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Prospective application of the risk analysis index to measure preoperative frailty in spinal tumor surgery: A single center outcomes analysis

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ABSTRACT

Introduction: Surgeons are frequently faced with challenging clinical dilemmas evaluating whether the benefits of surgery outweigh the substantial risks routinely encountered with spinal tumor surgery. The Clinical Risk Analysis Index (RAI-C) is a robust frailty tool administered via a patient-friendly questionnaire that strives to augment preoperative risk stratification. The objective of the study was to prospectively measure frailty with RAI-C and track postoperative outcomes after spinal tumor surgery.

Methods: Patients surgically treated for spinal tumors were followed prospectively from 7/2020–7/2022 at a single tertiary center. RAI-C was ascertained during preoperative visits and verified by the provider. The RAI-C scores were assessed in relation to postoperative functional status (measured by modified Rankin Scale score [mRS]) at the last follow-up visit.

Results: Of 39 patients, 47% were robust (RAI 0–20), 26% normal (21–30), 16% frail (31–40), and 11% severely frail (RAI 41+).). Pathology included primary (59%) and metastatic (41%) tumors with corresponding mRS>2 rates of 17% and 38%, respectively. Tumors were classified as extradural (49%), intradural extramedullary (46%), or intradural intramedullary (5.4%) with mRS>2 rates of 28%, 24%, and 50%, respectively. RAI-C had a positive association with mRS>2 at follow-up: 16% for robust, 20% for normal, 43% for frail, and 67% for severely frail. The two deaths in the series had the highest RAI-C scores (45 and 46) and were patients with metastatic cancer. The RAI-C was a robust and diagnostically accurate predictor of mRS>2 in receiver operating characteristic curve analysis (C-statistic: 0.70, 95 CI: 0.49–0.90).

Conclusions: The findings exemplify the clinical utility of RAI-C frailty scoring for prediction of outcomes after spinal tumor surgery and it has potential to help in the surgical decision-making process as well as surgical consent. As a preliminary case series, the authors intend to provide additional data with a larger sample size and longer follow-up duration in a future study.

1. Introduction

1.1. Background

Spinal tumors are a serious pathology, that arise most commonly secondary to metastasis (~70%).[1] Due to the scarcity of spinal oncology cases in comparison to the surgical treatment of chronic degenerative spine disease, research has been comparatively limited regarding the clinical course and treatment=.[2] Neurosurgeons are frequently faced with a challenging dilemma of whether the substantial risks of surgical treatment for spinal tumor patients justify aggressively pursuing the surgical goals of mitigation of neurological deficits, obtaining histopathological specimen, and/or improving survival.[3] A key consideration in the decision whether to recommend surgery, is whether a patient has the physiological reserve to recover sufficiently to return to functional independence free of postoperative complications. The latter is critical in patients with terminal disease undergoing non-curative surgery to

Abbreviations: eLOS, extended length of stay; mFI-5, 5-factor modified frailty index; NSQIP, National Surgical Quality Improvement Program; RAI-C, Clinical Risk Analysis Index; ROC, receiver operating characteristic curv.

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Abbreviations

ACS-NSQIP	American College of Surgeons National Surgical Quality Improvement Program
CCI	Charlson Comorbidity Index
CVA	Cerebrovascular Accident
eLOS	Extended Length of Stay
EMR	Electronic Medical Record
IQR	Interquartile Range
mFI	Modified Frailty Index
mRS	Modified Rankin Score
MSTFI	Metastatic Spinal Tumor Frailty Index
RAI	Risk Analysis Index
RAI-A	Risk Analysis Index-Administrative
RAI-C	Risk Analysis Index-Clinical
ROC	Receiver Operating Characteristic

prolong and maximize their quality of life. It is well known that patients with a higher burden of disease are generally more likely to have complications after spinal tumor surgery.[1] A prior nationwide cross-sectional analysis for spinal tumor surgery discovered that patients with advanced age, multiple comorbidities, and postoperative complications had worse discharge outcomes.[4] However, prior studies rarely combined solely preoperative, baseline health parameters, into a readily useable clinical tool for outcome prediction.[4] The RAI-C strives to capture a patient's baseline level of frailty, prior to any acute illness/neurological injury.

2. Rationale

Frailty, a measure of baseline physiological reserve, is a powerful predictor of outcomes after surgical procedures.[5–10] Frail patients across the spectrum of surgical subspecialties have been shown to experience more postoperative complications, adverse discharge disposition, and increased mortality rates.[6,9–12] The Clinical Risk Analysis Index (RAI-C) questionnaire and scoring system is a quantitatively robust frailty measurement developed and validated by Hall et al to predict mortality in surgical populations derived from administrative databases and clinical settings.[8,13] The RAI-C is administered with a patient-friendly questionnaire to gather information on age, biological sex, cancer status, cognition, baseline functional status, and key medical history (renal failure, congestive heart failure, unintentional weight loss, poor appetite). The impact of RAI-C on outcomes after spinal tumor surgery has not been previously reported.

2.1. Objectives

The objective of the present study was to measure preoperative baseline frailty (as measured by RAI-C) and track postoperative outcomes in spinal tumor surgery. To our knowledge, this is the first known prospective application of the RAI-C to this patient population.

3. Methods

3.1. Study design

The study was designed as a preliminary case series from a single center, prospective, cohort study. The study was reviewed and approved by the local Institutional Review Board as part of a large prospective frailty initiative in adult patients undergoing operative procedures across surgical specialties.

3.2. Participants

Adult (≥18 years) patients surgically treated for spinal tumors (7/2022 to 7/2022) completed the RAI-C questionnaire prior to neurosurgical intervention. Follow-up duration varied based upon clinical indication for continued follow-up. Functional status outcomes were ascertained from the last available follow-up documented.

3.3. Frailty screening

The RAI-C was ascertained during preoperative encounters using a standardized questionnaire and verified by the surgical provider. The RAI-C questionnaire and points assigned was adapted from *Annals of Surgery* manuscript by Arya et al, as depicted in Table 1 and Table 2.[8] The answers to questions are provided by the patient and/or surrogate with guidance from a healthcare provider. RAI-C scoring was seamlessly integrated into our clinical workflow via dot phrase in the electronic medical record system. RAI-C was recorded as a data point along with a comprehensive list of other preoperative, perioperative, and postoperative patient characteristics. RAI-C was compared to the commonly

Table 1
Recalibrated Prospective RAI-C, adapted from *Arya et al in Annals of Surgery*.[8]

Variable	Revised RAI-C	
Sex	3	
Age*Cancer	**w/o cancer**	**w/cancer**
< = 19	**0**	**28**
20–24	**1**	**29**
25–29	**4**	**29**
30–34	**6**	**30**
35–39	**8**	**30**
40–44	**10**	**31**
45–49	**12**	**31**
50–54	**14**	**32**
55–59	**16**	**32**
60–64	**18**	**33**
65–69	**20**	**34**
70–74	**22**	**34**
75–79	**24**	**35**
80–84	**26**	**35**
85–89	**28**	**36**
90–94	**30**	**36**
95–99	**32**	**37**
100+	**34**	**37**
Unintentional weight loss > 10 lbs., 3 mo.	**4**	
Poor Appetite	**4**	
Renal failure	**8**	
Chronic/Congestive Heart Failure	**5**	
Shortness of Breath at rest	**3**	
Resident other than Ind. Living	**1**	
ADL*Cog score	**w/o cog**	**w/cog**
0	**0**	**5**
1	**1**	**6**
2	**2**	**6**
3	**3**	**7**
4	**4**	**8**
5	**4**	**8**
6	**5**	**9**
7	**6**	**10**
8	**7**	**11**
9	**8**	**11**
10	**9**	**12**
11	**10**	**13**
12	**11**	**13**
13	**11**	**14**
14	**12**	**15**
15	**13**	**15**
16	**14**	**16**

Abbreviation: lbs., pounds; mo., months; w/o cog, without cognitive skills or status deterioration within past 3 months; w/cog, with cognitive skills or status deterioration within past 3 months.

Table 2
RAI-C Activities of Daily Living & Cognitive Decline, adapted from Arya et al in Annals of Surgery.[8]

Mobility/ Locomotion	Eating	Toilet Use	Personal Hygiene
0 – Independent	0 – Independent	0 – Independent	0 – Independent
1 – Supervised	1 – Supervised	1 – Supervised	1 – Supervised
2 – Limited Assistance	2 – Limited Assistance	2 – Limited Assistance	2 – Limited Assistance
3 - Extensive Assistance	3 - Extensive Assistance	3 - Extensive Assistance	3 - Extensive Assistance
4 - Total Dependence	4 - Total Dependence	4 - Total Dependence	4 - Total Dependence

utilized 5-factor modified frailty index (mFI-5), which is a predominantly comorbidity focused index. The primary outcome of interest was modified Rankin Scale score (mRS) > 2 (unfavorable functional status) at last follow-up (mean ± standard deviation of 10 ± 10 weeks, range 1–48 weeks).

3.4. Statistical methods

The IBM SPSS version 28 statistical software was utilized for all analyses. Statistical significance was set *a priori* to alpha of 0.05 with the understanding that additional, descriptively significant, trends would also be discussed. Statistical tests included Pearson chi-square test (categorical crosstabulation), Wilcoxon rank sum (continuous predictor by binary outcome), and Cochran-Armitage trend test (ordinal predictor by binary outcome for trends). Receiver operating characteristic (ROC) curve analysis was utilized to assess the discriminatory accuracy of RAI score for prediction of primary outcome.

4. Results

A total of 39 patients had preoperative RAI-C frailty scoring and underwent spinal tumor surgery. The median (interquartile range [IQR] age was 52 (40–66). Pathology included primary (59%) and metastatic (41%) tumors with corresponding mRS>2 rates of 17% and 38%, respectively (Table 3). Tumors were classified as extradural (49%), intradural extramedullary (46%), or intradural intramedullary (5.4%) with mRS>2 rates of 28%, 24%, and 50%, respectively (Table 3).

Frail (RAI-C>30) vs. not frail patients had significantly higher rates of mortality (P = 0.013), mRS>2 at follow-up (P = 0.041), and lack of functional improvement postop (P = 0.038) (Fig. 1). Descriptively, frailty was also associated with higher rates of extended length of stay (eLOS), non-home discharge disposition, and readmission but these comparisons did not reach statistical significance (P > 0.05, Fig. 1).

Patients were stratified by RAI-C frailty score into robust (47%, RAI 0–20), normal (26%, RAI 21–30), frail (16%, RAI 31–40), and severely frail (11%, RAI 41+). Uptrend in RAI-C score corresponded with increasing rate of mRS>2 (P = 0.025, Fig. 2). Trend tests for age group and mFI-5 frailty did not reach significance (P > 0.05, Fig. 2). Aside from frailty, patients with hyponatremia (67% vs. 23%, P = 0.098), elevated creatinine (100% vs. 20%, P = 0.003), and hypoalbuminemia (67% vs. 0%, P = 0.035) were at higher risk for adverse postoperative outcome (Table 3).

In ROC curve analysis, RAI-C frailty score predicted mRS>2 with acceptable discriminatory accuracy (C statistic: 0.70, 95% CI: 0.49–0.90). By comparison, mFI-5 demonstrated subpar discriminatory accuracy (C statistic: 0.65, 95% CI: 0.44–0.87) (Fig. 3).

5. Discussion

Spinal tumors are surgically treated to reduce pain, improve functional status, obtain histopathological tissue, and/or improve survivorship. However, these procedures are frequently complex and are associated with high rates of complications and increased mortality.[14–17] Thus, particularly with metastatic cases, it is critical to select patients with favorable benefit/risk ratio who are likely to swiftly recover and avoid prolonging suffering. The informed consent process is augmented whenever clinically validated prognostic tools are available. Herein, the authors present the first known prospective analysis of RAI-C frailty scoring in a cohort of patients undergoing spine tumor surgery. The preliminary results of a long-term prospective study were promising, showing that RAI-C reliably predicts unfavorable postoperative functional status (mRS>2). Of note, severely frail patients (RAI-C 41+) had exceedingly high rates of morbidity (75% mRS>2) and mortality (50%, 2/4). The only two deaths occurred in severely frail patients with metastatic cancer (RAI-C 45 and 46) at 8 weeks and 16 weeks postoperatively. One of the two mortality cases had an mFI-5 score of 0 (not frail/robust), which highlights the limitations of this comorbidity-driven frailty index. While severe frailty was associated with worse outcomes, there remains a spectrum of frailty, with a fair number of patients having reasonable outcome goals that warrant future discussion and research to attempt risk mitigation preoperatively.

The preliminary findings build upon a foundation of extensive frailty research in the neurosurgical literature. To our knowledge, this represents the second known RAI-C series in a neurosurgical patient population and the first in patients with spinal tumors. Within neurosurgery, the superiority of frailty to chronological patient age has been demonstrated repeatedly and has become accepted. The RAI-C strikes an optimal balance between clinical ease-of-use, quantitative robustness, and

Table 3
Baseline demographic, clinical characteristics, and outcomes for 39 patients undergoing spinal tumor resection from a prospective frailty database.

Characteristics	N = 39	mRS>2
Overall	39	10 (26)
Age in years	52 (40, 66)	
Age quartiles[a]		a
1st	8 (21)	0 (0)
2nd	10 (26)	4 (40)
3rd	10 (26)	1 (10)
4th	10 (26)	5 (50)
Biological Sex		
Male	23 (59)	8 (35)
Female	16 (41)	2 (13)
Tumor Source		
Primary spinal	23 (59)	4 (17)
Metastatic	16 (41)	6 (38)
Tumor Compartment		
Extradural	18 (49)	5 (28)
Intradural extramedullary	17 (46)	4 (24)
Intradural intramedullary	2 (5.4)	1 (50)
Tumor Location		
Cervical	11 (28)	3 (27)
Thoracic	16 (41)	5 (31)
Spine	12 (31)	2 (17)
mFI-5		
Robust	21 (54)	4 (19)
Normal	8 (21)	1 (13)
Frail	7 (18)	3 (43)
Severely frail	3 (8)	2 (67)
RAI-C[a]		a
Robust (0–20)	19 (49)	3 (16)
Normal (21–30)	10 (26)	2 (20)
Frail (31–40)	6 (15)	2 (33)
Severely frail (>40)	4 (10)	3 (75)
Hyponatremia (<135)[b]	3 (8)	2 (67)
Creatinine Elevated[a]	3 (8)	3 (100)[a]
Hypoalbuminemia[a]	3 (8)	2 (67)[a]
Leukocytosis	8 (21)	2 (25)
Thrombocytopenia (PLT<100 k)	1 (3)	0 (0)
Anemia (Hct <36)[b]	8 (21)	1 (100)[b]

Results reported as no. patients (%) unless otherwise specified.
[a] Statistically significant with P < 0.05.
[b] Statistical trend with P < 0.10.

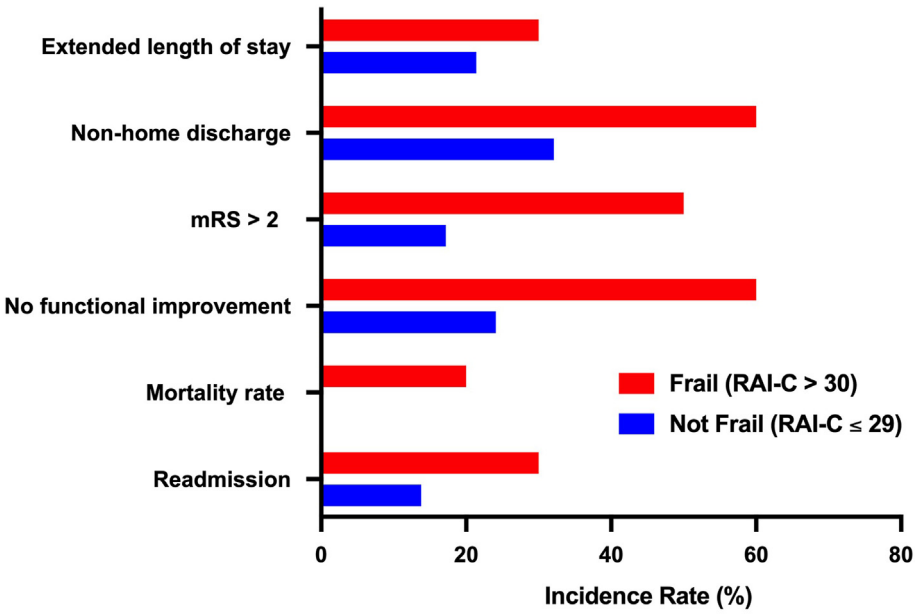

Fig. 1. Frailty (RAI-C > 30) and postoperative outcomes after spine tumor surgery.

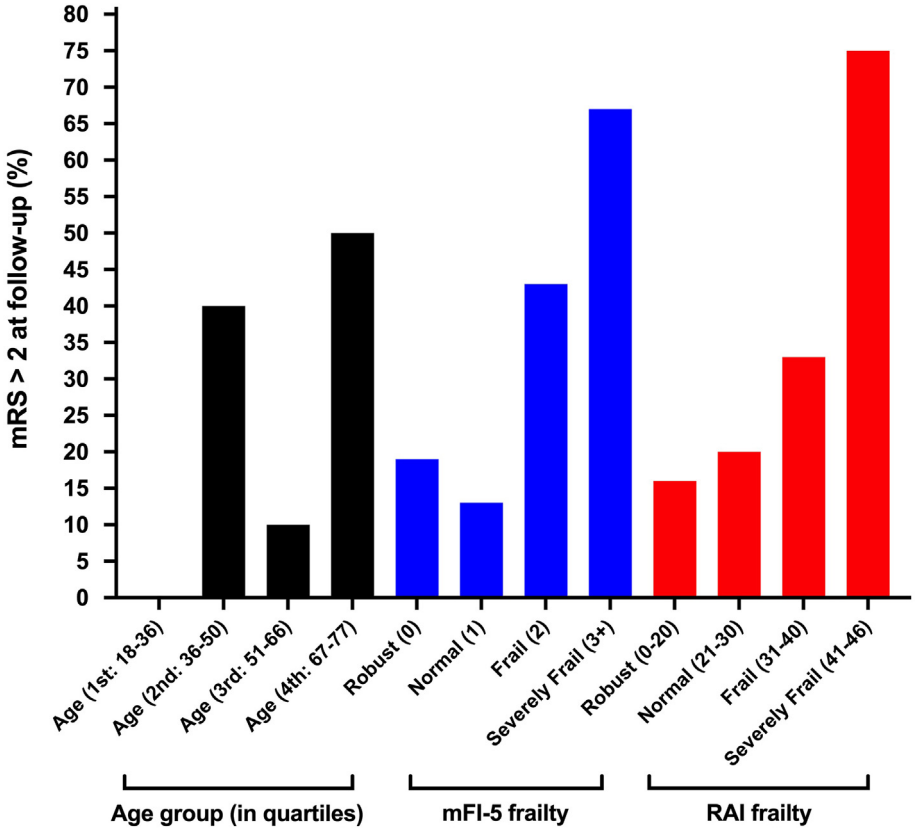

Fig. 2. Event rate of modified Rankin Scale score >2 (unfavorable functional outcome) at last follow-up by age groups and frailty status (measured by mFI-5 and RAI-C). The Cochran Armitage proportional test of trends was significant for RAI frailty groupings (P = 0.025) but not age group or mFI-5 frailty.

widespread generalizability across surgical patient populations. In the digital age with disease-specific information readily available to patients and their families, frailty tools add a patient-specific, personalized, perspective to assist surgeons with patient counseling. A reliable and easy-to-administer frailty tool bolsters a surgeon's arsenal with complex decision-making.

Other studies have proven the generalizability of RAI and its superiority in predicting short- and long-term mortality across surgical specialties.[8,18–20] Agarwal et al analyzed impact of frailty on outcomes after spine surgery (all) in a prospective cohort study of 688 patients.[21] They found that RAI-C was associated with increased risk of readmission and postoperative mortality after spine surgery. The surgical population

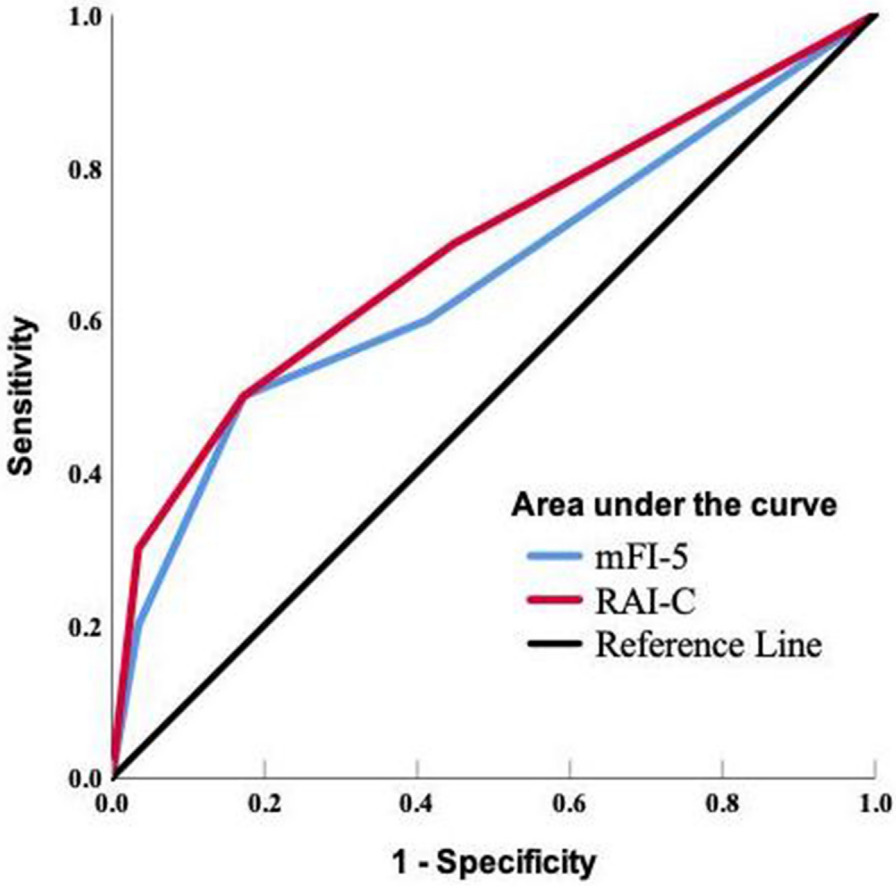

Fig. 3. Receiver operating characteristic (ROC) curve analysis showing discriminative ability of mFI-5 and RAI-C for prediction of mRS >2 (unfavorable functional outcome at follow-up).

included only 18 spinal tumor cases who were not analyzed independently as a patient population. George et al found that RAI was an independent risk factor for 30-day and 90-day mortality after noncardiac surgical patients with regards to low-and-moderate stress procedures[18] One limitation was the inability to analyze at the patient level as the data was deidentified at the case level. Also, the ACS-NSQIP did not separate the all-cause mortality from mortality related directly to the procedure.[18] Overall, RAI has numerous advantages as it is easily translatable to clinical settings and exposes suboptimal outcomes after surgery.[19,22,23] The present series, while limited in sample size, provides preliminary statistical results the authors plan to utilize in forward planning of a long-term prospective study.

Several prior studies have utilized alternative indices to predict outcomes after spinal tumor surgery. In a retrospective analysis of 4662 spinal tumor surgeries (ACS-NSQIP 2015–2019), Kazim et al found that baseline frailty (as measured by mFI-5) was more robust predictor than chronological age for predicting outcomes after spinal tumor surgery.[24] Specifically, the "severely frail" had the highest rates of 30 day mortality, readmission, reoperation, postoperative complications and LOS.[24] However, the mFI-5 is a comorbidity-driven index that does not comprehensively assess a patient's baseline physiological reserve for surgery. This is exemplified by the patient in our series with RAI of 46 (severely frail) but mFI-5 score of 0 (robust) who suffered postoperative mortality.

Ramos et al developed and tested the "metastatic spinal tumor frailty index (MSTFI) in a database of 4583 patients derived from a nationwide administrative discharge database.[25,26] They found associations between MSTFI and prolonged hospital stay, readmission rate, and inpatient mortality. However, the MSTFI "frailty index" included measures of surgical complexity (e.g., emergent/urgent admission and anterior/combined surgical approach) rather than exclusively parameters of frailty (baseline physiological reserve).[25] Furthermore, critical components of frailty that are essential to the concept of frailty affecting surgical outcomes, including chronological age, cancer status, cognitive status, and baseline functional status were not included.[25] Lakomkim et al compared modified Charlson Index (CCI) mFI-5, and ASA score in spine surgery using the 2008–2014 NSQIP and found that CCI demonstrated superior predictive capacity compared to mFI and ASA.[27]

The present single-center prospective study address key limitations of prior nationwide database driven frailty studies which have strength in sample size but are limited by cross-sectional design, poor granularity, and lack of information for post-operative functional status.[1,25–28] Overall, large national database analyses provide helpful overviews that identify associations warranting resource allocation in prospective study designs. However, such analyses are hindered by limited information for pre-/post-operative functional status, limited follow-up, poor granularity for diagnoses/procedures, and retrospective design.[24] The present study supports prior NSQIP nationwide findings that frailty is strongly linked to postoperative outcomes after spinal tumor surgery.[24] While quantitatively inferior to the RAI-C, frailty measured by mFI-5 in this prospective series was also associated with poor postoperative outcomes.

5.1. Limitations

This was a preliminary analysis from an ongoing large prospective frailty series at the authors' institution. Despite limited sample size, we found it imperative to disclose early descriptive trends warranting attention. Thus, outcome analysis was limited for several important postoperative variables due to sparse event rate (e.g., mortality, major complication, readmission/reoperation). Furthermore, our study cohort

was heterogeneous with a mixture of primary and metastatic spinal tumors, which presents additional generalizability limitations. However, the RAI-C frailty score is adept at accounting for disease severity attributed to metastatic cancer. Age with or without disseminated cancer is a key interaction term within the RAI-C index. For example, a 75 year-old without cancer would receive 4 points for age whereas a 75-year-old with cancer would receive 18 points. Patients with metastatic cancer are also more likely to have unintentional weight loss and poor appetite, which contribute additional frailty points. Future prospective RAI-C studies with larger sample size would ideally have the statistical power to separate primary and metastatic spinal tumor patients into separate analyses. Spinal tumors in this cohort were described by tumor source (primary vs. metastatic) and tumor compartment (extradural vs. intradural extramedullary vs. intradural intramedullary). Thus, we were able to describe variations in outcome by type of spinal tumor. However, the limited sample size hindered distinct frailty analysis stratified by tumor source and tumor compartment. The RAI-C score itself, while quantitatively robust and easy to administer, is not without its own limitations that warrant continuous re-evaluation moving forward. Follow-up duration for patients included towards the end of the study period is presently limited and expected to improve over time. The RAI-C was administered at a single U.S. neurosurgical department and may or may not generalize to other departments across the globe. Administration of the RAI-C screening form integrates seamlessly into our clinic flow with the assistance of our clinic staff. However, the authors recommend that all scores, particularly in operative candidates, are confirmed by surgeons. Overall, despite the limitations, the findings have guided early quality improvement strategies and inform preoperative decision making in our neurosurgical clinics.

6. Conclusion

The Clinical Risk Analysis Index (RAI-C) is a robust frailty measure easily administered via patient-friendly questionnaire that strives to augment preoperative risk stratification. The present study is the first known prospective application of the RAI-C to measure baseline frailty and track postoperative outcomes after spinal tumor surgery. The results emphasize the clinical utility of RAI-C in predicting postoperative morbidity/mortality while highlighting the limitations of comorbidity-driven frailty indices. As a preliminary report, the authors intend to provide additional data with longer follow-up duration in a future study.

Credit author statement

Remy L. Link: Investigation, Resources, Writing-Original Draft. **Kavelin Rumalla:** Methodology, Software, Validation, Formal Analysis, Writing Original Draft. **Evan N. Courville:** Visualization, Writing-Review and Editing. **Joanna M. Roy:** Visualization, Writing-Review and Editing. **Syed Faraz Kazim:** Conceptualization, Methodology, Supervision. **Christian A. Bowers:** Conceptualization, Methodology, Supervision. **Meic H. Schmidt:** Conceptualization, Methodology, Supervision, Project Administration.

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Declaration of competing interest

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

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