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Outstanding Paper

Prospective comparison of one-year survival in patients treated operatively and nonoperatively for spinal metastatic disease: results of the prospective observational study of spinal metastasis treatment (POST)

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Introduction

A sea-change occurred in the field of spine surgery in 2005 following the landmark publication of Patchell et al [1]. regarding the efficacy of spine surgery for restoration of ambulatory function in patients with spinal metastatic disease. In the succeeding 15 years, enthusiasm grew for surgical interventions as a standard treatment option for patients with spinal metastases [2]. Several investigations touted that surgery not only preserved ambulatory ability but also improved survival [3−6]. There was a concern that many of these investigations were confounded by selection bias and controversy remains regarding the utility of spine surgery in subsets of patients with spinal metastases based on baseline neurologic status [7]. To address this, we planned an analysis that accounted for confounding by indication and compared patients treated operatively and nonoperatively for spinal metastases within the Prospective Observational study of Spinal metastasis Treatment (POST) [2,8]. We hypothesized that patients treated surgically would have superior one-year survival to those managed nonoperatively.

Methods

This study was conducted among patients enrolled in the POST study (2017−2019) [2]. Enrollment details, inclusion criteria, and study protocol have been published previously [2]. The study was approved through institutional review before commencement and patients consented before participation. The investigation was registered with clinicaltrials.gov (NCT03224650). Eligible patients were adults presenting for initial treatment of spinal metastases at participating centers and received operative, or nonoperative, management [2]. Patients were treated based on shared decision-making and as directed by treating clinicians. Overall, the POST investigation was powered to detect differences in survival at 1-year based on the New England Spinal Metastasis Score (NESMS) at presentation [2,8]. Enrollment was structured to create a comparative balance between operative and nonoperative cohorts with a 2:3 ratio. The date of enrollment was considered time-zero and patients were followed to one of two time-points: death or 365 days following enrollment [2]. In cases where patients initially managed nonoperatively subsequently received surgery, we extended surveillance to 365 days following the date of surgery. Sixty-four percent of eligible participants consented to be enrolled, with 80 individuals receiving surgical intervention as the initial treatment strategy and an additional 7 crossovers from nonoperative to surgical management. Data for this analysis was finalized on July 31, 2021.

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Table 1
Demographic and clinical characteristics of the operative and nonoperative cohorts*

Characteristic	Nonoperative	Operative	p-value
Age (mean, SD)	60.2 (11.9)	60.8 (11.9)	.24
Biologic Sex	-	-	.11
Male Sex	62(51)	54 (62)	-
Female Sex	60 (49)	33 (38)	-
White	102 (84)	76 (87)	.45
Body Mass Index (mean, SD)	26.9 (6.1)	27.7 (6.1)	.22
Number of Co-morbidities (mean, SD)	2.5 (0.9)	2.3 (0.8)	.04
Serum Albumin	-	-	.86
Albumin <3.5g/dL	35 (29)	24 (28)	-
Albumin ≥3.5g/dL	87 (71)	63 (72)	-
Ambulatory Status at Presentation	-	-	.39
Independent Ambulator	76 (62)	49 (56)	-
Ambulatory with Assistance/Non-ambulatory	46 (38)	38 (44)	-
Performance Status	-	-	.50
Poor	11 (9)	11 (13)	-
Moderate	40 (33)	32 (37)	-
Good	71 (58)	44 (51)	-
Neurologic Status at Presentation	-	-	.008
Neurologic Intact	97 (80)	52 (60)	-
Neurologic Deficits	24 (20)	34 (39)	-
Bone Metastases	72 (59)	42 (48)	.12
Visceral Metastases	66 (54)	44 (51)	.62
Type of Lesion	-	-	.05
Blastic	29 (24)	13 (15)	-
Mixed (lytic/blastic)	32 (26)	15 (18)	-
Lytic	61 (50)	57 (67)	-
New England Spinal Metastases Score	-	-	.69
0	16 (13)	14 (16)	-
1	29 (24)	23 (26)	-
2	52 (43)	30 (34)	-
3	25 (20)	20 (23)	-
Tokuhashi Score (mean/SD)	8.5 (2.9)	8.3 (2.9)	.53
Tomita Score (mean/SD)	5.9 (2.5)	5.9 (2.8)	.94
Spinal Instability Neoplastic (SINS) Score (mean/SD)	9.7 (3.0)	11 (3.2)	.004

* All values are presented as raw number and percentage (rounded to the nearest whole number) except where noted.

Per study protocol, the primary outcome for the analysis presented here was survival at 1-year following treatment initiation [2]. The primary predictor was treatment, categorized as operative, or nonoperative management. Cross-overs were handled via statistical cloning [9]. Unadjusted comparisons between the operative and nonoperative cohorts were made using chi-square tests for categorical variables and the Wilcoxon rank-sum test for non-parametric, continuous data. Survival was assessed using Kaplan-Meier curves. Per protocol, we developed a propensity score around the likelihood for surgical intervention using age, biologic sex, co-morbidities, primary tumor, neurologic symptoms, and NESMS at presentation based on our conceptual model [2]. Inclusion of the NESMS in the propensity score is supported by prior work validating the association between the NESMS and 1-year survival in this cohort [8]. The propensity score was used in final adjusted models for survival at 1-year, presented using odds ratios (OR) and 95% confidence intervals (CI). Calibration was evaluated using observed to expected plots and Hosmer-Lemeshow testing [10].

Results

We considered 87 instances of surgical intervention and 122 cases of nonoperative treatment. The average age of both cohorts approximated 60.5 years. Lung cancer was the most common primary tumor (20%), followed by breast (16%) and prostate (14%). The thoracic spine was the most common site of surgical intervention (70%). The majority of surgeries consisted of fusion-based procedures (79%), including 26 corpectomies. Combined chemotherapy and radiation was the most common nonoperative modality (80%).

There was a reasonable balance across socio-demographic and clinical characteristics between the operative and nonoperative cohorts (Table). There was no significant difference in primary tumor between groups, with lung cancer the most common in nonoperative (20%) and operative (18%) cohorts (p=.12). Relatively normal distribution was also appreciated across all prognostic scoring utilities. Overall, 50% of the cohort died by 1-year following presentation (105/209). In the operative group, the mortality rate

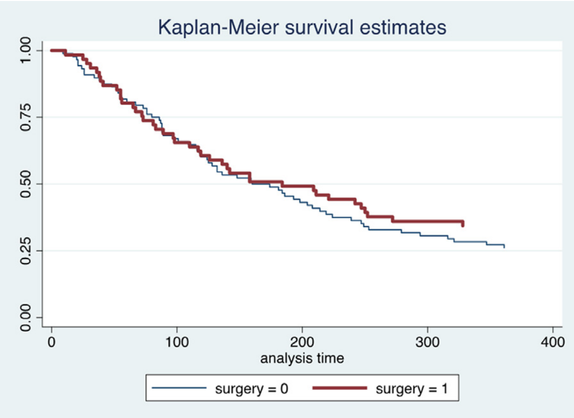

Fig. 1. Kaplan-Meier survival curves for patients treated operatively (surgery=1) and nonoperatively (surgery=0) over the course of the first year following presentation.

was 46% at 1-year, as compared to 54% in the nonoperative cohort (Figure). This represented a 25% reduction in the odds of mortality (OR 0.75; 95% CI 0.43, 1.30) but was not significantly different (p=.3). Following propensity score adjustment, accounting for confounding by indication in the decision for surgery, surgical intervention offered a 28% reduction in the odds of mortality (OR 0.72; 95% CI 0.40, 1.29) but still did not demonstrate statistical significance (p=.27). There was no evidence of statistical lack of fit (p=.39) with good calibration on observed to expected plots (Appendix 1).

Discussion

This is the first investigation we are aware of that prospectively compares operative and nonoperative treatment in patients with spinal metastases while accounting for selection and indication bias in the decision for treatment. This work is advantaged by its prospective nature as well as broad and representative variation in clinical parameters across both operative and nonoperative cohorts, including ambulatory capacity and neurologic status. Given the relatively large size of the sample, we were able to account for confounders using propensity score adjustment and cloning for treatment crossovers [9,10].

We believe that our findings add to a growing body of evidence that indicates surgical intervention is not uniformly beneficial across all individuals with spinal metastases. Although the benefits of surgery for patients with neurologic deficits, acute loss of ambulatory function, and spinal instability are incontrovertible [1,3,7], robust evidence is lacking for those without neurologic compromise or impaired ambulatory function [7,8]. We demonstrated an 8-percentage point difference in 1-year survival that, based on power estimates, would require a sample of over 1,200 patients in total to demonstrate significance given high near-term mortality. While it is interesting that propensity adjustment slightly increased the advantage for surgery, the estimated 25% to 28% reduction in the odds of mortality should be balanced against the risks associated with these high-intensity interventions and relatively low survival rates, irrespective of treatment strategy [7,8]. This may be especially important in instances where the metastatic process is largely asymptomatic, or if patients do not manifest neurologic deficits or impaired ambulatory ability.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.spinee.2022.02.004.

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