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Original Article

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Baseline Frailty Measured by the Risk Analysis Index and 30-Day Mortality After Surgery for Spinal Malignancy: Analysis of a Prospective Registry (2011–2020)

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Objective: To evaluate the prognostic utility of baseline frailty, measured by the Risk Analysis Index (RAI), for prediction of postoperative mortality among patients with spinal malignancy (SM) undergoing resection.
Methods: SM surgery cases were queried from the American College of Surgeons – National Surgical Quality Improvement Program database (2011–2020). The relationship between preoperative RAI frailty score and increasing rate of primary endpoint (mortality or discharge to hospice within 30 days, "mortality/hospice") were assessed. Discriminatory accuracy was assessed by computation of C-statistics (with 95% confidence interval [CI]) in receiver operating characteristic (ROC) curve analysis.
Results: A total of 2,235 cases were stratified by RAI score: 0–20, 22.7%; 21–30, 11.9%; 31–40, 54.7%; and ≥41, 10.7%. The rate of mortality/hospice was 6.5%, which increased linearly with increasing RAI score ($p < 0.001$). RAI was also associated with increasing rates of major complication, extended length of stay, and nonhome discharge (all $p < 0.05$). The RAI demonstrated acceptable discriminatory accuracy for prediction of primary endpoint (C-statistic, 0.717; 95% CI, 0.697–0.735). In pairwise ROC comparison, RAI demonstrated superiority versus modified frailty index-5 and chronological age ($p < 0.001$).
Conclusion: Preoperative frailty, as measured by RAI, is a robust predictor of mortality/hospice after SM surgery. The frailty score may be applied in clinical settings using a user-friendly calculator, deployed here: https://nsgyfrailtyoutcomeslab.shinyapps.io/spinalMalignancyRAI/.

Keywords: Frailty, Risk Analysis Index, Spinal tumor, Metastatic, Spinal oncology, National Surgical Quality Improvement Program

INTRODUCTION

Spinal malignancies (SMs) are often associated with significant morbidity and reduced quality of life from neurological deficits and/or fracture-associated pain. These patients commonly present with pain and/or focal neurologic deficits. Spine metastases were found to be the most common osseous destination for secondary malignancy (70%).[1,2] Recent literature reported 15.67% of patients diagnosed with a solid tumor have spinal metastasis; 9.6% of patients with SM will develop epidural spinal cord compression and 12.6% will experience pathologic compression fractures.[3] Although primary central nervous

system malignancies are less common, 2.9% occur in the spinal cord or cauda equina regions.[4] Despite a low incidence of primary spinal neoplasms (0.77 per 100,000), their incidence peaks at the 75–84 year age group (1.80 per 100,000 in individuals), which is relevant to research studying frailty's impact on SM surgery.[5]

There is an increased risk of developing primary malignancy with increasing age, and people are living longer thanks to advancements in medical science and cancer management. Due to improved rates of survival of cancer patients, there is a higher incidence of older patients presenting with a greater cancer disease burden with spinal metastasis, in addition to the peak incidence of primary SMs that accompanies increasing patient age until the 75–84 year group.[6] Therefore, it is becoming even more important to accurately measure preoperative risk and quantify frailty as a measure of physiologic reserve, as surgical outcomes prediction cannot be based on age alone for risk stratification.[7-10] The majority of previous frailty studies in the neurosurgical literature have used the 11- or 5-modified frailty index (mFI), the mFI-11 or mFI-5, respectively. The Risk Analysis Index (RAI) is a robust frailty index originally developed and validated in surgical populations.[11-13] The RAI is uniquely versatile for both clinical prospective application with a patient-centered questionnaire and for large retrospective database analysis. However, the generalizability of RAI to neurosurgical spinal oncology is currently unknown.

The objective of the present study is to evaluate the predictive ability of the RAI for 30-day mortality and other adverse postoperative outcomes in patients undergoing surgical intervention for a SM using data from a large multicenter, clinical surgical registry representing over 700 hospitals across 49 U.S. states and 11 countries.

MATERIALS AND METHODS

1. Study Design

The present study, designed as a secondary analysis of a prospective surgical registry, was conducted in accordance with STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines.

2. Data Source

The patient population was derived from the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database. The ACS-NSQIP is a prospective, peer-controlled, validated database for quantifying 30-day surgical outcomes. NSQIP data are prospectively entered at each participating hospital by ACS-trained surgical clinical reviewers to improve consistency and reliability. The present study was performed under the data user agreement of the ACS with our institution and was approved by Institutional Review Board of University of New Mexico (Study ID 21-315). Given the deidentified nature of the information in NSQIP database, patient consent was neither sought nor required.

3. Participants

The malignant spinal tumor patient population was queried from the NSQIP (2011–2020) using a combination of Current Procedural Terminology (CPT) codes and International Classification for Disease (ICD), 9th and 10th Revision, Clinical Modification codes (Table 1). Initial query using exclusively primary CPT codes yielded 7,851 records. The postoperative diagnoses fields in NSQIP ("PODIAG") further narrowed the search to 2,235 records using prespecified ICD codes (Table 1).

4. Predictor Variables

The primary predictor of interest was preoperative frailty, measured by the RAI score. The RAI was originally developed and validated for compatibility with the ACS-NSQIP database.[12] RAI has been previously utilized to predict outcomes in patients undergoing spine surgery.[14,15] The revised RAI score, as described by Arya et al.,[12] was computed using standard NSQIP variables: age, sex, disseminated cancer ("DISCANC"), weight loss ("WTLOSS"), renal failure ("RENAFAIL; DIALYSIS"), congestive heart failure ("HXCHF"), shortness of breath ("DYSPNEA"), functional status ("FNSTATUS2"), and living status ("TRANST" = nursing home or chronic care facility). The mFI-5, a readily utilized risk index in neurooncological literature, was computed and analyzed for comparative purposes alongside RAI.[7,16-18] mFI-5 has a 5-point maximum score, with 1 point given to each positive variable. mFI-5 score was calculated from NSQIP using the cumulative score of nonindependent functional status ("FNSTATUS2"), diabetes mellitus ("DIABETES"), chronic obstructive pulmonary disease ("HXCOPD"), and congestive heart failure ("HXCHF").

5. Primary and Secondary Outcomes

The primary outcome for this study was mortality within 30 days of surgery and/or discharge to hospice, which was calculated using the NSQIP variables "DOPERTOD" (days from operation to death for mortality) and "DISCHDEST" (hospital discharge destination). The secondary outcomes were non-

Table 1. List of CPT, ICD-9-CM, and ICD-10-CM codes used to identify SM surgery cases from the NSQIP database 2011–2020

Coding system	Code	Description
CPT	63275-63280	Laminectomy for biopsy/excision of extradural spinal neoplasm
	63280-63283	Laminectomy for biopsy/excision of intradural extramedullary spinal neoplasm
	63285-63287	Laminectomy for biopsy/excision of intradural intramedullary spinal neoplasm
	63290	Laminectomy for biopsy/excision of combined intradural/extradural spinal neoplasm
	63300-63303	Vertebral corpectomy for excision of extradural spinal neoplasm
	63304-63307	Vertebral corpectomy for excision of intradural spinal neoplasm
ICD-9-CM	170.2	Malignant neoplasm of vertebral column excluding sacrum and coccyx
	170.6	Malignant neoplasm of pelvic bones, sacrum, and coccyx
	192.2	Malignant neoplasm of spinal cord
	192.3	Malignant neoplasm of spinal meninges
	198.3-198.5	Secondary malignant neoplasm of brain and spinal cord
	733.13	Pathological fracture of vertebrae
	239.7	Neoplasm of uncertain behavior other parts of central nervous system
ICD-10-CM	C41.2	Malignant neoplasm of vertebral column
	C72	Malignant neoplasm of spinal cord
	C79.49	Malignant neoplasm of other parts of central nervous system
	C79.51	Secondary malignant neoplasm of bone
	D43.4	Neoplasm of uncertain behavior of spinal cord
	M48.50X	Pathological fracture in neoplastic disease, unspecified site
	M84.68	Pathological fracture in other disease, other site

CPT, Current Procedural Terminology; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; SM, spinal malignancy; NSQIP, National Surgical Quality Improvement Program.

home discharge disposition (NHD), extended length of hospital stay (ELOS), major complication occurrence, and Clavien-Dindo grade IV complication occurrence (CD IV). CD IV complications include life-threatening complications that require intensive care unit management. Major complication occurrences were defined by one or more instances of prolonged intubation (defined as greater than 48 hours), unplanned reintubation, sepsis, septic shock, pneumonia, deep venous thrombosis/thrombophlebitis, pulmonary embolism, cerebrovascular accident/stroke with neurological deficit, acute renal failure, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, superficial surgical site infection (SSI), deep incisional SSI, organ space SSI, or wound dehiscence.

6. Statistical Methods

Statistical analyses were performed with a combination of R Project for Statistical Computing ver. 4.2.1 (The R Foundation, Vienna, Austria) (https://www.R-project.org/), IBM SPSS Statistics ver. 28.0 (IBM Co., Armonk, NY, USA), GraphPad Prism ver. 9.0 (GraphPad Software Inc., La Jolla, CA, USA), and MedCalc for Windows ver. 19.4 (MedCalc Software, Ostend, Belgium). Statistical significance was set *a priori* to alpha of 0.05. The R gtsummary package was utilized to generate descriptive statistics for the spine tumor surgery cohort.[19] RAI was analyzed as a continuous variable and categorized into a base "nonfrail" category of 0–20 and subsequent ascending 5-point bins (e.g., 21–25, 26–30). The binning scheme was defined *a priori* and arbitrary in nature to avoid scoring biases associated with tiers.[20] The Cochran-Armitage trend test was utilized to determine significance of proportional trends (frailty score bin vs. binary outcomes). Discriminatory accuracy of frailty score for primary outcome was quantified using C-statistics (with 95% confidence interval [CI]) and interpreted using standard criteria per Hosmer-Lemeshow.[19] A C-statistic >0.7 was indicative of adequate discriminatory accuracy.[21,22] The relative discriminatory superiority of RAI (vs. increasing chronological age and mFI-5) was assessed using pairwise receiver operating characteristic (ROC) comparison (DeLong) tests. The R, packages rms and shiny

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Table 2. Demographics, clinical characteristics, and baseline frailty in patients undergoing surgery for SM, subgroup by primary endpoint (mortality/hospice), ACS-NSQIP 2011–2020 (N = 2,235)

Variable	All cohort	Primary endpoint (mortality/hospice)		p-value
		No	Yes	
Total patients	2,235	2,099	136	
Age (yr), median (IQR)	61 (52–70)	61 (52–70)	66 (58–73)	0.003
Female sex (biological)	865 (39)	822 (39)	43 (32)	0.080
Race				0.640
White	1,476 (66)	1,381 (66)	95 (70)	
Black	218 (9.8)	204 (9.7)	14 (10)	
Asian	98 (4.4)	94 (4.5)	4 (2.9)	
Other	443 (20)	420 (20)	23 (17)	
Hispanic ethnicity	162 (7.2)	156 (7.4)	6 (4.4)	
Body mass index (kg/m^2), median (IQR)	27.0 (23.5–30.5)	27.0 (23.5–30.5)	26.0 (22.0–30.0)	0.04
Acute care transfer	423 (19)	385 (18)	38 (28)	0.006
RAI, median (IQR)	34 (26–42)	34 (26–42)	37 (34–41)	< 0.001
RAI categorical bins				< 0.001
0–20	507 (23)	498 (24)	9 (6.6)	
21–25	173 (7.7)	169 (8.1)	4 (2.9)	
26–30	93 (4.2)	90 (4.3)	3 (2.2)	
31–35	635 (28)	605 (29)	30 (22)	
36–40	587 (26)	540 (26)	47 (35)	
41–45	172 (7.7)	145 (6.9)	27 (20)	
46–50	51 (2.3)	41 (2.0)	10 (7.4)	
≥ 51	17 (0.8)	11 (0.5)	6 (4.4)	
mFI-5				< 0.001
0	1,079 (48)	1,031 (49)	48 (35)	
1	807 (36)	759 (36)	48 (35)	
2	301 (13)	272 (13)	29 (21)	
3	44 (2.0)	37 (1.8)	7 (5.1)	
4	4 (0.2)	0 (0)	4 (2.9)	

Values are presented as number of patients (%) unless otherwise indicated.
SM, spinal malignancy; ACS-NSQIP, American College of Surgeons – National Surgical Quality Improvement Program; IQR, interquartile range; RAI, Risk Analysis Index; mFI-5, modified frailty index-5.

were used to generate an interactive Risk Analysis Index and Malignant Spinal Tumor Surgery Outcomes calculator found at the following website: https://nsgyfrailtyoutcomeslab.shinyapps.io/spinalMalignancyRAI/.[23-25]

RESULTS

1. Participants and Descriptive Statistics

There were 2,235 patients that underwent SM surgery and 507 were RAI 0–20, 266 were RAI 21–30, 1,222 were RAI 31–40, and 240 were RAI ≥41. Baseline demographics, clinical characteristics, and baseline frailty status are summarized in Table 2. The median (interquartile range) age was 61 (52–70) and 39% were female.

2. RAI and Mortality Within 30 Days of Operation

The rate of primary outcome (30-day mortality/hospice) was 6.1% (N = 136). This was significantly associated with increasing frailty by RAI (Fig. 1). RAI demonstrated adequate discriminatory accuracy for prediction of the primary endpoint in ROC

analysis (C-statistic, 0.717; 95% CI, 0.697–0.735) (Fig. 2). On pairwise ROC comparison, RAI score had superior discriminatory accuracy compared to mFI-5 and increasing chronological age (both p < 0.001, DeLong test, Fig. 2).

3. Complications, ELOS, and NHD

There were 181 major complication occurrences (8.1%), 126 CD IV occurrences (5.6%), 937 NHDs (42%), 571 ELOS (26%), within 30 days. Increasing RAI score (in stepwise 5-point bins) was statistically significantly associated with increasing occurrence rate of major complication, CD IV, ELOS, and NHD (Table 3, Fig. 3).

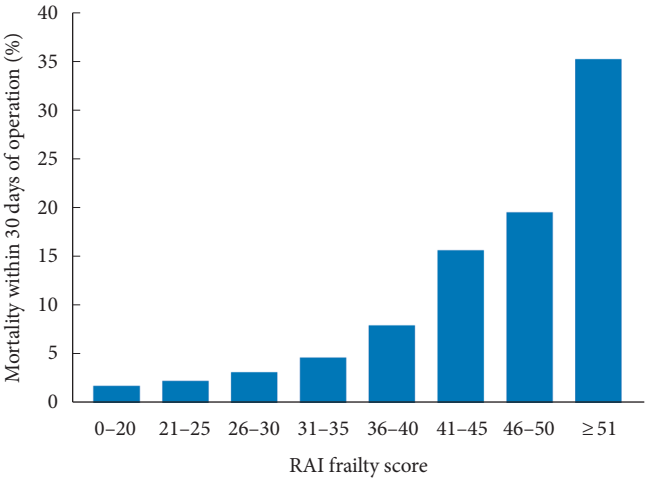

Fig. 1. Incidence rate of mortality within 30 days of operation stratified by preoperative RAI frailty score, ACS-NSQIP 2011–2020 (N = 2,235). RAI, Risk Analysis Index; ACS-NSQIP, American College of Surgeons – National Surgical Quality Improvement Program.

DISCUSSION

In this analysis of 2,235 SM patients undergoing surgical treatment in a prospective surgical registry, increasing frailty, as measured by the RAI, provided discriminatory accuracy for prediction of postoperative mortality/hospice discharge. Increasing RAI scores were also associated with the other secondary outcomes consisting of major complications, CD IV, NHD, and ELOS. Comparative ROC curve analysis demonstrated the superior discrimination of the RAI compared to the mFI-5 and

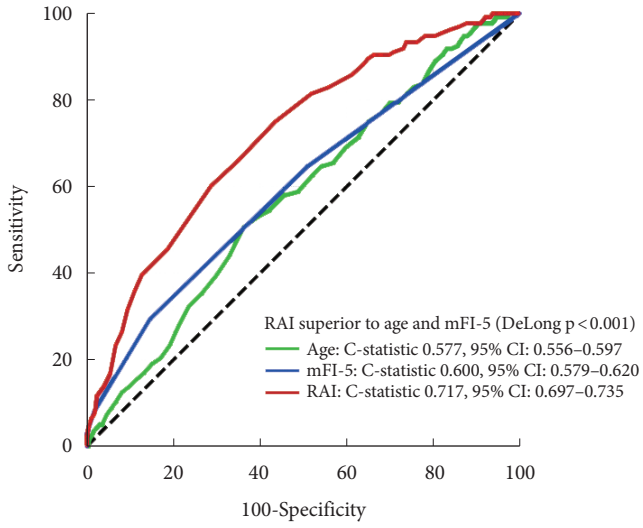

Fig. 2. Risk Analysis Index (RAI) with superior discriminatory accuracy for primary endpoint of 30-day mortality compared to age and mFI-5 (DeLong pairwise comparison, p < 0.001), ACS-NSQIP, 2011–2020 (N = 2,235). ACS-NSQIP, American College of Surgeons – National Surgical Quality Improvement Program; mFI-5, modified frailty index-5; CI, confidence interval.

Table 3. Postoperative complications, discharge outcomes, and 30-day outcomes after surgery for SM stratified by RAI frailty score, ACS-NSQIP 2011–2020 (N = 2,235)

Variable	All cohort	RAI category				p-value
		0–20	21–30	31–40	≥41	
Total patient	2,235	507	266	1,222	240	
Postoperative major complication	181 (8.1)	29 (5.7)	19 (7.1)	104 (8.5)	29 (12.1)	0.022
Clavien-Dindo IV complication	126 (5.6)	17 (3.4)	15 (5.6)	69 (5.6)	25 (10.4)	0.002
Extended length of stay	571 (25.5)	89 (17.6)	63 (23.7)	318 (26.0)	101 (42.1)	< 0.001
Nonhome discharge disposition	937 (41.9)	146 (28.8)	119 (44.7)	521 (42.6)	151 (62.9)	< 0.001
Mortality within 30 days of operation	136 (6.1)	9 (1.8)	7 (2.6)	77 (6.3)	43 (17.9)	< 0.001
Mortality or hospice	146 (6.5)	9 (1.8)	8 (3.0)	85 (7.0)	44 (18.3)	< 0.001

Values are presented as number of patients (%).
SM, spinal malignancy; RAI, Risk Analysis Index; ACS-NSQIP, American College of Surgeons – National Surgical Quality Improvement Program.

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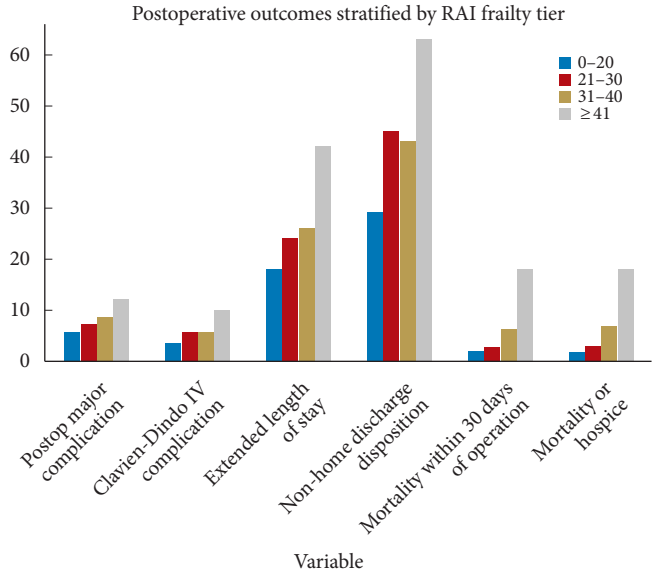

Fig. 3. Postoperative outcomes stratified by RAI frailty tier, ACS-NSQIP 2011–2020 (N = 2,235). RAI, Risk Analysis Index; ACS-NSQIP, American College of Surgeons – National Surgical Quality Improvement Program.

chronological age in prediction of the primary endpoint. These results may improve informed consent and surgical decision-making by enabling more accurate preoperative surgical risk prediction.

Few studies have similarly examined the use of frailty tools for outcome prediction in SM patients.[7] Many studies have described the importance of capturing frailty for preoperative risk assessment, moreover accurate frailty measurement and prediction is exceedingly crucial for SM patients who are often among the most frail due to their metastatic disease or SMs, advanced chronologic age, prior radiotherapy, and the necessity of surgical intervention despite these factors.[8,26-28] Hersh et al.[9] established that the mFI-5 and Metastatic Spinal Tumor Frailty Index (MSTFI) were superior to the widely used Charlson Comorbidity Index, supporting the well-established tenet that increasing frailty, and not just comorbidity accounting, robustly predict outcomes. A recent meta-analysis determined mFI-5 correlates better with postoperative complication prediction, while MSTFI predicts mortality better.[8] However, other scholars found the MSTFI had poor discrimination in predicting mortality and postoperative complications for SM patients in a single center machine learning study.[29] Another retrospective cohort study from a single institution similarly concluded that the mFI-5 did not accurately predict outcomes in surgically treated SM patients.[30] In a series of surgical SM patients treated at a single comprehensive cancer center, Ehresman et al.[31] analyzed specific preoperative comorbidities to create a web-based calculator predicting non-home discharge disposition. Preoperative albumin values, emergency status, and increasing complexity of the surgical procedure are established variables known to affect postoperative outcomes.[32-36] In addition to functional dependence, knowledge of the primary site of cancer, number, and site of metastases play a role in risk stratification in patients with metastatic spinal tumors.[37,38] However, these variables do not quantify the baseline physiological reserve of a patient (i.e., frailty) even in conjunction with the mFI-5.[33,39-41] Hall and colleagues adapted the Minimum Data Set Mortality Risk Index-Revised as a tool for the prospective or retrospective calculation of frailty. The 14-variables captured by RAI to create a frailty score have been recalibrated and validated across multiple surgical specialties.[11,42-45]

Prior studies have robustly demonstrated the predictive value of mFI-5 for poor postoperative outcomes in various surgical populations, including SM.[8,46] However, the mFI-5 is limited as a unidimensional scale, merely consisting of 4 comorbidities plus a binary functional assessment of independent versus dependent status (fully dependent or partially dependent). The RAI incorporates multiple domains of frailty by assessing comorbidities, functional status, nutritional baseline, mental status, and transfer status. The RAI's more comprehensive assessment of physiologic reserve in patients with SM is reflected by its superior discrimination in mortality/hospice prediction (compared to mFI-5) in patients with SMs. This study also adds support to the previous literature that also refutes the notion that frailty simply increases in proportion with chronological age.[47,48] Rather, frailty and chronological age need to be independently assessed preoperatively to accurately predict risk associated with any potential surgical intervention.[47,49] As such, the predictive ability of RAI plays a vital role in this cohort where the prevalence of primary SMs increases with age and improved rates of cancer survival predispose to the risk of future metastasis.[6,49] This study complements the growing body of literature validating the use of RAI in predicting adverse postoperative outcomes in neurosurgical spine patient populations.[50,51]

Frailty assessment at clinic visits could guide preoperative counseling and prehabilitation efforts to prevent adverse outcomes in elective spine surgery procedures.[52] The ease of calculating frailty scores could play a role in the extent of their incorporation into routine clinical practice.[53] For instance, scores like the Hospital Frailty Risk Score (HFRS) are calculated from over a 100 ICD-10 codes.[54] Although it is unclear as to how well HFRS is currently being utilized in clinical practice, one might imagine that calculating frailty scores based on HFRS might

prove challenging.[55] RAI, on the other hand, can be calculated using a 14-item questionnaire by the caregiver. Prior literature has described its ease of calculation in prospective cohorts of patients undergoing spine surgery.[50,56]

While not the primary endpoint, the RAI was also associated with ELOS, NHD, major complications, and CD IV complications. These adverse outcomes impact the patient and their family, but also increase the cost and burden on the healthcare system.[57] The elevated risk of poor outcomes with higher RAI scores highlights the importance of preoperative counseling with patients and families for more precise risk-benefit estimation.[58,59] As our analysis demonstrates the superiority of RAI over mFI-5 in terms of discriminatory accuracy for predicting mortality and since increasing RAI is associated with all the other adverse outcomes, clinicians may consider implementing RAI scoring during the preoperative surgical evaluation of SM patients.

RAI score was modified according to criteria described in prior studies to compute the score without the preoperative cognitive decline variable since this variable is no longer available in the NSQIP database.[20] The NSQIP only supplies a single ICD diagnosis field called "PODIAG" (postoperative diagnosis) and thus ICD codes cannot be utilized to define diagnoses other than the primary surgical diagnosis. There are also limitations related to specific outcomes of interest for the surgical treatment of SM. The NSQIP does not record postoperative functional outcomes such as urinary/bowel incontinence or other neurological deficits. Spinal cord compression is typically an indication for emergent/urgent surgical decompression and restoration. Information on quality of life or symptom improvement after surgery would add value to future research as it relates to RAI frailty indexing preoperatively. Additionally, variables critical in neurooncology research are not recorded in the NSQIP such as tumor size, surgical approach, and extent of resection. Furthermore, ICD coding is inherently difficult in distinguishing primary from metastatic neoplasms (Table 1). Thus, the authors opted to include all "malignant" spinal tumors. Further prospective research using qualitative data may provide better insight into discrete outcomes between these 2 groups that was unable to be performed in our retrospective analysis. Similarly, the MSTFI is not available using NSQIP, which we could not compare in this study to retrospective RAI. However, further prospective RAI studies can compare MSTFI in this patient population. Despite these limitations, this study is robust, with a large sample size of 2,235 patients, providing the necessary statistical power to analyze the prognostic utility of the RAI score.

CONCLUSION

Preoperative frailty, measured by the RAI score, was a predictor of postoperative mortality and/or hospice discharge in patients undergoing resection of SMs. Increased RAI scores are not only highly predictive of 30-day mortality or discharge to hospice, but are also associated with major complications, CD IV complications, ELOS, and NHD. Of note, the RAI demonstrated superior discrimination as compared to mFI-5 and age for outcome prediction. The frailty analysis may be translated to the bedside with a user-friendly application. The present work provides a foundation for frailty research in patients with SMs, including ongoing prospective clinical studies at the authors' institution.

NOTES

Conflict of Interest: In order to comply with the Hospital Participation Agreement (HPA) that is agreed to between the ACS and participating sites, facility identifiers as well as geographic information regarding the case have been removed. The HPA stipulates that the ACS does not identify participating sites. Site identification could be possible even with blinded identifiers through advanced statistics. A stipulation of access to the PUF is completion of the Data Use Agreement that strictly prohibits attempts to identify hospitals, health care providers, or patients. The authors have nothing to disclose.

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