Prognostic Factors Associated With Surviving Less Than 3 Months vs Greater Than 3 Years Specific to Spine Stereotactic Body Radiotherapy and Late Adverse Events

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BACKGROUND: Patient selection is critical for spine stereotactic body radiotherapy (SBRT) given potential for serious adverse effects and the associated costs.
OBJECTIVE: To identify prognostic factors associated with dying within 3 mo, or living greater than 3 yr, following spine SBRT, to better inform patient selection.
METHODS: Patients living ≤3 mo after spine SBRT and >3 yr after spine SBRT were identified, and multivariable regression analyses were performed. We report serious late toxicities observed, including vertebral compression fractures (VCF) and plexopathy.
RESULTS: A total of 605 patients (1406 spine segments) were treated from 2009 to 2018. A total of 51 patients (8.4%) lived ≤3 mo, and 79 patients (13%) survived >3 yr. Significant differences in baseline features were observed. On multivariable analysis, nonbreast/prostate primaries (odds ratio [ORs]: 28.8-104.2, $P = .0004$), eastern cooperative oncology group (ECOG) ≥2 (OR: 23.7, 95% CI: 3.2-177, $P = .0020$), polymetastatic disease (OR: 6.715, 95% CI: 1.89-23.85, $P = .0032$), painful lesions (OR: 3.833-8.898, $P = .0118$), and paraspinal disease (OR: 2.874, 95% CI: 1.118-7.393, $P = .0288$) were prognostic for ≤3 mo survival. The 3- and 5-yr rates of VCF were 10.4% and 14.4%, respectively, and 3- and 5-yr rates of plexopathy were 2.2% and 5.1%, respectively. A single duodenal perforation was observed, and there was no radiation myelopathy events.
CONCLUSION: Shorter survival after spine SBRT was seen in patients with less radiosensitive histologies (ie, not breast or prostate), ECOG ≥2, and polymetastatic disease. Pain and paraspinal disease were also associated with poor survival. Fractionated spine SBRT confers a low risk of late serious adverse events.

KEY WORDS: Spine, Metastases, SBRT, Poor prognosis, Survival, Patient selection

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The spine is a common site of metastatic dissemination and can cause significant morbidity and mortality. Traditionally, conventional palliative external beam radiotherapy (cEBRT) with a low uniform dose was standard of care for metastatic spine disease, and associated with an overall and complete pain response rate of 60% to 70% and ~20%, respectively.[1] Tumor control with palliative cEBRT is not well studied, as this was historically not an intent of treatment. In contrast, the goal of spine SBRT is local tumor ablation. SBRT requires millimetric precision to avoid overdosing neural structures, which can lead to devastating consequences, such as paralysis. Multiple series support high rates of local control from 80% to 95%, and excellent pain relief with a phase 2 trial reporting 40% complete pain response.[2-4] Importantly, high rates of local control are observed even in radioresistant histologies, that previously exhibited poor response with cEBRT.[5] With novel systemic agents, metastatic cancer patients are living

ABBREVIATIONS: cEBRT, conventional palliative external beam radiotherapy; **CI,** confidence interval; **ECOG,** eastern cooperative oncology group; **SBRT,** stereotactic body radiotherapy; **SINS,** Spinal Instability Neoplastic Score; **VCF,** vertebral compression fracture

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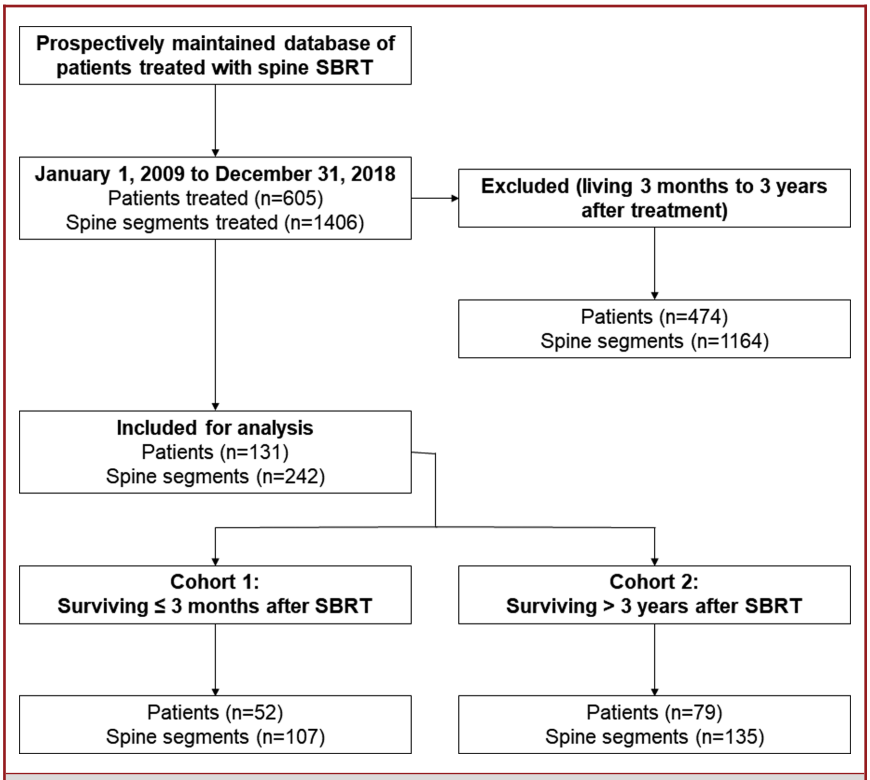

FIGURE 1. *Patient flow chart. Identification process for patients included for analysis.*

longer making durable tumor and pain control achieved with SBRT an increasingly important objective.

SBRT requires significantly more resources including specialized equipment, additional planning, and treatment time, as well as expertise. This comes at considerable expense, and cost-effectiveness analyses estimate the treatment cost of single fraction SBRT to be 9-fold higher than cEBRT.[6] Additionally, risk of adverse events such as vertebral compression fracture (VCF) and late neurological injury (myelopathy and peripheral nerve dysfunction) is higher. It is critical to ascertain which patients benefit most from more intensive treatment.

In surgical practice, a minimum prognosis of 3 mo is necessary to be considered for operative intervention,[7] and the American Society for Radiation Oncology Evidence-Based Guideline also suggested a similar minimum 3-mo prognosis for SBRT.[8,9] Lastly, specific to spine SBRT, the reporting of RTOG-0631 in abstract form challenges the application of spine SBRT to patients with 3-mo survival given the lack of symptomatic benefit compared to cEBRT at the 3-mo primary endpoint.[10] As a result, there is a need to identify factors associated with a ≤3-mo survival to inform patient selection. The purpose of this study was to identify prognostic factors associated with ≤3 mo of life following spine SBRT, as compared to those surviving >3 yr. Additionally, we report late serious adverse effects, including VCF and brachial/lumbosacral plexopathy.

METHODS

Study Design

A prospectively maintained database of 605 patients (1406 spine segments) treated with spine SBRT, between January 2009 and December 2018, was reviewed (Figure 1). This study was approved by our Research Ethics Board, and consent was exempted because of the retrospective nature of this study. Patients who died ≤3 mo after SBRT and those who survived >3 yr were included. Demographics including gender, performance status, age, primary cancer, oligometastatic disease (≤5 metastases) or polymetastatic disease (>5 metastases), visceral and/or brain metastases, and treatment indication (de novo, postoperative, or retreatment) were collected. Radioresistant malignancies included renal cell carcinoma, sarcoma, melanoma, colorectal cancer, and thyroid cancer. Tumor factors including SINS (Spinal Instability Neoplastic Score), epidural grade, and presence of paraspinal disease along with dose fractionation were studied. Our treatment technique has been reported,[11] and patients were followed per institutional protocol, including clinic assessment and full spine magnetic resonance imaging every 2 to 3 mo. We report serious adverse events in the 3-yr surviving cohort. Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Statistical Methods

Clinical factors were reported per patient and tumor factors per segment amongst each cohort. Logistic regression analysis was used to

assess for potential predictors of living ≤3 mo after spine SBRT. A generalized linear mixed model with binary outcome (living ≤3 mo vs >3 yr) was used to assess the impact of patient and tumor factors per spinal segment. Predictors with *P*-value < .2 on univariate analysis were selected for multivariable analysis. Analyses were performed for local control, considering death as competing risk. All *P*-values were 2-sided, and for the statistical analyses, a $P < .05$ was considered statistically significant. Analyses were performed using version 9.4 of the SAS system for Windows, 2002-2012 SAS Institute Inc (Cary, North Carolina).

RESULTS

Participants

A total of 52 and 79 patients, corresponding to 107 and 135 segments, respectively, survived ≤3 mo and >3 yr following spine SBRT (Table 1). The 52-patient cohort living ≤3 mo after spine SBRT represented a total of 8.4% of patients treated with spine SBRT, and the 79-patient cohort living >3 yr represented 12.7% of patients. Those with colorectal cancer had the highest proportion of patients living ≤3 mo (12/41 total colorectal cancer patients in the entire 605-patient cohort; Table 2). Features of patients with non small cell lung cancer and renal cell carcinoma receiving targeted therapy or immunotherapy are detailed in **Table**, **Supplemental Digital Content**. Median survival for those living ≤3 mo was 58 d (range: 11-91 d), and median follow-up for those living >3 yr was 4 yr (range: 3.0-8.6 yr). 67.3% of patients living ≤3 mo and 96.3% of patients surviving >3 yr were treated with 2 fraction regimens.

Baseline Patient and Tumor Factors

Many baseline factors were significantly different between groups (Table 1; Figures 2 and 3). No patient with breast cancer survived ≤3 mo after SBRT. Patients living ≤3 mo were more likely to have poor performance status, neurological deficits, radioresistant primary cancers, polymetastatic disease, and prior radiotherapy to the treatment site. Approximately 71% of those dying within 3 mo of treatment were eastern cooperative oncology group (ECOG)0-1. These patients also had higher frequency of paraspinal disease, baseline VCF, and to be treated with more fractionated regimens.

Features Associated With Living ≤3 Months

On univariable analysis, polymetastatic disease, nonbreast or prostate primary cancer, lung/liver or brain metastases, ECOG performance status ≥2, male gender, poor neurological status, duration from diagnosis to treatment, pain, and paraspinal disease were statistically significant predictors of living ≤3 mo after spine SBRT. Age, treatment indication, presence of VCF, and epidural disease status were not significant.

On multivariable analysis (Table 3), nonbreast/prostate primary cancer (odds ratio [OR]: 104.18, 95% CI: >8.28, $P = .0004$), ECOG performance status ≥2 (OR: 23.7, 95% CI: 3.17-177, $P = .0020$), and polymetastatic disease (OR: 6.715, 95% CI: 1.891-23.849, $P = .0032$) were associated with living ≤3 mo after spine SBRT. Segments with paraspinal disease had higher risk dying ≤3 mo after spine SBRT (OR: 2.874, 95% CI: 1.118-7.393, $P = .0288$). Those with painful spinal lesions (as assessed by SINS) were more likely to die within 3 mo of treatment (OR: 3.833-8.898, $P = .0118$). There was a trend towards significance for presence of liver and/or lung metastases (OR: 4.063 and 5.863, $P = .0556$).

Local Control

In those who survived at least 3 yr, local failure at 3 yr was 12.5% (95% CI: 6.8%-18.3%), and at 5 yr was 14.4% (95% CI: 5.2%-23.6%). There was variation in local failure depending on histology, with radioresistant histologies at a greater risk with a 3-yr failure rate of 25% vs 7.2% for those breast/prostate metastases.

Early Deaths and Acute Serious Adverse Events

Three patients (5.8%) who lived ≤3 mo after spine SBRT died of causes potentially relating to spine disease. Two patients experienced neurological deterioration relating to progression of nontreated sites, one patient had a significant episode of flare of pain after treatment, and one patient had cardiac complications relating to dehydration.

Systemic Therapy in Those Living ≤3 Months

Almost half of the patients (47.1%) living ≤3 mo had received ≥2 lines, and 45.8% had received ≥4 lines of systemic therapy prior to SBRT (Table 1). One patient had received 7 lines of systemic therapy; systemic therapy was administered to 66.7% of patients within 3 mo of death.

Late Toxicities

In patients living >3 yr, there were a total of 13 (9.6%) cases of new VCF and 6 (4.4%) of progression of existing VCFs (Figure 4). This occurred at a median of 24.0 mo after spine SBRT (range: 1.97-98.7 mo). The incidence of VCF was 2.2% at 1 yr, 7.4% at 2 yr, 10.4% at 3 yr, and 14.4% at 5 yr.

A total of 6 cases of plexopathy (1 brachial and 5 lumbosacral plexopathy) were observed (Table 4). These occurred at a median of 35.7 mo (range: 10.9-41.9 mo). Plexopathy at 1, 2, 3, and 5 yr was 0.74%, 1.5%, 2.2%, and 5.1%, respectively. Three patients had 3 courses of radiotherapy (cEBRT then SBRT twice) to the site of toxicity, 2 had 2 courses of SBRT, and a single patient had plexopathy after 1 course of SBRT. We observed a single case of duodenal perforation after 3 courses of SBRT to the same spinal site (2 spines and 1 para-aortic node close to the target spinal segment); this patient died ≤3 mo after spine SBRT. There were no cases of radiation myelopathy.

DISCUSSION

Key Results

With evolving technology and the ability to offer more aggressive palliative treatments, prognostication of survival is a

TABLE 1. Comparison of Patient Characteristics in Those Living ≤3 Months Compared to Those Living >3 Years, per Patient Treated

	Died within 3 mo (n = 51)	Living longer than 3 yr (n = 79)	*P* value
Gender			
Female	20 (39.2%)	48 (60.8%)	**.0163**
Male	31 (60.8%)	31 (39.2%)	
ECOG			
0-1	36 (70.6%)	75 (94.9%)	**.0001**
≥2	15 (29.4%)	4 (5.1%)	
Age at diagnosis			
Median (range)	69 (27.11-89)	67 (29-90)	.4864
Duration from diagnosis to treatment			
Median (range)	1.53 (0.08-19.85)	3.87 (0.05-27.86)	**.0406**
Neurological status			
Normal	40 (78.4%)	75 (94.9%)	**.0048**
Abnormal	11 (21.6%)	4 (5.1%)	
Primary cancer			
Breast	0 (0%)	35 (44.3%)	**<.0001**
Colon	12 (23.5%)	2 (2.5%)	
NSCLC	16 (31.4%)	11 (13.9%)	
Prostate	3 (5.9%)	20 (25.3%)	
Renal	11 (21.6%)	5 (6.4%)	
Other	9 (17.6%)	6 (7.6%)	
Histologic classification			
Radioresistant	24 (47.1%)	11 (13.9%)	**<.0001**
Radiosensitive	27 (52.9%)	68 (86.1%)	
Oligometastatic disease			
Yes	14 (27.5%)	63 (79.8%)	**<.0001**
No	37 (72.5%)	16 (20.2%)	
Previous surgery at site			
Yes	10 (19.6%)	10 (12.7%)	.2836
No	41 (80.4%)	69 (87.3%)	
Previous RT at site			
Yes	14 (27.5%)	8 (10.1%)	**.0101**
No	37 (72.5%)	71 (89.9%)	
Brain metastases			
Yes	13 (25.5%)	7 (8.9%)	**.0103**
No	38 (74.5%)	72 (91.1%)	
Liver or lung metastases			
Both	10 (19.6%)	5 (6.3%)	**<.0001**
Liver	9 (17.6%)	8 (10.1%)	
Lung	21 (41.2%)	9 (11.4%)	
None	11 (21.6%)	57 (72.2%)	
Treatment indication			
De novo	30 (58.8%)	62 (78.5%)	**.0172**
Postop	5 (9.8%)	8 (10.1%)	
Retreat	16 (31.4%)	9 (11.4%)	
Number of lines of systemic therapy			
0-1	27 (52.9%)	N/A	N/A
2-3	13 (25.5%)		
4-7	11 (21.6%)		
Systemic therapy within 3 mo of data of death			
Yes	24 (66.7%)	N/A	N/A
No	12 (33.3%)		

TABLE 1. Continued

	Segments treated in those that lived ≤3 mo (n = 107)	Segments treated in those living >3 yr (n = 135)	*P* value
Location within spine			
Cervical	18 (16.8%)	12 (8.9%)	.9929
Thoracic	51 (47.7%)	76 (56.3%)	
Lumbar	33 (30.8%)	34 (25.2%)	
Sacral	5 (4.7%)	13 (9.6%)	
Dose fractionation			
18-24 Gy/1#	2 (1.9%)	0 (0%)	**<.0001**
20-28 Gy/2#	72 (67.3%)	130 (96.3%)	
24 Gy/3#	3 (2.8%)	1 (0.7%)	
30 Gy/4-5#	30 (28.0%)	4 (3.0%)	
Paraspinal extension			
Yes	56 (52.3%)	31 (22.0%)	.5513
No	51 (47.7%)	104 (77.0%)	
Bilsky epidural grade			
1A	9 (16.7%)	10 (26.3%)	.8876
1B	15 (27.8%)	7 (18.4%)	
1C/2/3	30 (55.5%)	21 (55.3%)	
SINS classification			
Stable	40 (37.4%)	81 (60.0%)	.9449
Potentially unstable	57 (53.3%)	49 (36.3%)	
Unstable	10 (9.3%)	5 (3.7%)	
Baseline VCF			
Yes	35 (32.7%)	23 (17.0%)	.7259
No	72 (67.3%)	112 (83.0%)	

NSCLC: non small cell lung cancer; RCC: renal cell carcinoma.
Bold signifies statistical significance.

critical component in decision-making. The appropriateness of spine SBRT should be considered within this context. Physician prognostication based on experience and clinical acumen alone can be inaccurate, and quantification and modeling of data can often be of aid in this process.[12] We observed that 8.4% of patients lived ≤3 mo of spine SBRT. These patients tended to have nonbreast/prostate histology, poor performance status, polymetastatic disease, painful lesions, and paraspinal disease.

Interpretation

Within our cohort, challenges in patient selection and physician prognostication are also observed in the decision for active systemic therapy. Two-thirds of those patients who lived ≤3 mo from the time of spine SBRT also received systemic therapy (cytotoxic chemotherapy, immunotherapy, or targeted nonhormonal oral agents). This illustrates that these patients were not in hospice and deemed by multiple physicians fit to receive aggressive palliative treatments, reinforcing the need for better modeling of survival to spare these patients potentially toxic treatments in their last months of life.

Nonbreast/prostate primary cancers, poor performance status, extensive metastatic disease, pain, and paraspinal disease were predictive of living ≤3 mo after spine SBRT. Patients with breast and prostate cancer typically exhibit slower disease progression with longer survival. Recent major trials in metastatic breast cancer demonstrate survival of 58% at 3.5 yr[13] and in metastatic prostate cancer, 3-yr survival of 80%.[14] Given prolonged survival in these patients, long-term local control is important and supports the use of SBRT in this group of favorable risk patients. Ongoing clinical trials will inform this endpoint along with long-term pain control, as 3-mo pain control has historically been the primary outcome of interest. Performance status reflects function, which implicates treatment tolerability and independently predicts survival.[15] In prior spine SBRT series, poor performance status is consistently identified as a feature of patients with poor prognosis.[16-18] This is only a component of survival prediction, as reflected by 71% of those dying ≤3 mo of treatment being ECOG 0-1. Interest in defining an oligometastatic state has increased, with evidence suggesting focal therapies to limited metastatic disease yields better survival and progression outcomes.[19,20] Our study supports this, as those

TABLE 2. Proportion of Patients Treated Between 2009 and 2018 Who Die ≤3 Months After Treatment and Live >3 Years After Treatment, by Histology

	Patients treated (total = 605 patients)	Number of patients who live ≤3 mo (as percent of total patients treated with that histology)	Number of patients who live >3 yr (as percent of total patients treated with that histology)
Breast cancer	120	0 (0%)	35 (29.2%)
Prostate cancer	98	3 (3.1%)	20 (20.4%)
Colorectal cancer	41	12 (29.3%)	2 (4.9%)
NSCLC	113	16 (14.2%)	11 (9.7%)
Renal cell carcinoma	104	11 (10.6%)	5 (4.8%)
Melanoma	20	1 (5.0%)	2 (10.0%)
Thyroid cancer	12	0 (0%)	2 (16.7%)
Other[a]	97	8 (8.2%)	2 (2.1%)

[a]Other includes histologies such as anal canal cancer, bladder/urothelial cancer, esophageal cancer, endometrial cancer, cervix cancer, primary head and neck cancers, primary skin cancer, sarcoma, and unknown primary cancers.

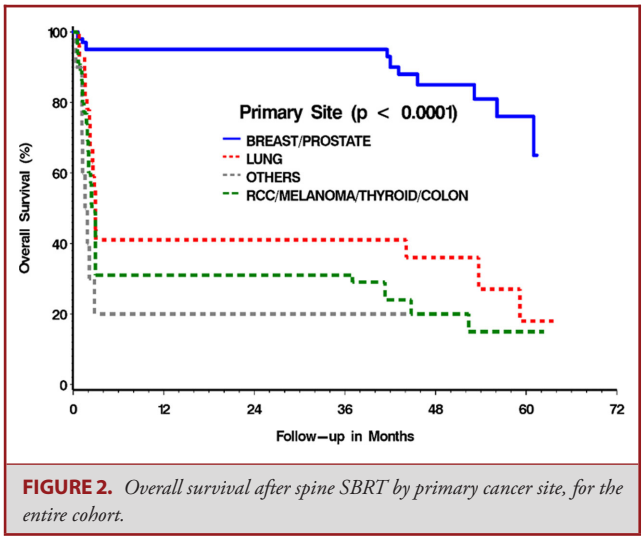

FIGURE 2. *Overall survival after spine SBRT by primary cancer site, for the entire cohort.*

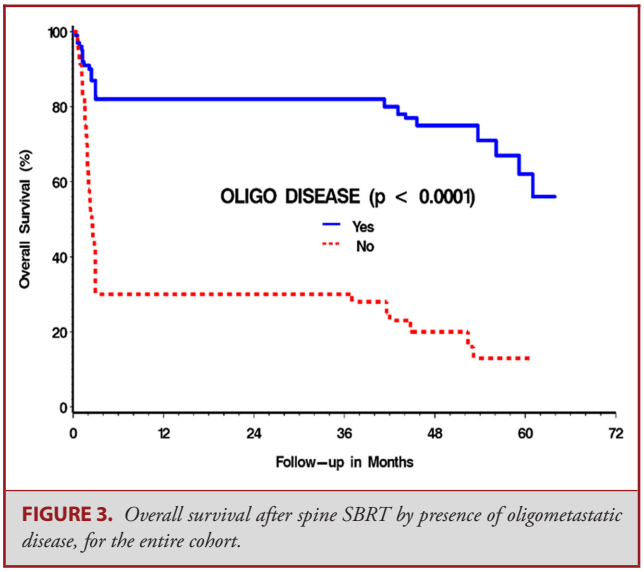

FIGURE 3. *Overall survival after spine SBRT by presence of oligometastatic disease, for the entire cohort.*

with polymetastatic disease were more likely to live ≤3 mo after treatment. To our knowledge, tumor factors have not previously been included as part of survival outcomes after spine SBRT. Patients with paraspinal disease and painful metastases were more likely to have shorter survival. Paraspinal disease may reflect a greater burden of disease in the spine and potentially reflect biologically more aggressive disease. In the surgical realm, pain has been associated with poor survival and may contribute to poor performance status because of symptom burden.[21,22] In Pointillart et al's[21] prospective study spine surgery for metastatic disease, pretreatment pain scores ≥6 determined by self-assessment on a 0 (no pain) to 10 (worst pain) scale were associated with worse survival after surgery (hazard ratio 1.988, $P = .0134$). We are unable to comment on pain response to treatment, which may better support this hypothesis, and ongoing randomized clinical trials may inform this endpoint.

Generalizability

Two indices have been developed to aid decision making in spine SBRT. A recursive partitioning analysis identified 3 factors that were most prognostic for survival—age, performance status, and time from diagnosis.[16] This study also identified a difference in survival based on radioresistant breast/prostate and other histologies. The Prognostic Index for Spinal Metastases outlines groups that would most benefit from spine SBRT.[17,18] This factors gender, performance status, previous surgery and previous radiotherapy, other visceral metastases, and time from diagnosis to metastasis. Our findings are consistent and utilize a strict ≤3 mo survival cutoff that has historically been suggested to

TABLE 3. Multivariable Analysis for Predictors of Dying ≤3 Months After Receiving Spine SBRT

	Overall *P* value	Specific *P* value	OR	95% CI Lower	95% CI Upper
Presence of widespread metastases (non-oligometastatic)	**.0032**	.0032	6.715	1.891	23.849
Lung cancer vs breast/prostate	**.0004**	<.0001	31.138	4.797	202.122
Nonbreast/prostate vs breast/prostate		.02693	104.184	8.282	>999.999
Radioresistant histology vs breast/prostate		.0242	28.839	4.913	169.291
Presence of liver metastases	.0556	.4575	4.063	0.850	19.415
Presence of lung metastases		.1136	5.863	1.290	26.644
ECOG ≥2	**.0020**	.0020	23.697	3.172	177.011
Pain free lesion (vs occasional pain)	**.0118**	.2145	3.833	1.222	12.029
Pain free lesion (vs other)		.0048	8.898	1.978	40.02
Paraspinal disease	**.0288**	.0288	2.874	1.118	7.393

be the absolute minimal prognosis to benefit from more intensive treatment such as surgery, and such a cutoff should be used for advanced radiotherapy techniques such as SBRT.

In the surgical setting, patient selection is critical because of potential for immediate morbidity and mortality. Verlaan et al[7] evaluated characteristics of 1266 patients undergoing spine surgery for metastatic spinal disease. Those living ≤3 mo had worse performance status and were older, whereas those with longer survival had lower spinal disease burden and favorable tumor histology. In their series, 84% of patients who died ≤3 mo of surgery died because of progression of the malignant process rather than surgical complications. Radiotherapy may be advantageous here, where patients can start systemic therapy sooner. Dea et al[23] reviewed 253 patients undergoing surgery for spinal metastases and compared those with survivals less than and greater than 3 mo. Those surviving ≤3 mo after had worse baseline performance status, pain, and quality of life.

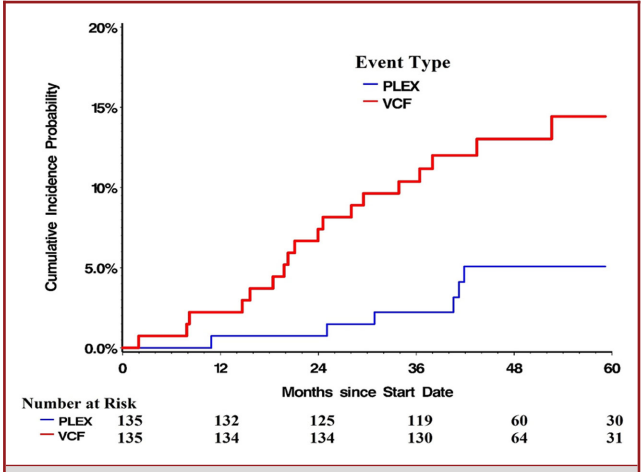

FIGURE 4. *Cumulative incidence of vertebral compression fracture (VCF) and plexopathy (PLEX) after spine SBRT with number at risk.*

Toxicities

The rate of VCF at 3 yr was 10.4% and plexopathy 2.2%. Peripheral nerve injury occurred between 11 and 42 mo (median: 36 mo) after the initial course of SBRT, and 5 of 6 patients were exposed to more than one course of radiotherapy. Stubblefield et al[24] reported 14 similar events amongst 557 segments treated with SBRT amongst 447 patients. These patients received between 18 and 26 Gy in a single fraction, whereas our usual de novo regimen is 24 Gy in 2 fractions or 30 Gy in 4 to 5 fractions when retreating or in the presence of large bulky volumes. The tolerance of peripheral nerves to SBRT dose fractionations is poorly understood and given potential devastating neurological sequelae, warrants further study. VCF was expected and our rate is consistent with the literature.[25,26] No radiation myelopathy was observed. A single duodenal perforation was observed that was nonfatal and occurred after multiple courses of SBRT to the same spinal segment.

Limitations

We are limited by the relatively low number of deaths within 3 mo of SBRT and those who survived longer than 3 yr. Secondly, we are unable to quantify systemic therapy time factors such as duration of response, which undoubtedly influences prognosis. Lastly, death is often multifactorial, and comorbidities contribute towards the success and availability of life-sustaining measures towards end of life. We attribute 3 deaths to progression of spine disease itself. Cause of death was generally because of overall progression of disease. The Charlson index may be informative as it has been reported as the strongest predictor of survival after surgery for spinal metastases.[27]

CONCLUSION

Overall, within a large cohort of over 600 patients including over 1400 segments treated with spine SBRT, 8.4% of patients die within 3 mo of treatment. Patients with less radiosensitive

TABLE 4. Late Noncompression Fracture Toxicities Observed After Spine SBRT

ID	Toxicity	Age	Primary cancer	Location	Time from initial SBRT course to toxicity	Local radiotherapy courses (months prior to event)
1	Brachial plexopathy	76	Prostate	C7	40 mo	1. 20 Gy/5 fractions (51 mo) 2. 30 Gy/4 fractions (40 mo) 3. 30 Gy/4 fractions (4 mo)
2	Lumbosacral plexopathy	61	NSCLC	S1	11 mo	1. 24 Gy/2 fractions (11 mo)
3	Lumbosacral plexopathy	68	Breast	L4-5	41 mo	1. 24 Gy/2 fractions (41 mo) 2. 24 Gy/2 fractions (29 mo)
4	Lumbosacral plexopathy	82	Melanoma	S1	30 mo	1. 24 Gy/2 fractions (30 mo) 2. 30 Gy/4 fractions (16 mo) 3. 30 Gy/5 fractions (14 mo)
5	Lumbosacral plexopathy	54	Colon	L4-5	25 mo	1. 24 Gy/2 fractions (25 mo) 2. 30 Gy/4 fractions (21 mo) 3. 35 Gy/5 fractions (15 mo)
6	Lumbosacral plexopathy	60	Prostate	L5	41 mo	1. 24 Gy/2 fractions (41 mo) 2. 30 Gy/4 fractions (6 mo)
7	Duodenal perforation	78	RCC	T11-L1	17 mo	1. 24 Gy/2 fractions (17 mo) 2. 30 Gy/5 fractions (to local lymph node; 12 mo) 3. 30 Gy/4 fractions (5 mo)

histologies (ie, not breast or prostate), ECOG $\geq$2, and polymetastatic disease had shorter survival after spine SBRT. Other factors such as presence of paraspinal disease and painful metastases represent further tumor-related factors to consider when selecting patients for spine SBRT. Late serious toxicities such as plexopathy are rare and were observed predominantly in heavily radiated patients, even in patients surviving several years after spine SBRT.

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Supplemental Digital Content. Table. Breakdown of patients with NSCLC and RCC by cohort, who received targeted therapy or immunotherapy.

COMMENT

In this large single center retrospective study of prospectively collected data, the authors aim to identify factors associated with dying within 3 mo or living more than 3 yr after SBRT treatment. They found that non favorable histologies (nonbreast/prostate primaries), poor performance status, widespread metastatic disease, painful lesions and paraspinal disease was associated with short survival.

Their results support data from surgical series where poor performance status is consistently associated with short survival. Proper patient selection is crucial when using more invasive and costlier treatment like surgery and SBRT. As opposed to surgery, which can immediately improve stability, neurology or pain, the main goal of SBRT is towards better local control rates and thus might be futile in someone with poor survival, especially considering the added resources, time, and cost of SBRT compared to conventional radiation therapy and similar short term pain control.

As this treatment modality is increasingly utilized in many centers, another key message of this paper is their much-needed description of the late toxicities associated with SBRT. Vertebral compression fractured occurred in 10.4% at 3 yr, which is lower than previously reported. No radiation myelopathy and a very low rate of plexopathy (2.2% at 3 yr) was reported, even in long survivors which will definitely support the use of this treatment modality to increase local control in patients expected to outlive local control conferred by conventional techniques.

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