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Assessing the utility of a prognostication model to predict 1-year mortality in patients receiving radiation therapy for spinal metastases

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Abstract

Background Context: Predicting survival outcomes after radiation therapy alone for metastatic disease of the spine is a challenging task that is important to guiding treatment decisions (e.g., determining dose fractionation and intensity). The New England Spinal Metastasis Score (NESMS) was recently introduced and validated in independent cohorts as a tool to predict 1-year survival following surgery for spinal metastases. This metric is composed of 3 factors: pre-operative albumin, ambulatory status, and modified Bauer score, with the total score ranging from 0 to 3.

Purpose: The purpose of this study is to assess the applicability of the NESMS model to predict 1-year survival among patients treated with radiation therapy alone for spinal metastases.

Study Design/Setting: This study is a retrospective analysis.

Patient Sample: This sample included 290 patients who underwent conventional radiation therapy alone for spinal metastases.

Outcome Measures: Patients' NESMS scores (comprised of ambulatory status, pre-treatment serum albumin, and modified Bauer score) were assessed as well as their 1-year overall survival rates following radiation for metastatic disease of the spine.

Methods: This study is a single-institution retrospective analysis of 290 patients treated with conventional radiation alone for spinal metastases from 2008 to 2013. The predictive value of the NESMS was assessed using multivariable logistic regression modeling, adjusted for potential confounding variables.

Results: This analysis indicated that patients with lower NESMS scores had higher rates of 1-year mortality. Multivariable analysis demonstrated a strong association between lower NESMS scores and lower rates of survival.

Conclusions: The NESMS score is a simple prognostic scheme that requires clinical data that is often readily available and has been validated in independent cohorts of surgical patients. This study serves to validate the utility of the NESMS composite score to predict 1-year mortality in patients treated with radiation alone for spinal metastases.

Introduction:

An estimated 5-10% of all cancer patients experience spinal metastasis over the course of their disease, with the most common tumors being breast, prostate, and lung [1]. These lesions are often accompanied by significant morbidity and present with symptoms including back pain, compression fracture, radiculopathy, and myelopathy. Treatment decisions can be complicated and frequently involve a multidisciplinary team of surgeons, medical oncologists, and radiation oncologists. For many patients, radiation therapy (RT) is the primary treatment for spine metastases, particularly in patients who are not surgical candidates and have limited life expectancy [2–4]. These patients often have advanced disease, and accurately assessing prognosis is thus critical in identifying optimal candidates for spinal RT as well as determining suitable dose/fractionation regimens.

Currently, the validated prognostic tools to predict mortality following spinal RT for metastatic disease in a general population are limited, with most validated models in patients with spinal cord compression [5–8]. Among patients with spinal metastases treated with surgery, a number of clinical schemes have been developed to predict post-operative mortality and/or guide treatment decisions, which take into account factors including tumor characteristics, extent of metastatic disease, neurological symptoms, and radiological data [9–12]. Among these prognostic tools, the modified Bauer score (which reflects tumor histology and presence of visceral and/or skeletal metastases) is frequently used by spine surgeons and has demonstrated predictive value for mortality among surgical candidates, with a lower score predicting for worse survival [13]. Recently, Ghori and colleagues sought to further improve on the predictive value of the modified Bauer with the development of the New England Spinal Metastasis Score (NESMS) to predict 1-year survival following surgery for spinal metastasis [14]. The NESMS is

composed of 3 factors: pre-operative albumin, ambulatory status, and modified Bauer score, with the total score ranging from 0 to 3. In the cohort of n=318 patients used to develop the scoring system, the NESMS was able to explain 74% of the variation in 1-year survival, compared to the modified Bauer score alone, which predicted only 64% of the variation in 1-year survival. The NESMS has subsequently been validated in independent cohorts as a predictor of 1-year survival following surgery for spinal metastasis, again with a lower score predicting for worse survival [15], as well as short-term outcomes including 30- and 90-day mortality [16,17].

Though these published results have helped clinicians better prognosticate in surgical patients, little is known about the utility of such clinical tools among patients undergoing RT for spinal metastases, despite the frequency at which RT is used for metastatic disease to the spine. Given that the NESMS reflects patient and disease characteristics that would likely affect post-treatment mortality outcomes in both surgical and non-surgical patients, we sought to validate the predictive value of the NESMS in a non-operative population. The purpose of this study is to assess the applicability of the NESMS model to predict 1-year survival among patients treated with radiation therapy alone for spinal metastases.

Materials and Methods:

This investigation was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board. This was a retrospective analysis of patients treated with conventional radiation therapy for spinal metastasis at Dana-Farber/Brigham & Women's Cancer Center from January 2008 through December 2013. A composite NESMS score was calculated for each patient (**Table 1**). Patients received 2 points if their modified Bauer score (which assigns 1 point for breast, kidney, lymphoma, or multiple myeloma primary tumor histology, 1 point if the primary tumor histology

is not lung cancer, 1 point if the patient has no visceral metastases, and 1 point if the patient has one solitary skeletal metastasis) was ≥ 3 , and 0 points if modified Bauer score was ≤ 2 ; 1 point if the patient had an intact or impaired ambulatory status (vs. non-ambulatory); and 1 point if the patient's pretreatment albumin was ≥ 3.5 g/dL. The maximum NESMS is a score of 3 because there was no statistical difference between a score of 3 and a score of 4 in the original analysis establishing the NESMS model. Of note, that the categorization of ambulatory status in this study differs slightly from the original NESMS scoring system, which scores 0 points if the patient is non-ambulatory or had impaired ambulatory status, and 1 point if the patient had an intact ambulatory status. We found that assessing impaired vs. intact ambulatory status retrospectively is often difficult and unreliable. Thus, we found ambulatory or impaired ambulation vs. non-ambulatory to be a more clinically useful, reproducible, and accurate categorization for the purpose of this analysis.

For patients with more than one course of spine RT, only the first treatment course was included in the analysis. Patients were excluded if they had incomplete data to assign an NESMS score, including missing or outdated (>30 days prior to initiation of RT) serum albumin levels. Descriptive statistics were used to characterize patients at study entry. Fisher's exact test and logistic regression model were used to evaluate the association between NESMS score and 1-year survival. The method of Kaplan-Meier was used to characterize overall survival, defined as time from completion of RT to death or date last known alive.

Results:

Patient Demographics and Clinical Characteristics

A total of 290 patients who received conventional RT alone for metastatic disease to the spine and had complete follow-up through 1-year post treatment completion (including documented date of death during this period if relevant) were included in this analysis. Median follow-up was 57.2 months among patients who were still alive as of this analysis. Eight patients who received conventional RT alone who were lost to follow-up prior to 1-year post-treatment completion were excluded from analysis. Patient demographics including age, gender, race, performance status, and tumor histology are summarized in **Table 2**. The median age at receipt of radiation was 62 (standard deviation: 12.7, range: 23-97). The majority of patients (260/290, 89.7%) had a modified Bauer score ≤ 2 , and 30 patients (10.3%) had a modified Bauer score ≥ 3 . Median albumin was 3.7 g/dL (standard deviation: 0.60 g/dL), and the majority of patients (258/290, 89.0%) had intact or impaired ambulatory status.

Composite Score and Mortality

The majority of patients had a composite NESMS score of 2 points (148/290, 51.0%). Twenty-nine patients (10.0%) had the highest composite NESMS score of 3 points, 94 patients (32.4%) had composite NESMS score of 1 point, and 19 patients (6.6%) had a composite score of 0 points. A total of 13 (44.8%) of patients with NESMS score of 3 died within one year, compared to 103 (69.6%) of patients with score 2, 83 (88.3%) of patients with score of 1, and 17 (89.5%) of patients with NESMS score of 0 ($P < 0.001$) (**Table 3**). The median overall survival was 15.2 months for patients with score of 3, 6.6 months for score of 2, 1.3 months for score of 1, and 1.1 months for score of 0 ($P < 0.0001$) (**Figure 1**).

Unadjusted and Adjusted Analyses

Unadjusted analysis (**Table 4**) indicated that, as compared to patients with NESMS score of 3, patients with NESMS score of 2 had a 64% reduction in the odds of 1-year overall survival (OS) (odds ratio [OR] 0.36; 95% CI 0.16, 0.80; $P = 0.012$). Those with a score of 1 had an 89% reduction (OR 0.11; 95% CI 0.04, 0.283; $P < 0.0001$), and patients with a score of 0 had a 90% reduction (OR 0.10; 95% CI 0.02, 0.49; $P = 0.005$). Adjusted multivariable analysis that accounted for demographic variables (age, gender, and race) demonstrated similar results. As compared to patients with NESMS score of 3, patients with NESMS score 2 had a 60% reduction in odds of 1-year OS (OR 0.40; 95% CI 0.17, 0.91; $P = 0.029$). Patients with score of 1 had an 87% reduction (OR 0.13; 95% CI 0.05, 0.33; $P < 0.0001$), and patients with a score of 0 had an 89% reduction (OR 0.11; 95% CI 0.02, 0.57, $P = 0.009$) in 1-year OS (**Table 5**).

Discussion:

The ability to accurately assess prognosis has a significant impact on treatment decisions for patients with spinal metastases. Despite the importance of prognostication in patients who are potential candidates for spine RT, there are few clinical tools in use that dependably predict survival in patients undergoing palliative RT for metastatic disease to the spine. We sought to assess whether the NESMS prognostication model established by Ghori et al. in patients undergoing surgery for spinal metastases demonstrated predictive value in an independent cohort of patients who underwent conventional RT alone for spinal metastatic disease.

Our analysis revealed significantly lower 1-year survival rates for patients with lower NESMS scores, with scores of 3, 2, 1, and 0 demonstrating 44.8%, 69.6%, 88.3%, and 89.5%

rates of death within 1 year, respectively. Both unadjusted model and model adjusted for age, gender, and race, demonstrated a significant reduction in the odds of 1-year survival for lower NESMS scores. To our knowledge, this is the first study examining the utility of a prognostication scheme in patients treated with RT for spinal metastases in the absence of spinal cord compression. Thus, it is important to note that these results be validated in independent cohorts to further strengthen the utility of the NESMS score in this clinical setting. Nevertheless, our findings indicate that the NESMS scoring system, though developed as a prognosticator of surgical patients, performed well in predicting 1-year mortality in patients treated with conventional RT alone for spinal metastases.

Our findings demonstrated similar results compared to a recently published validation of the NESMS to predict 1-year mortality in surgical patients by Goodwin and colleagues [15]. We found similar reductions in odds ratio for each NESMS score: For NESMS score 0, Goodwin et al. report an adjusted OR of 0.09, compared to 0.11 in our results; an adjusted OR of 0.12 for NESMS score 1 compared to 0.13 in our results; and an adjusted OR of 0.37 for NESMS score 3 compared to 0.40 in our results. Given that the NESMS reflects both tumor-specific factors as well as the patient's overall health, it is not unexpected that the scoring system would perform similarly in both operative and non-operative patient cohorts. While the NESMS is one of many prognostication schemes for surgical patients, other scoring systems (the Tomita score, Sioutos score, Tokuhashi score, van der Linden score, and Katagiri score) [9,11,18–20] have had variable degrees of validation in independent cohorts. Furthermore, these scoring systems generally emphasize disease characteristics (including extent of metastases, tumor histology, previous treatment, and rate of lesion growth) and do not incorporate other indicators of the patient's overall health, aside from performance status (a component of the Katagiri, Tokuhashi, and van

der Linden scoring systems). In contrast, the NESMS accounts for both tumor characteristics as well as albumin and ambulatory status, which reflect more of the patient's overall health status in addition to the patient's disease characteristics.

As is the case for any retrospective analysis, this study is not without limitations. The patients included in this analysis were treated at a single academic institution, which may not reflect the clinical practice patterns or patient populations of other institutions. In addition, the fact that all of these patients underwent spinal RT introduces selection bias, though we adjusted for demographic factors in order to best minimize this effect. Our data set also had few patients in the lowest NESMS score category of 0, which likely reflects the fact that these patients often do not undergo RT and thus were not included in the cohort. Of note, OS outcomes for patients with NESMS score of 0 and 1 were somewhat similar (1.1 months and 1.3 months, respectively), and the reduction in adjusted odds ratio of 1-year survival were also similar (0.11 and 0.13, respectively). It is possible that these two groups of patients are better reflected in a single group rather than two separate scoring categories, though this may also be a result of few patients with score of 0 included in this analysis. It should also be noted that our slight difference in categorization of ambulatory status in this study (0 points if the patient was non-ambulatory and 1 point if the patient had intact or impaired ambulatory status) as compared to the original NESMS (0 points if the patient is non-ambulatory or had impaired ambulatory status, and 1 point if the patient had intact ambulatory status) may limit direct comparison to the original NESMS results. Finally, it is worth emphasizing that while prognosis does impact treatment decisions, many other factors, such as symptom relief and quality of life, should also guide management.

Conclusions:

Predicting survival outcomes after radiation therapy alone for metastatic disease of the spine is a challenging task that is important to guiding treatment decisions (e.g., determining dose fractionation and intensity). The New England Spinal Metastasis Score (NESMS) was recently introduced as a tool to predict 1-year survival following surgery for spinal metastases and has also been validated in independent cohorts of surgical patients. In contrast, there is limited data on the development of new prognostication schemes or applicability of existing schemes to patients with spinal metastases treated with RT, particularly in the absence of spinal cord compression. Our results demonstrate the NESMS score is able to predict 1-year survival in patients treated with conventional RT alone for spinal metastases. Given that the NESMS indicated similar reductions in odds ratio of 1-year survival for operative and non-operative cohorts, future work may explore the applicability of the NESMS for any patient with spinal metastatic disease, regardless of how that patient is subsequently managed. Expanding to this cohort would also likely increase the number of patients with NESMS score of 0, which included the fewest number of patients in both this study and in previous validations. With further validation in non-operative independent cohorts, the NESMS score can help further guide treatment decisions for patients with metastatic disease to the spine.

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Parameter		NESMS Points
Modified Bauer Score components	Modified Bauer points	N/A
Primary tumor is NOT lung	1	N/A
Primary tumor is breast or kidney	1	N/A
Solitary skeletal metastasis	1	N/A
No visceral metastasis	1	N/A
Modified Bauer score		
≤2		0
≥3		2
Serum albumin		
<3.5 g/dL		0
≥3.5 g/dL		1
Ambulatory status*		
Non-ambulatory		0
Intact or impaired		1

Table 1. The New England Spinal Metastasis Score (NESMS) and its components. The components are summed, with a ceiling score of 3.

*Note that the original NESMS dichotomizes ambulatory status as impaired/non-ambulatory vs. intact ambulatory status.

	N	%
Age		
Median	62	
Range	23-97	
Gender		
Female	137	47.2%
Male	153	52.8%
Race		
Caucasian	242	86.7%
Hispanic/Latino	7	2.5%
Black/AA	23	8.2%
Asian	4	1.4%
Other	3	1.1%
Unknown	11	
ECOG PS		
0	40	13.8%
1	126	43.5%
2	65	22.4%
3	53	18.3%
4	6	2.1%
Histology		
Breast	49	16.9%
Lung	82	28.3%
Prostate	51	17.6%
Other	108	37.2%
Modified Bauer Score		
≤2	260	89.7%
3	30	10.3%
Serum Albumin		
<3.5 g/dL	108	37.2%
≥3.5 g/dL	182	62.8%
Ambulatory Status		
Intact or impaired	258	89.0%
Non-ambulatory	32	11.0%
NESMS		
0	19	6.6%
1	94	32.4%
2	148	51.0%
3	29	10.0%

Table 2: Patient characteristics (N=290)

NESMS score	Number of patients	1-year mortality (%)	Lost to follow-up by 1 year ¹
0	19	17 (89.5)	1
1	94	83 (88.3)	0
2	148	103 (69.6)	7
3	29	13 (44.8)	0
P-value (Fisher's exact)	-	<.0001	-

Table 3: Distribution of 1-year mortality by NESMS score. ¹Patients lost to follow-up by 1 year were excluded from the analysis of 1-year survival.

NESMS score	Number of patients	Odds Ratio	95% CI	p-value
0	19	0.10	0.019, 0.492	0.005
1	94	0.11	0.041, 0.283	<.0001
2	148	0.36	0.158, 0.799	0.012
3	29	Reference	-	-
Total	290 ¹	-	-	-

Table 4: Unadjusted effects of the NESMS score on survival at 1 year. ¹Patients lost to follow-up by 1 year were excluded from the analysis of 1-year survival.

NESMS score	Number of patients	Odds Ratio	95% CI	p-value
0	19	0.11	0.021, 0.568	0.009
1	94	0.13	0.047, 0.334	<.0001
2	148	0.40	0.174, 0.908	0.029
3	29	Reference	-	-
Total	290 ¹	-	-	-

Table 5: Effects of the NESMS score on survival at 1 year with adjustment for age, gender and race. Age at RT start is analyzed as continuous variable; race is dichotomized as white vs. other (including unknown). ¹Patients lost to follow-up by 1 year were excluded from the analysis of 1-year survival.

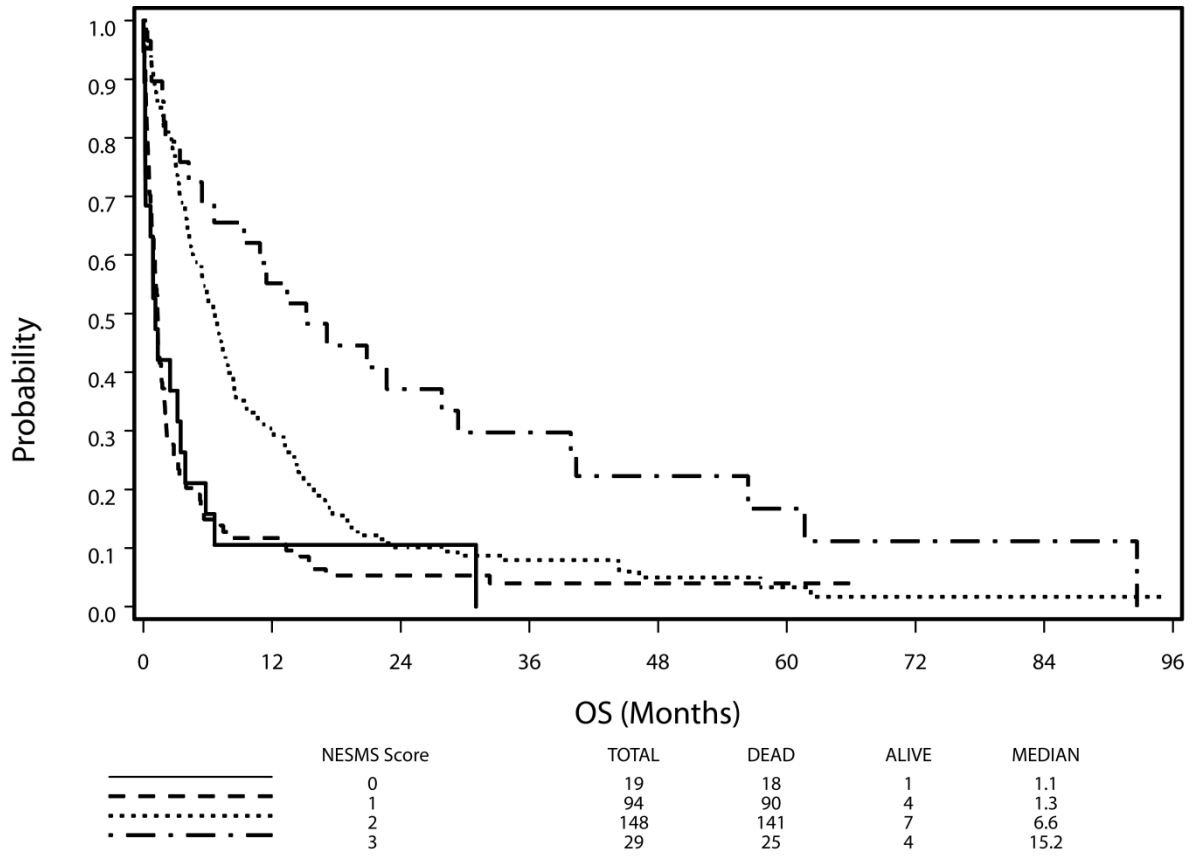


Figure 1: Overall survival (OS) by NESMS score.