1976)* 36: 1977–1986
- Arrigo RT, Kalanithi P, Cheng I, Alamin T, Carragee EJ, Mindea SA, Boakye M (2011) Predictors of survival after surgical treatment of spinal metastasis. *Neurosurgery* 68:674–681
- Quan GM, Vital JM, Aurouer N, Obeid I, Palussiere J, Diallo A, Pointillart V (2011) Surgery improves pain, function and quality of life in patients with spinal metastases: a prospective study on 118 patients. *Eur Spine J* 20:1970–1978
- Williams BJ, Fox BD, Sciubba DM, Suki D, Tu SM, Kuban D, Gokaslan ZL, Rhines LD, Rao G (2009) Surgical management of prostate cancer metastatic to the spine. *J Neurosurg Spine* 10:414–422
- Wise JJ, Fischgrund JS, Herkowitz HN, Montgomery D, Kurz LT (1999) Complication, survival rates, and risk factors of surgery for metastatic disease of the spine. *Spine (Phila Pa 1976)* 24:1943–1951
- Arrigo RT, Kalanithi P, Cheng I, Alamin T, Carragee EJ, Mindea SA, Boakye M, Park J (2011) Charlson score is a robust predictor of 30-day complications following spinal metastasis surgery. *Spine (Phila Pa 1976)* 36:E1274–E1280
- Demura S, Kawahara N, Murakami H, Nambu K, Kato S, Yoshioka K, Okayama T, Tomita K (2009) Surgical site infection in spinal metastasis: risk factors and countermeasures. *Spine (Phila Pa 1976)* 34:635–639
- Shehadi JA, Sciubba DM, Suk I, Suki D, Maldaun MV, McCutcheon IE, Nader R, Theriault R, Rhines LD, Gokaslan ZL (2007) Surgical treatment strategies and outcome in patients with breast cancer metastatic to the spine: a review of 87 patients. *Eur Spine J* 16:1179–1192
- Seo SH, Hur H, An CW, Yi X, Kim JY, Han SU, Cho YK (2011) Operative risk factors in gastric cancer surgery for elderly patients. *J Gastric Cancer* 11:116–121
- Schoenfeld AJ, Ochoa LM, Bader JO, Belmont PJ Jr (2011) Risk factors for immediate postoperative complications and mortality following spine surgery: a study of 3475 patients from the national surgical quality improvement program. *J Bone Jt Surg Am* 93:1577–1582
- Cloyd JM, Acosta FL Jr, Cloyd C, Ames CP (2010) Effects of age on perioperative complications of extensive multilevel thoracolumbar spinal fusion surgery. *J Neurosurg Spine* 12:402–408
- Lau D, El-Sayed AM, Ziewacz JE, Jayachandran P, Huq FS, Zamora-Berridi GJ, Davis MC, Sullivan SE (2012) Postoperative outcomes following closed head injury and craniotomy for evacuation of hematoma in patients older than 80 years. *J Neurosurg* 116:234–245
- Lans TE, van der Pol C, Wouters MW, Schmitz PI, van Geel AN (2009) Complications in wound healing after chest wall resection in cancer patients; a multivariate analysis of 220 patients. *J Thorac Oncol* 4:639–643
- Payne WG, Naidu DK, Wheeler CK, Barkoe D, Mentis M, Salas RE, Smith DJ Jr, Robson MC (2008) Wound healing in patients with cancer. *Eplasty* 8:e9
- Byrne M, Reynolds JV, O'Donnell JS, Keogan M, White B, Murphy S, Maher SG, Pidgeon GP (2010) Long-term activation of the pro-coagulant response after neoadjuvant chemoradiation and major cancer surgery. *Br J Cancer* 102:73–79
- Huppert J, Beaurain J, Steib JP, Bernard P, Dufour T, Hovorka I, Stecken J, Dam-Hieu P, Fuentes JM, Vital JM, Vila T, Aubourg L (2011) Comparison between single- and multi-level patients: clinical and radiological outcomes 2 years after cervical disc replacement. *Eur Spine J* 20:1417–1426
- Lettice JJ, Kula TA, Derby R, Kim BJ, Lee SH, Seo KS (2005) Does the number of levels affect lumbar fusion outcome? *Spine (Phila Pa 1976)* 30:675–681
- Lawrence VA, Hilsenbeck SG, Mulrow CD, Dhanda R, Sapp J, Page CP (1995) Incidence and hospital stay for cardiac and pulmonary complications after abdominal surgery. *J Gen Intern Med* 10:671–678
- Polanczyk CA, Marcantonio E, Goldman L, Rohde LE, Orav J, Mangione CM, Lee TH (2001) Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med* 134:637–643
- Falicov A, Fisher CG, Sparkes J, Boyd MC, Wing PC, Dvorak MF (2006) Impact of surgical intervention on quality of life in patients with spinal metastases. *Spine (Phila Pa 1976)* 31:2849–2856
- Fujibayashi S, Neo M, Miyaki K, Nakayama T, Nakamura T (2010) The value of palliative surgery for metastatic spinal disease: satisfaction of patients and their families. *Spine J* 10:42–49