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Sarcopenia Predicts Overall Survival in Patients with Lung, Breast, Prostate, or Myeloma Spine Metastases Undergoing Stereotactic Body Radiation Therapy (SBRT), Independent of Histology

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This work has been previously presented as oral presentations at the Joint AANS/CNS Spine Section Annual Meeting in Orlando, Florida, on March 16, 2018, and at the American Association of Neurological Surgeons Annual Meeting in New Orleans, Louisiana, on April 23, 2018.

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Received, October 18, 2018.
Accepted, March 11, 2019.

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BACKGROUND: Predicting survival of patients with spinal metastases would help stratify treatments from aggressive to palliation.

OBJECTIVE: To evaluate whether sarcopenia predicts survival in patients with lung, breast, prostate, or multiple myeloma spinal metastases.

METHODS: Psoas muscle measurements in patients with spinal metastasis were taken from computed tomography scans at 2 time points: at first episode of stereotactic body radiation therapy (SBRT) and from the most recent scan available. Overall survival and hazard ratios were calculated with multivariate cox proportional hazards regression analyses.

RESULTS: In 417 patients with spinal metastases, 40% had lung cancer, 27% breast, 21% prostate, and 11% myeloma. Overall survival was not associated with age, sex, ethnicity, levels treated, or SBRT volume. Multivariate analysis showed patients in the lowest psoas tertile had shorter survival (222 d, 95% CI = 185-323 d) as compared to the largest tertile (579 d, 95% CI = 405-815 d), (HR1.54, $P = .005$). Median psoas size as a cutoff value was also strongly predictive for survival (HR1.48, $P = .002$). Survival was independent of tumor histology. The psoas/vertebral body ratio was also successful in predicting overall survival independent of tumor histology and gender (HR1.52, $P < .01$). Kaplan–Meier survival curves visually represent survival ($P = .0005$).

CONCLUSION: In patients with spine metastases, psoas muscle size as a hallmark of frailty/sarcopenia is an objective, simple, and effective way to identify patients who are at risk for shorter survival, regardless of tumor histology. This information can be used to help with surgical decision making in patients with advanced cancer, as patients with small psoas sizes are at higher risk of death.

KEY WORDS: Frailty, Medical oncology, Metastasis, Sarcopenia, Spine

Neurosurgery 0:1–12, 2019 DOI:10.1093/neuros/nyz216 www.neurosurgery-online.com

Creating valid, accurate, and reliable markers of overall survival in the field of oncology would optimize treatment allocation (whether chemotherapy, radiation, surgery, or palliation) for vulnerable cancer patients. This concept is especially relevant to patients who have spinal metastases, as according to the TNM Classification of Malignant Tumors, most of these patients will have stage IV disease and, by definition, will have the lowest rate of survival. However, select patients often routinely undergo resource-intensive surgery for their metastatic spinal disease, as it has been shown that combined surgical resection and radiation is superior to radiotherapy alone in terms of overall survival, neurological outcome, and pain control.[1-7] Unfortunately, these procedures are not only expensive and potentially morbid (with the development of a complication removing any survival benefit),[8-13] they ultimately delay the definitive oncologic treatments of chemotherapy and radiotherapy.[14]

ABBREVIATIONS: CT, computed tomography; **HR,** hazard ratios; **mFI,** modified frailty index; **SBRT,** stereotactic body radiation therapy

In a cost-conscious environment with limited resources, both patients and society will gain when aggressive and expensive cancer treatment, whether it be surgery, radiation, chemotherapy, or a combination, is reserved only for those patients most likely to benefit.[15] Outcome models may offer providers, families, and patients with objective end-of-life data to help guide treatment decision making, but current models for patients with spine metastasis are insufficient and focus on single histologies.[16-19] In choosing whether surgery is appropriate for spinal metastasis, scoring systems have been developed to guide surgical decision making,[14,20-23] but validity studies have identified inaccuracies in predicting postoperative morbidity and overall survival.[7,24-26] New objective measurements to provide realistic and accurate expectations for overall survival and fitness for treatments in patients with spine metastases would prove beneficial in stratifying and selecting therapeutic options.

One of the hallmarks of human senescence is that of frailty, which has been defined as a decreased reserve to physiologic stressors.[27,28] Identifying a frail patient carries clinical importance, as this population is at an increased risk for postoperative morbidity and mortality.[29,30] The direct measurement of frailty is impractical,[31,32] and so sarcopenia (lack of muscle mass) has been used successfully as a surrogate to predict postoperative outcomes,[33-37] including after lumbar spine surgery.[38] During oncologic surgery, sarcopenia has been used to identify patients at risk for postoperative morbidity and shorter progression-free survival,[39-42] and it has been revealed that the association of increased muscle mass and longer overall survival is independent of a surgical procedure.[43-49]

We have previously shown that sarcopenic patients with lung cancer spinal metastases have decreased overall survival.[50] In this study, we expanded our previous approach to use the frailty/sarcopenia paradigm to predict overall survival in patients with lung, breast, prostate, or myeloma spinal metastases. Our hypothesis is that sarcopenia can be used as a unique predictor of overall mortality in patients with spine metastasis.

METHODS

Study Design, Setting, and Participants

This study was conducted after approval from our Institutional Review Board (IRB no. 4370), and no patient consent was required because of the retrospective nature of this study. From an index of patients having undergone stereotactic body radiation therapy (SBRT) for metastatic spine cancer at our institution from 2002 to 2012, we retrospectively identified those with lung, breast, prostate, or multiple myeloma. In patients with both lung and breast or prostate cancer, the lung cancer diagnosis was used for analysis. Although external beam radiation therapy is typically used for myeloma spinal metastases, the patients in this cohort were carefully selected to receive SBRT. Recommendations were made by consensus opinion at a multidisciplinary spine tumor board attended by radiation oncologists, neurosurgeons, neuroradiologists, and medical oncologists.

Data Sources, Variables, Bias, and Study Size

The primary data source was the electronic medical record. Morphometric analysis of the psoas muscle at the L4 vertebral level was performed using previously described methodology.[50-53] Briefly, the area (in centimeters squared) of each patient's psoas muscle was measured and recorded. In addition, the L4 vertebral body area was measured and recorded in the same fashion. This methodology was applied to computed tomography (CT) scans at two time points, the closest (within 200 d) to the first SBRT (SBRT-CT), as well as to the most recent CT available (recent CT). Although only a small percentage of patients received spine surgery (15%), most procedures (~70%) occurred within 200 d of the first SBRT as well. The primary outcome was overall survival from imaging. Other demographic variables such as age, gender, ethnicity, number of spinal levels treated, type of cancer, spine surgery, medication use (bisphosphonates and antiangiogenesis), post-SBRT chemotherapy, and SBRT target volume were also considered. A 5 factor modified frailty index (mFI) at the time of first SBRT was also included.[54] The mFI has been shown to be a powerful indicator of a patient's overall health status, predicting survival and morbidity after surgical procedures.[55,56] Given the retrospective nature of this study, we are unable to account for unintended bias as well as for study size.

Quantitative Variables and Statistical Methods

Psoas muscle sizes were divided into tertiles according to average psoas area. To account for gender-specific differences, male and female psoas sizes were divided into separate groups and stratified accordingly, except where otherwise stated. In addition, the ratio of the average psoas area to the L4 vertebral body area (P: VBA ratio) was also measured; this was done to account for patients of smaller stature, who are not necessarily frailer. The rationale is that both vertebral body size and psoas size are dependent on stature under normal physiologic conditions; however, whereas psoas size can decrease with frailty/sarcopenia, vertebral body size should not, and so, the ratio may correct for stature-related psoas size differences. The use of this ratio had been described previously.[50] In addition to stratifying our cohort into tertiles, analysis of those above and below the median psoas size was also performed. The primary outcome was overall survival, which was calculated from the date of the patient's CT scan to date of death or last follow-up. The median survival time (in days) along with the corresponding 95% confidence interval were computed using Kaplan–Meier estimates for all patients, as well as for the variables of interest. Cox proportional hazards regression analyses were done to estimate the hazard ratios (HR) and test for differences in the variables of interest. This was used for both the univariate and multivariate analyses. The testing level was set at 0.05. All analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Participants and Descriptive Data

There were 417 patients with spinal metastases from lung cancer, breast cancer, prostate cancer, or multiple myeloma that had recent imaging available and 369 patients with imaging available at SBRT. Seven patients had both lung and breast or prostate cancer. The SBRT-CT cohort had an average age of 65.3 yr, with about equal split of males and females, and 53%

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of patients Caucasian, 39% African American, and 5% other (Table 1). Of these patients, 40% received single-level SBRT and 15% underwent a spinal surgical procedure. The demographics for the recent CT cohort patients are similar (Table 1).

Outcome Data and Main Results

The median survival of SBRT-CT patients was 356 d (95% CI = 298-445 d) and for recent CT patients it was 173 d (95% CI = 140-204 d). Table 2 illustrates the univariate relationship of median overall survival with patient demographic and medical information, with HR and *P* values for specific variables of interest. Patient age, gender, ethnicity, number of levels treated with SBRT, and mFI did not affect overall survival. The SBRT-CT cohort survival was affected by spine surgery, bisphosphonate use, antiangiogenesis medication use, post-SBRT chemotherapy, and SBRT target volume. Overall survival was associated with primary tumor histology and with myeloma patients having significantly longer survival compared to the other three groups ($P < .001$).

Table 3 illustrates the relationship of median overall survival with morphometric measurements (sarcopenia), with HR with *P* values for the variables of interest. Average psoas size significantly predicted overall survival. In the SBRT cohort and after multivariate analysis, patients in the 1st tertile (smallest muscle area) for average psoas size had significantly shorter survival than those in the 3rd tertile (largest muscle area): 222 d vs 579, HR 1.54 (95% CI = 1.14-2.09), $P = .005$. Median psoas size also predicted survival in this population of patients, with patients above median having a longer lifespan (HR 1.48, $P = .002$). The ratio of average psoas size to vertebral body area (P: VBA ratio) showed similar results; 1st tertile had significantly shorter survival than the 3rd tertile (HR 1.45, $P = .019$). Patients above the median for P: VBA ratio had significantly longer survival (HR 1.32, $P = .024$).

The recent CT cohort also had statistically significant findings after multivariate analysis. Not only did the 1st and 3rd tertiles have significant differences in survival (HR 2.02, $P < .001$), but differences were also observed when comparing the 1st and 2nd tertiles (HR 1.36, $P = .024$) and the 2nd and 3rd tertiles (HR 1.48, $P = .005$). Median psoas size was strongly predictive of survival in this cohort (HR 1.73, $P < .001$), and the P: VBA ratio showed significance when comparing the medians (HR 1.52, $P < .001$), 1st vs 3rd tertiles (HR 1.87, $P < .001$), and 2nd vs 3rd tertiles (HR 1.65, $P < .001$), but not 1st vs 2nd tertiles. Kaplan–Meier survival curves of the SBRT cohort illustrate the differences in survival between different tertiles (Figure 1, log-rank test, $P = .0005$).

Because of gender-specific differences, our previous model relied on splitting male and female psoas sizes into separate groups. One of our hypotheses is that the P: VBA ratio should account for gender-specific differences, and so repeat calculations were performed without separating males and females (Table 4). P: VBA ratio tertiles significantly predicted survival of the overall population in both the SBRT-CT and the recent CT cohorts. In the SBRT-CT cohort, patients in the 1st tertile had significantly shorter survival than those in the 3rd tertile, HR 1.52 (95% CI = 1.11-2.09), $P = .009$. Patients in the 2nd tertile also had significantly longer survival than those in the 3rd tertile, HR 1.54 (95% CI = 1.14-2.09), $P = .005$. Patients above the median for P: VBA ratio also had significantly longer survival as well, HR 1.37 (95% CI = 1.06-1.77), $P = .014$. Similar results and trends were observed in the recent CT cohort. The nongendered cutoffs in the SBRT-CT cohort (Table 4) consistently produced stronger and more significant predictions than the gendered cutoffs (Table 3). Kaplan–Meier survival curves of the SBRT-CT cohort illustrate the ability of the P: VBA ratio to differentiate survival (Figure 2), log-rank $P = .0001$.

DISCUSSION

Key Results

Our results highlight the utility of morphometric analysis of psoas size as a surrogate for frailty/sarcopenia in predicting overall survival in patients with a variety of cancers. This study illustrates that patients with spinal metastases (from lung, breast, prostate, or multiple myeloma) and clinical signs of sarcopenia, as measured by psoas size, have decreased overall survival. This survival difference was irrespective of primary tumor histology, as well as other demographic, oncologic, functional, and therapeutic factors on multivariate analysis. The ability to predict overall survival of patients with different types of cancer in different stages of disease (stage IV for prostate, lung, and breast only) using a single methodology (psoas size measurements) is novel and implies that the frailty/sarcopenia technique can be broadly applied to assist in oncologic decision making. These findings are consistent with our previously published work,[50] as well as with the literature generally, which suggests that frailty/sarcopenia is an accurate marker of a patient's overall health and subsequently their ability to survive malignancy.

Interpretation

As we show that the frailty/sarcopenia paradigm can predict overall survival independent of tumor histology and stage of disease, these results have broad implications within the field of oncology. All of the patients with lung, breast, and prostate cancer had stage IV disease by the nature of having distant bony metastases; whereas multiple myeloma is staged independently of osseous metastasis,[57] the burden of bony disease has been shown to independently decrease quality of life as well as increase the risk of mortality.[58-60] We were able to identify that psoas size and P: VBA ratio can accurately predict overall survival in patients with late stage disease, regardless of primary cancer type. The P: VBA ratio also allows for gender-neutral cut-points, with the potential of introducing a single numerical value that can be applied clinically to predict survival. This process can theoretically be applied to any patients with spine metastasis to predict overall survival, irrespective of their primary tumor type.

TABLE 1. Demographic Information

Variable		CT Within 200 d of First SBRT					Most Recent CT				
		All patients (N = 369)	Lung (N = 163)	Breast (N = 96)	Prostate (N = 75)	Myeloma (N = 35)	All patients (N = 417)	Lung (N = 168)	Breast (N = 114)	Prostate (N = 89)	Myeloma (N = 46)
Age at CT	Mean (SD)	65.3 (11.5)	65.3 (11.2)	61.7 (12.3)	71.6 (8.6)	61.7 (11.0)	66.3 (11.4)	65.3 (11.3)	63.5 (12.2)	72.8 (8.5)	64.4 (10.6)
Gender	Male	182 (49%)	86 (53%)	0 (0%)	75 (100%)	21 (60%)	210 (50%)	90 (54%)	0 (0%)	89 (100%)	31 (67%)
	Female	187 (51%)	77 (47%)	96 (100%)	0 (0%)	14 (40%)	207 (50%)	78 (46%)	114 (100%)	0 (0%)	15 (33%)
Ethnicity	Caucasian	195 (53%)	102 (63%)	51 (53%)	28 (37%)	14 (40%)	217 (52%)	104 (62%)	61 (54%)	33 (37%)	19 (41%)
	African American	143 (39%)	49 (30%)	34 (35%)	40 (53%)	20 (57%)	168 (40%)	52 (31%)	42 (37%)	48 (54%)	26 (57%)
	Other	17 (5%)	7 (4%)	7 (7%)	2 (3%)	1 (3%)	18 (4%)	7 (4%)	7 (6%)	3 (3%)	1 (2%)
	N/A	14 (4%)	5 (3%)	4 (4%)	5 (7%)	0 (0%)	14 (3%)	5 (3%)	4 (4%)	5 (6%)	0 (0%)
Number of treated levels	1	146 (40%)	75 (46%)	34 (36%)	23 (31%)	14 (40%)	168 (40%)	78 (46%)	42 (37%)	29 (33%)	19 (41%)
	2	110 (30%)	55 (34%)	25 (26%)	21 (28%)	9 (26%)	123 (30%)	55 (33%)	31 (27%)	24 (27%)	13 (28%)
	3	65 (18%)	22 (13%)	20 (21%)	17 (23%)	6 (17%)	67 (16%)	23 (14%)	20 (18%)	17 (19%)	7 (15%)
	4+	46 (13%)	11 (7%)	16 (17%)	13 (18%)	6 (17%)	57 (14%)	12 (7%)	20 (18%)	18 (20%)	7 (15%)
Spine surgery	Yes	55 (15%)	20 (12%)	13 (14%)	10 (13%)	12 (34%)	61 (15%)	20 (12%)	16 (14%)	12 (13%)	13 (28%)
	No	314 (85%)	143 (88%)	83 (86%)	65 (87%)	23 (66%)	356 (85%)	148 (88%)	98 (86%)	77 (87%)	33 (72%)
Bisphosphonates	Yes	197 (53%)	53 (33%)	71 (74%)	50 (67%)	23 (66%)	228 (55%)	54 (32%)	84 (74%)	59 (66%)	31 (67%)
	No	172 (47%)	110 (67%)	25 (26%)	25 (33%)	12 (34%)	189 (45%)	114 (68%)	30 (26%)	30 (34%)	15 (33%)
Anti-angiogenesis Meds	Yes	129 (35%)	46 (28%)	51 (53%)	8 (11%)	24 (69%)	148 (35%)	46 (27%)	58 (51%)	10 (11%)	34 (74%)
	No	240 (65%)	117 (72%)	45 (47%)	67 (89%)	11 (31%)	269 (65%)	122 (73%)	56 (49%)	79 (89%)	12 (26%)
Post-SBRT chemotherapy	Yes	268 (73%)	98 (60%)	85 (89%)	55 (73%)	30 (86%)	306 (74%)	102 (61%)	101 (87%)	63 (72%)	40 (87%)
	No	101 (27%)	65 (40%)	11 (11%)	20 (27%)	5 (14%)	110 (26%)	66 (39%)	12 (11%)	25 (28%)	6 (13%)
5-Factor modified frailty index	0	94 (25%)	44 (27%)	23 (24%)	17 (23%)	10 (29%)	110 (26%)	45 (27%)	31 (27%)	23 (26%)	11 (24%)
	1	146 (40%)	69 (42%)	30 (31%)	28 (37%)	19 (54%)	164 (39%)	71 (42%)	35 (31%)	32 (36%)	26 (57%)
	2	83 (22%)	32 (20%)	22 (23%)	23 (31%)	6 (17%)	91 (22%)	23 (20%)	25 (22%)	24 (27%)	9 (20%)
	3	35 (9%)	14 (9%)	14 (15%)	7 (9%)	0 (0%)	38 (9%)	14 (8%)	15 (13%)	9 (10%)	0 (0%)
	4	9 (2%)	3 (2%)	6 (6%)	0 (0%)	0 (0%)	10 (2%)	3 (2%)	7 (6%)	0 (0%)	0 (0%)
	5	2 (1%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	3 (1%)	2 (1%)	1 (1%)	0 (0%)	0 (0%)
SBRT target volume (cc)	Mean (SD)	74.58 (69.36)	50.93 (38.25)	73.44 (76.92)	118.7 (88.86)	90.71 (63.69)	76.56 (71.89)	51.68 (39.25)	79.66 (85.44)	118.0 (88.05)	83.07 (58.74)
SBRT target volume (cc)	0 to 30	73 (22%)	46 (33%)	19 (22%)	3 (5%)	5 (14%)	82 (23%)	47 (33%)	24 (24%)	3 (4%)	8 (17%)
	>30 to 50	81 (25%)	39 (28%)	27 (31%)	10 (16%)	5 (14%)	85 (24%)	40 (28%)	27 (27%)	12 (17%)	6 (13%)
	>50 to 100	93 (29%)	41 (29%)	22 (25%)	17 (27%)	13 (37%)	105 (29%)	42 (29%)	25 (25%)	19 (27%)	19 (41%)
	>100	79 (24%)	13 (9%)	20 (23%)	34 (53%)	12 (34%)	89 (25%)	14 (10%)	25 (25%)	37 (52%)	13 (28%)
Primary cancer	Lung	163 (44%)					168 (40%)				
	Breast	96 (26%)					114 (27%)				
	Prostate	75 (20%)					89 (21%)				
	Myeloma	35 (9%)					46 (11%)				

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TABLE 2. The Effects of Patient Demographics on Survival

Variable		CT Within 200 d of First SBRT			Most recent CT		
		Median survival in days (95% CI)	Unadjusted Hazard Ratio (95% CI)	*P* value	Median survival in days (95% CI)	Unadjusted Hazard Ratio (95% CI)	*P* value
Age at CT		(Increase of 10 years)	1.09 (0.98, 1.20)	.107	(Increase of 10 years)	1.04 (0.94, 1.14)	.475
Gender	Male	332 (261, 471)	1.06 (0.85, 1.3)	.585	191 (138, 234)	0.88 (0.72, 1.09)	.238
	Female	391.5 (298, 502)	Ref		157 (115, 201)	Ref	
Ethnicity	Caucasian	340 (272, 434)	Ref	.184	179 (145, 222)	Ref	.381
	African American	433 (302, 600)	0.84 (0.66, 1.06)		162 (115, 230)	0.84 (0.68, 1.05)	
	Other	191 (40, NA)	0.71 (0.38, 1.36)		132 (40, NA)	0.75 (0.41, 1.38)	
	N/A	211.5 (48, 519)	1.42 (0.77, 2.61)		85 (33, 519)	1.09 (0.59, 2.00)	
Number of treated levels	Single	348 (222, 435)	1.00 (0.8, 1.25)	.985	179 (124, 237)	0.86 (0.7, 1.07)	.174
	Multiple	391.5 (306, 525)	Ref		173 (132, 211)	Ref	
Spine surgery	Yes	513 (299, 965)	0.68 (0.46, 0.94)	*.019	201 (115, 280)	0.82 (0.6, 1.11)	.194
	No	337 (272, 431)	Ref		168 (133, 204)	Ref	
Bisphosphonates	Yes	587 (497, 722)	0.55 (0.44, 0.69)	* < .001	168 (129, 210)	0.99 (0.8, 1.22)	.893
	No	191 (153, 237)	Ref		173 (133, 224)	Ref	
Anti-angiogenesis meds	Yes	525 (356, 688)	0.78 (0.62, 0.98)	*.034	210 (157, 257)	0.9 (0.72, 1.12)	.327
	No	291 (222, 387)	Ref		156 (120, 191)	Ref	
Post-SBRT chemotherapy	Yes	513 (405, 602)	0.46 (0.36, 0.58)	* < .001	190 (157, 248)	0.72 (0.57, 0.91)	*.005
	No	142.5 (87, 204)	Ref		115 (79, 179)	Ref	
5-factor modified frailty index	0	404 (282, 682)	Ref	.388	204 (132, 265)	Ref	.421
	1	330 (253, 479)	1.21 (0.91,1.61)		179 (132, 226)	1.12 (0.86,1.46)	
	2	340 (218, 497)	1.32 (0.95, 1.82)		131 (100, 208)	1.28 (0.95, 1.74)	
	3+	395 (180, 191)	1.19 (0.80, 1.76)		156 (95, 246)	1.21 (0.83, 1.37)	
SBRT target volume (cc)		(Increase over 10 cc)	0.98 (0.96, 1.0)	*.042	(Increase over 10cc)	1.01 (0.99, 1.02)	.491
SBRT target volume (cc)	0 to 30	237 (172, 379)	Ref	.169	185 (116, 237)	Ref	.802
	>30 to 50	319 (222, 525)	0.81 (0.57, 1.15)		197 (139, 282)	0.9 (0.65, 1.27)	
	>50 to 100	337 (222, 481)	0.85 (0.61, 1.19)		167 (101, 280)	1.02 (0.75, 1.4)	
	>100	686 (483, 858)	0.68 (0.48, 0.967)		173 (126, 226)	1.06 (0.77, 1.47)	
Primary cancer	Lung	176.5 (140, 211)	7.04 (4.36, 11.36)	* < .001[1]	185.5 (146, 228)	2.74 (1.82, 4.1)	* < .001[2]
	Breast	707 (551, 1012)	2.15 (1.31, 3.51)		105 (74, 157)	2.83 (1.85, 4.33)	
	Prostate	477 (302, 717)	2.86 (1.73, 4.73)		124 (98, 203)	2.85 (1.84, 4.4)	
	Myeloma	1734 (1071, 4517)	Ref		989 (379, 2185)	Ref	

[1] $P < .003$ for all pairwise site comparisons, except for breast vs prostate with $P = .09$.
[2] $P < .001$ for comparison of Myeloma to each of the other sites; $P > .77$ for comparisons of all other sites.
*Indicates statistical significance, $P < .05$.

The timing of imaging is crucial. We present the data from 2 different time points, at the first SBRT and from the most recent scan available. The first SBRT is clinically relevant because it is when a patient with advanced oncologic disease receives their first radiation treatment for (usually newly diagnosed) spine metastases. This is commonly when a spine surgeon becomes involved in the patient's care to provide surgical decision making regarding the spine metastases. These patients are also at a similar stage of their disease, not only because of spread to the spine but also having sufficient functional status to be referred to and receive radiation. We also selected the most recent CT because it is conceptually similar to a patient with advanced and disseminated cancer coming through the emergency room and receiving imaging; spine surgeons in this context are again asked to comment on whether any of the spine metastases require surgical intervention, and so the most recent imaging is reviewed.

We observed noticeable differences in outcome between these 2 time points; SBRT-CT patients had survival affected by spine surgery, bisphosphonate use, antiangiogenesis medication use, post-SBRT chemotherapy, and SBRT target volume, whereas the recent CT patients did not. This is likely that at the time of SBRT, patients can still potentially be rescued (or at least provided

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TABLE 3. The Effects of Sarcopenia on Survival, Using Gender-Based Cutoffs

		CT within 200 d of First SBRT						Most recent CT					
				Unadjusted		Adjusted[1]				Unadjusted		Adjusted[1]	
Morphometric measurement		N	Median survival in days (95% CI)	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value	N	Median survival in days (95% CI)	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value
Average psoas tertiles	1st tertile	121	222 (185, 323)	1.33 (1.02, 1.74)	*.038 (1 vs 2)	1.28 (0.96, 1.69)	.09 (1 vs 2)	137	115 (91, 153)	1.47 (1.14, 1.90)	*.002 (1 vs 2)	1.36 (1.04, 1.77)	*.024 (1 vs 2)
	2nd tertile	124	360 (253, 525)	1.72 (1.31, 2.27)	* < .001 (1 vs 3)	1.54 (1.14, 2.09)	*.005 (1 vs 3)	141	157 (109, 222)	1.95 (1.51, 2.53)	* < .001 (1 vs 3)	2.02 (1.53, 2.66)	* < .001 (1 vs 3)
	3rd tertile	123	579 (405, 815)	1.3 (0.99, 1.71)	.064 (2 vs 3)	1.21 (0.90, 1.63)	.21 (2 vs 3)	139	298 (225, 423)	1.33 (1.02, 1.72)	*.034 (2 vs 3)	1.48 (1.12, 1.97)	*.005 (2 vs 3)
Average psoas Median	Less than median	184	263.5 (197, 989)	1.51 (1.21, 1.88)	* < .001	1.48 (1.15, 1.9)	*.002	209	124 (99, 157)	1.67 (1.35, 2.06)	* < .001	1.73 (1.38, 2.17)	* < .001
	Greater than median	184	513 (357, 673)	Ref		Ref		208	254 (205, 321)	Ref		Ref	
Ratio of Average Psoas to Vertebral Body Area	1st tertile	120	218 (157, 323)	1.37 (1.04, 1.79)	*.024 (1 vs 2)	1.22 (0.92, 1.62)	.17 (1 vs 2)	136	120 (88, 156)	1.24 (0.96, 1.59)	.1 (1 vs 2)	1.13 (0.87, 1.48)	.34 (1 vs 2)
	2nd tertile	122	340.5 (254, 497)	1.73 (1.32, 2.28)	* < .001 (1 vs 3)	1.45 (1.06, 1.99)	*.019 (1 vs 3)	139	185 (127, 218)	1.82 (1.4, 2.36)	* < .001 (1 vs 3)	1.87 (1.41, 2.48)	* < .001 (1 vs 3)
	3rd tertile	122	554 (405, 815)	1.27 (0.96, 1.68)	.091 (2 vs 3)	1.19 (0.88, 1.62)	.266 (2 vs 3)	138	286 (180, 423)	1.47 (1.13, 1.91)	*.003 (2 vs 3)	1.65 (1.25, 2.02)	* < .001 (2 vs 3)
Ratio of average psoas to vertebral body area	Less than median	181	250 (204, 353)	1.43 (1.15, 1.80)	*.001	1.32 (1.04, 1.69)	*.024	206	140 (107, 168)	1.52 (1.23, 1.88)	* < .001	1.52 (1.21, 1.90)	* < .001
	Greater than median	183	513 (337, 670)	Ref		Ref		207	234 (179, 302)	Ref		Ref	

[1]Adjusted for age, sex, race, number of levels (single vs multiple), surgery done, bisphosphonates use, antiangiogenesis medication use, modified Frailty Index, post-SBRT chemotherapy, and primary cancer site.
*Indicates statistical significance, $P < .05$

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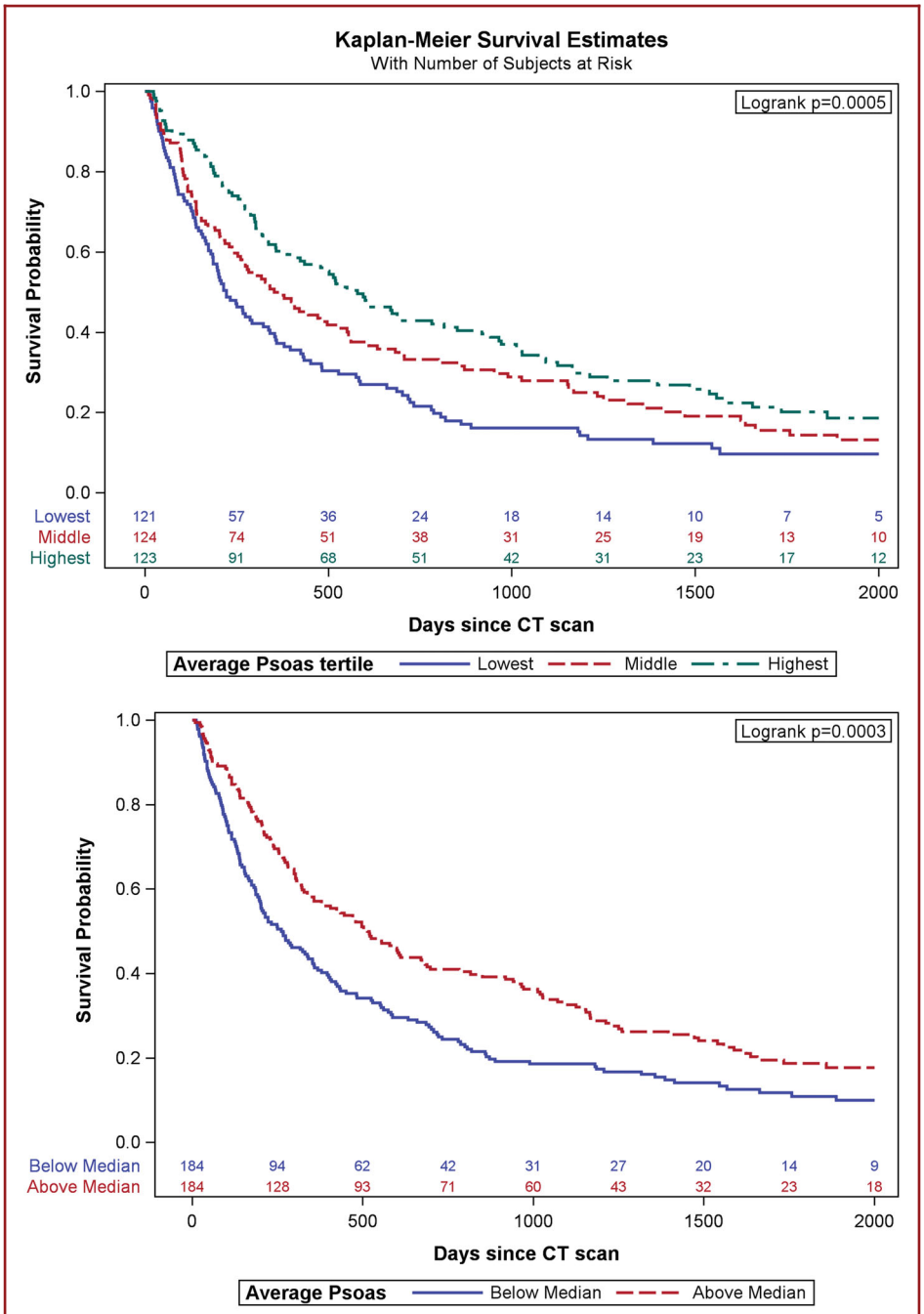

FIGURE 1. *Kaplan–Meier survival estimates of the SBRT-CT cohort using average and median psoas size. Multivariate analysis was employed to account for age, sex, ethnicity, number of levels (single vs multiple), surgery done, bisphosphonates use, antiangiogenesis medication use, modified Frailty Index, post-SBRT chemotherapy, and primary cancer site. Log-rank test shows statistically significant differences in overall survival.*

increased longevity) from their cancer with treatments (surgery, chemotherapy, and radiation). The timing of recent CT likely represents the final hospital admission before demise, when treatments have failed and few therapeutic options remain. This may also explain why recent CTs had a greater number of statistically significant results than SBRT-CT for average psoas size; patients with frailty/sarcopenia may be less likely to survive a serious hospital admission (timing of recent CT), whereas patients at the

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TABLE 4. The Effects of Sarcopenia on Survival, Using Nongendered Cutoffs

Morphometric measurement		CT Within 200 d of First SBRT						Most recent CT					
				Unadjusted		Adjusted[1]				Unadjusted		Adjusted[1]	
		N	Median survival in days (95% CI)	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value	N	Median survival in days (95% CI)	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value
Ratio of average psoas to vertebral body area	1st tertile	121 (64% female)	248 (186, 337)	1.13 (0.86, 1.48)	.375 (1 vs 2)	0.98 (0.74, 1.30)	.909 (1 vs 2)	137 (61% female)	126 (91, 157)	1.16 (0.91, 1.50)	.237 (1 vs 2)	1.07 (0.83, 1.38)	.63 (1 vs 2)
	2nd tertile	121 (51% female)	306 (237, 387)	1.81 (1.37, 2.38)	* < .001 (1 vs 3)	1.52 (1.11, 2.09)	*.009 (1 vs 3)	138 (54% female)	173 (116, 218)	1.83 (1.41, 2.37)	* < .001 (1 vs 3)	1.81 (1.36, 2.42)	* < .001 (1 vs 3)
	3rd tertile	122 (36% female)	606 (479, 1028)	1.6 (1.21, 2.11)	*.001 (2 vs 3)	1.54 (1.14, 2.09)	*.005 (2 vs 3)	138 (33% female)	280 (210, 423)	1.57 (1.21, 2.05)	* < .001 (2 vs 3)	1.7 (1.28, 2.37)	* < .001 (2 vs 3)
Ratio of average psoas to vertebral body area	Less than median	182 (62% female)	244 (200, 330)	1.56 (1.24, 1.95)	*.001	1.37 (1.06, 1.77)	*.014	206 (60% female)	138 (107, 168)	1.55 (1.25, 1.91)	* < .001	1.47 (1.17, 1.86)	* < .001
	Greater than median	182 (38% female)	551 (399, 698)	Ref		Ref		207 (38% female)	237 (180, 302)	Ref		Ref	

[1]Adjusted for age, sex, race, number of levels (single vs multiple), surgery done, bisphosphonates use, antiangiogenesis medication use, modified Frailty Index, post-SBRT chemotherapy, and primary cancer site.
*Indicates statistical significance, $P < .05$.

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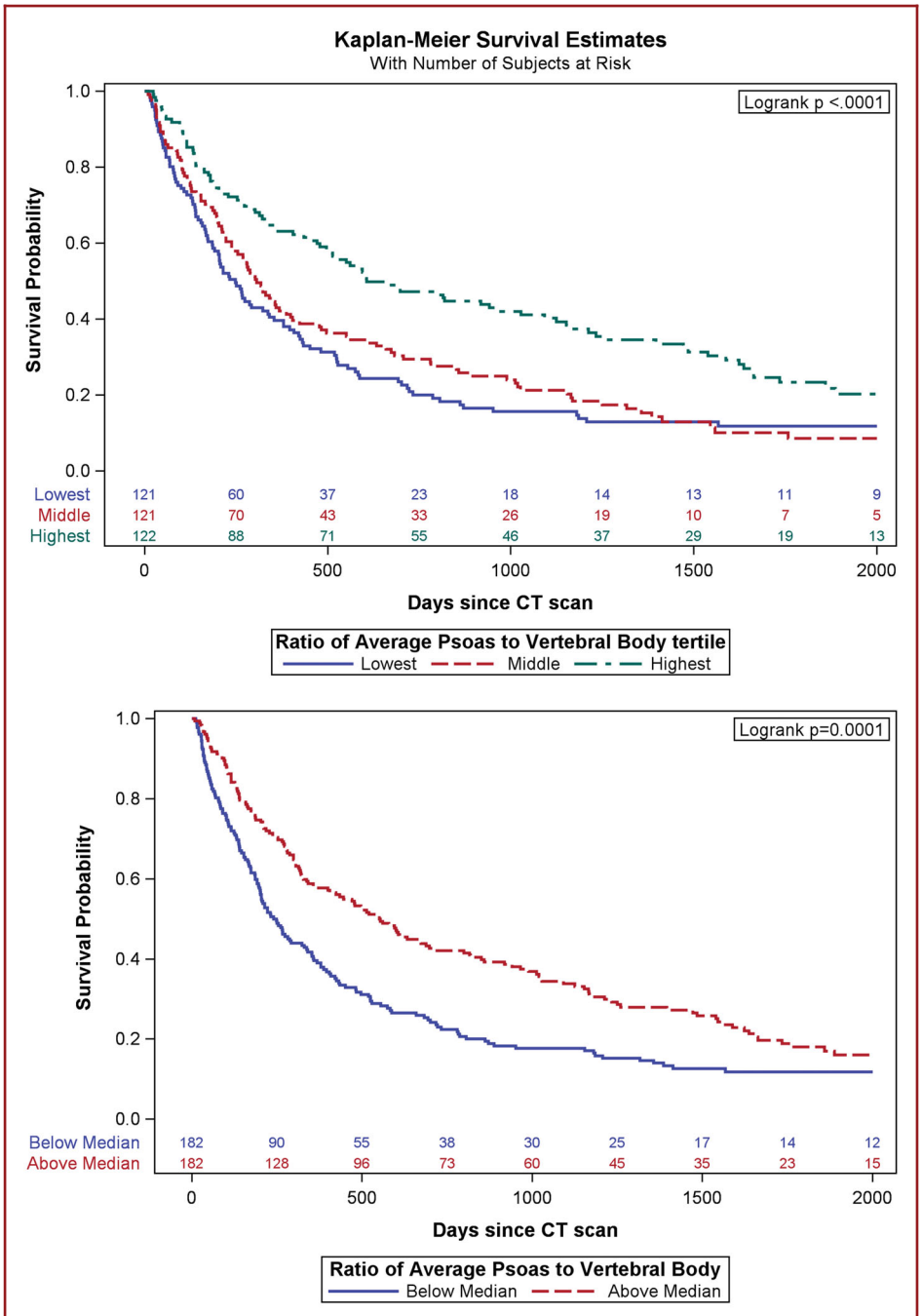

FIGURE 2. *Kaplan–Meier survival curves of the SBRT-CT cohort for psoas: vertebral body ratio using nongendered cutoffs. Kaplan–Meier survival estimates of the SBRT-CT cohort using the ratio of average psoas size to the vertebral body size, which accounts for patient body habitus. Multivariate analysis was employed to account for age, sex, ethnicity, number of levels (single vs multiple), surgery done, bisphosphonates use, antiangiogenesis medication use, modified Frailty Index, post-SBRT chemotherapy, and primary cancer site. Log-rank test shows statistically significant differences in overall survival.*

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timing of SBRT have other more important factors dictating survival (surgery, chemotherapy, and radiation). Interestingly, the P: VBA ratio was equally successful in predicting survival independent of timing of imaging, and the gender-neutral P: VBA ratio at the time of SBRT (Table 4) was a stronger predictor than gendered cutoffs at the same time-point (Table 3). More research is required to assess the validity of this technique.

Ultimately, treatment decision-making in patients with spine metastases is challenging. Most of these patients will have stage IV disease and given the cost-conscious healthcare environment, the decision to allocate and commit precious resources (ie, to perform surgery, radiation, or chemotherapy) to potentially terminally ill patients is difficult. Particularly with surgery, providers have to weigh the proven benefits[1-7] with inherent risks[8-13] in sick patients with a limited lifespan who are prone to postoperative morbidity. Objective measures to assess fitness for treatments or longevity would greatly assist in determining the patients most likely to benefit from specific treatments. Morphometric analysis of psoas size as a hallmark of frailty/sarcopenia provides an objective, simple, and effective way to assess the overall health and survival of patients independent of their type of cancer.

Limitations

Limitations of this study include its retrospective design from a single institution, and given the possibility of incomplete data in the EMR, there may be hidden bias unaccounted for in our analysis. We are limited by the agedness of our dataset; the patient population is from 2002-2012; therefore, we were unable to include newer and more novel chemotherapies, immunotherapies, and tumor markers, which are relevant in certain subtypes of cancer. We were also unable to include other indicators of patient health that required detailed past medical history, such as the Charlson Comorbidity Index. We were limited by the power of our study; the recent CT cohort identified statistically significant associations that were not seen on SBRT-CT, which may be due to the smaller sample size in this population. The study population also only included patients that underwent SBRT for their spinal metastatic disease, and thus does not include patients in earlier stages of malignancy or those who chose not to undergo radiation. However, given the usual practice at our institution, our belief is this missing population only represents a small percentage of the overall population. Prospective multicenter studies are needed to validate our findings.

Generalizability

This study is likely generalizable to all patients with lung, breast, prostate, or multiple myeloma spine metastases, as well as perhaps to all patients with spine metastases regardless of their primary cancer type. It is known that myeloma spine metastases is a different disease than lung, breast, and prostate spread to the spine, but performing additional analyses with myeloma patients excluded did not drastically affect our results (not shown), perhaps hinting at the broad utility of the frailty/sarcopenia paradigm in this context. Future research is required to assess whether morphometrics can predict morbidity and mortality in those patients referred to surgery, as only a small percentage of our patients underwent a surgical procedure. More work is also required to determine an appropriate cutoff psoas size, beneath which patients would be considered at risk. The gender-neutral values of P: VBA ratio has potential for introducing a single numerical value that can be applied clinically to predict survival (Table 4). As prior scoring systems designed to guide surgical decision making for patients with spine metastases[14,20-23] have shown poor accuracy in predicting postoperative morbidity and overall survival,[7,24-26] further research is needed to determine whether incorporating frailty/sarcopenia can improve the accuracy of these scoring systems. More work is needed to see if morphometrics can be used to predict survival in earlier stages of cancer. If validated, frailty/sarcopenia assessment via morphometric analysis of psoas size has the potential to tailor specific oncologic treatments.

CONCLUSION

Morphometric analysis of psoas size, as a hallmark of frailty/sarcopenia, predicts overall survival in patients with lung cancer, breast cancer, prostate cancer, and multiple myeloma metastases to the spine, independent of tumor histology and after multivariate analysis accounting for demographic, oncologic, functional, and therapeutic factors. This technique provides an objective, simple, and effective way to assess longevity. This information can be used to help with surgical decision making in patients with the same burden of disease, as patients with small psoas sizes are at higher risk of death. It can potentially assist in the appropriate stratification of patients who are candidates for chemotherapy, radiation, or surgery.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Lee holds consulting agreements with Medtronic and Monteris, and he has received honoraria from Varian Medical Systems. Dr Siddiqui received grants from Varian Medical Systems and Philips Medical; he has received honoraria from MD Anderson SBRT Symposium, St. John Providence Hospital, American College of Veterinary Radiology, and Wayne State University. Dr Chang holds consulting agreements with DepuySynthes and Globus, and he has received research support from Medtronic.

REFERENCES

1. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet North Am Ed*. 2005;366(9486):643-648.
2. Holman PJ, Suki D, McCutcheon I, Wolinsky JP, Rhines LD, Gokaslan ZL. Surgical management of metastatic disease of the lumbar spine: experience with 139 patients. *J Neurosurg Spine*. 2005;2(5):550-563.
3. Kim CH, Chung CK, Jahng TA, Kim HJ. Resumption of ambulatory status after surgery for nonambulatory patients with epidural spinal metastasis. *Spine J*. 2011;11(11):1015-1023.
4. Kim JM, Losina E, Bono CM, et al. Clinical outcome of metastatic spinal cord compression treated with surgical excision +/− radiation versus radiation therapy alone: a systematic review of literature. *Spine*. 2012;37(1):78-84.

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5. Bollen L, de Ruiter GC, Pondaag W, et al. Risk factors for survival of 106 surgically treated patients with symptomatic spinal epidural metastases. *Eur Spine J*. 2013;22(6):1408-1416.
6. Tatsui CE, Suki D, Rao G, et al. Factors affecting survival in 267 consecutive patients undergoing surgery for spinal metastasis from renal cell carcinoma. *SPI*. 2014;20(1):108-116.
7. Ghori AK, Leonard DA, Schoenfeld AJ, et al. Modeling 1-year survival after surgery on the metastatic spine. *Spine J*. 2015;15(11):2345-2350.
8. Choi D, Crockard A, Bunger C, et al. Review of metastatic spine tumour classification and indications for surgery: the consensus statement of the Global Spine Tumour Study Group. *Eur Spine J*. 2010;19(2):215-222.
9. Lee BH, Park JO, Kim HS, Park YC, Lee HM, Moon SH. Perioperative complication and surgical outcome in patients with spine metastases: retrospective 200-case series in a single institute. *Clin Neurol Neurosurg*. 2014;122:80-86.
10. Quraishi NA, Rajabian A, Spencer A, et al. Reoperation rates in the surgical treatment of spinal metastases. *Spine J*. 2015;15(3):S37-S43.
11. Janssen SJ, Teunis T, van Dijk E, et al. Validation of the spine oncology study group-outcomes questionnaire to assess quality of life in patients with metastatic spine disease. *Spine J*. 2017;17(6):768-776.
12. Choi D, Fox Z, Albert T, et al. Rapid improvements in pain and quality of life are sustained after surgery for spinal metastases in a large prospective cohort. *Br J Neurosurg*. 2016:1-8.
13. Dea N, Versteeg A, Fisher C, et al. Adverse events in emergency oncological spine surgery: a prospective analysis. *J Neurosurg Spine*. 2014;21(5):698-703.
14. Laufer I, Rubin DG, Lis E, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist*. 2013;18(6):744-751.
15. Escalante CP, Martin CG, Elting LS, Rubenstein EB. Medical futility and appropriate medical care in patients whose death is thought to be imminent. *Support Care Cancer*. 1997;5(4):274-280.
16. Rees M, Tekkis PP, Welsh FK, O'Rourke T, John TG. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer. *Ann Surg*. 2008;247(1):125-135.
17. Stillwell AP, Ho YH, Veitch C. Systematic review of prognostic factors related to overall survival in patients with stage IV colorectal cancer and unresectable metastases. *World J Surg*. 2011;35(3):684-692.
18. Caudle AS, Ross MI. Metastasectomy for Stage IV melanoma: for whom and how much? *Surg Oncol Clin N Am*. 2011;20(1):133-144.
19. Rutten MJ, van de Vrie R, Bruining A, et al. Predicting surgical outcome in patients with international federation of gynecology and obstetrics stage III or IV ovarian cancer using computed tomography. *Int J Gynecol Cancer*. 2015;25(3):407-415.
20. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine*. 2001;26(3):298-306.
21. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine*. 2005;30(19):2186-2191.
22. Fourney DR, Frangou EM, Ryken TC, et al. Spinal instability neoplastic score: an analysis of reliability and validity from the spine oncology study group. *J Clin Oncol*. 2011;29(22):3072-3077.
23. Schoenfeld AJ, Le HV, Marjoua Y, et al. Assessing the utility of a clinical prediction score regarding 30-day morbidity and mortality following metastatic spinal surgery: the New England Spinal Metastasis Score (NESMS). *Spine J*. 2016;16(4):482-490.
24. Quraishi NA, Manoharan SR, Arealis G, et al. Accuracy of the revised Tokuhashi score in predicting survival in patients with metastatic spinal cord compression (MSCC). *Eur Spine J*. 2013;22(S1):21-26.
25. Tabouret E, Cauvin C, Fuentes S, et al. Reassessment of scoring systems and prognostic factors for metastatic spinal cord compression. *Spine J*. 2015;15(5):944-950.
26. Zoccali C, Skoch J, Walter CM, Torabi M, Borgstrom M, Baaj AA. The Tokuhashi score: effectiveness and pitfalls. *Eur Spine J*. 2016;25(3):673-678.
27. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-M157.
28. Ruiz M, Cefalu C, Reske T. Frailty syndrome in geriatric medicine. *Am J Med Sci*. 2012;344(5):395-398.
29. Lee JS, He K, Harbaugh CM, et al. Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair. *J Vasc Surg*. 2011;53(4):912-917.
30. Cloney M, D'Amico R, Lebovic J, et al. Frailty in geriatric glioblastoma patients: a predictor of operative morbidity and outcome. *World Neurosurg*. 2016;89:362-367.
31. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg*. 2010;210(6):901-908.
32. Amrock LG, Deiner S. The implication of frailty on preoperative risk assessment. *Curr Opin Anaesthesiol*. 2014;27(3):330-335.
33. Englesbe MJ, Patel SP, He K, et al. Sarcopenia and mortality after liver transplantation. *J Am Coll Surg*. 2010;211(2):271-278.
34. Peng P, Hyder O, Firoozmand A, et al. Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. *J Gastrointest Surg*. 2012;16(8):1478-1486.
35. Englesbe MJ, Lee JS, He K, et al. Analytic morphomics, core muscle size, and surgical outcomes. *Ann Surg*. 2012;256(2):255-261.
36. Hasselager R, Gogenur I. Core muscle size assessed by perioperative abdominal CT scan is related to mortality, postoperative complications, and hospitalization after major abdominal surgery: a systematic review. *Langenbecks Arch Surg*. 2014;399(3):287-295.
37. Waits SA, Kim EK, Terjimanian MN, et al. Morphometric age and mortality after liver transplant. *JAMA Surg*. 2014;149(4):335-340.
38. Zakaria HM, Schultz L, Mossa-Basha F, Griffith B, Chang V. Morphometrics as a predictor of perioperative morbidity after lumbar spine surgery. *Neurosurg Focus*. 2015;39(4):E5.
39. Sheetz KH, Zhao L, Holcombe SA, et al. Decreased core muscle size is associated with worse patient survival following esophagectomy for cancer. *Dis Esophagus*. 2013;26(7):716-722.
40. Itoh S, Shirabe K, Matsumoto Y, et al. Effect of body composition on outcomes after hepatic resection for hepatocellular carcinoma. *Ann Surg Oncol*. 2014;21(9):3063-3068.
41. Miyamoto Y, Baba Y, Sakamoto Y, et al. Sarcopenia is a negative prognostic factor after curative resection of colorectal cancer. *Ann Surg Oncol*. 2015;22(8):2663-2668.
42. Kuroki LM, Mangano M, Allsworth JE, et al. Pre-operative assessment of muscle mass to predict surgical complications and prognosis in patients with endometrial cancer. *Ann Surg Oncol*. 2015;22(3):972-979.
43. Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sarcopenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. *Clin Cancer Res*. 2009;15(22):6973-6979.
44. Sabel MS, Lee J, Cai S, Englesbe MJ, Holcombe S, Wang S. Sarcopenia as a prognostic factor among patients with stage III melanoma. *Ann Surg Oncol*. 2011;18(13):3579-3585.
45. Parsons HA, Baracos VE, Dhillon N, Hong DS, Kurzrock R. Body composition, symptoms, and survival in advanced cancer patients referred to a phase I service. *PLoS One*. 2012;7(1):e29330.
46. Villasenor A, Ballard-Barbash R, Baumgartner K, et al. Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. *J Cancer Surviv*. 2012;6(4):398-406.
47. Lanic H, Kraut-Tauzia J, Modzelewski R, et al. Sarcopenia is an independent prognostic factor in elderly patients with diffuse large B-cell lymphoma treated with immunochemotherapy. *Leuk Lymphoma*. 2014;55(4):817-823.
48. Fujiwara N, Nakagawa H, Kudo Y, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. *J Hepatol*. 2015;63(1):131-140.
49. Harada K, Ida S, Baba Y, et al. Prognostic and clinical impact of sarcopenia in esophageal squamous cell carcinoma. *Dis Esophagus*. 2016;29(6):627-633.
50. Zakaria HM, Basheer A, Boyce-Fappiano D, et al. Application of morphometric analysis to patients with lung cancer metastasis to the spine: a clinical study. *Neurosurg Focus*. 2016;41(2):E12.
51. Zakaria HM, Elibe E, Macki M, et al. Morphometrics predicts overall survival in patients with multiple myeloma spine metastasis: A retrospective cohort study. *Surg Neurol Int*. 2018;9(1):172.
52. Zakaria HM, Massie L, Basheer A, et al. Application of morphometrics as a predictor for survival in female patients with breast cancer spinal metastasis: a retrospective cohort study. *Spine J*. 2018;18(10):1798-1803.
53. Zakaria HM, Massie L, Basheer A, et al. Application of morphometrics as a predictor for survival in patients with prostate cancer metastasis to the spine. *World Neurosurg*. 2018;114:e913-e919.

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54. Subramaniam S, Aalberg JJ, Soriano RP, Divino CM. New 5-Factor modified frailty index using American college of surgeons NSQIP data. *J Am Coll Surg*. 2018;226(2):173-181.e8.
55. Ali R, Schwalb JM, Nerenz DR, Antoine HJ, Rubinfeld I. Use of the modified frailty index to predict 30-day morbidity and mortality from spine surgery. *J Neurosurg Spine*. 2016;25(4):537-541.
56. Panayi AC, Orkaby AR, Sakthivel D, et al. Impact of frailty on outcomes in surgical patients: a systematic review and meta-analysis. *The Am J Surg*. published online: November 27, 2018. (doi: 10.1016/j.amjsurg.2018.11.020).
57. Kumar SK, Callander NS, Alsina M, et al. Multiple Myeloma, Version 3.2017, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2017;15(2):230-269.
58. Terpos E, Politou M, Rahemtulla A. New insights into the pathophysiology and management of bone disease in multiple myeloma. *Br J Haematol*. 2003;123(5):758-769.
59. Cocks K, Cohen D, Wisloff F, et al. An international field study of the reliability and validity of a disease-specific questionnaire module (the QLQ-MY20) in assessing the quality of life of patients with multiple myeloma. *Eur J Cancer*. 2007;43(11):1670-1678.
60. Boland E, Eiser C, Ezaydi Y, Greenfield DM, Ahmedzai SH, Snowden JA. Living with advanced but stable multiple myeloma: a study of the symptom burden and cumulative effects of disease and intensive (hematopoietic stem cell transplant-based) treatment on health-related quality of life. *J Pain Symptom Manage*. 2013;46(5):671-680.

Acknowledgments

We thank Susan MacPhee-Gray for editorial assistance.

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