World Neurosurgery: X 23 (2024) 100286

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x

Frailty Predicts 30-day mortality following major complications in neurosurgery patients: The risk analysis index has superior discrimination compared to modified frailty index-5 and increasing patient age

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ARTICLE INFO

Keywords:
Frailty
Risk analysis index
Modified frailty Index-5
Clavien Dindo
Major complications
30-Day mortality

ABSTRACT

Background: Postoperative complications after cranial or spine surgery are prevalent, and frailty can be a key contributing patient factor. Therefore, we evaluated frailty's impact on 30-day mortality. We compared the discrimination for risk analysis index (RAI), modified frailty index-5 (mFI-5) and increasing patient age for predicting 30-day mortality.

Methods: Patients with major complications following neurosurgery procedures between 2012- 2020 in the ACS-NSQIP database were included. We employed receiver operating characteristic (ROC) curve and examined discrimination thresholds for RAI, mFI-5, and increasing patient age for 30-day mortality. Independent relationships were examined using multivariable analysis.

Results: There were 19,096 patients included in the study and in the ROC analysis for 30-day mortality, RAI showed superior discriminant validity threshold C-statistic 0.655 (95% CI: 0.644-0.666), compared to mFI-5 C-statistic 0.570 (95% CI 0.559-0.581), and increasing patient age C-statistic 0.607 (95% CI 0.595-0.619). When the patient population was divided into subsets based on the procedures type (spinal, cranial or other), spine procedures had the highest discriminant validity threshold for RAI (Cstatistic 0.717). Furthermore, there was a frailty risk tier dose response relationship with 30-day mortalityy ($p<0.001$).

Conclusion: When a major complication arises after neurosurgical procedures, frail patients have a higher likelihood of dying within 30 days than their non-frail counterparts. The RAI demonstrated a higher discriminant validity threshold than mFI-5 and increasing patient age, making it a more clinically relevant tool for identifying and stratifying patients by frailty risk tiers. These findings highlight the importance of initiatives geared toward optimizing frail patients, to mitigate long-term disability.

1. Introduction

In the present paradigm of quality-metric-based payment, it is crucial to anticipate surgical complications and undertake measures to reduce them during perioperative planning and management.[1] Postoperative complications contribute to the high rates of morbidity and mortality observed following neurosurgical procedures.[2] Over 94,000 people residing in the United States are estimated to receive a new central nervous system (CNS) tumor diagnosis in 2023.[3] The surgical removal of operable tumors is paramount to the treatment of CNS malignancy and is a lifesaving procedure for many; however, tumor resection has inherent risks, with some institutions reporting postoperative complication rates as high as 27%.[4]

Similarly, spine procedures are associated with high rates of postoperative complications (11.2%), with blood loss necessitating transfusion and reoperation within 30 days as the most common complications following either cranial or spine procedures.[5] Although

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https://doi.org/10.1016/j.wnsx.2024.100286
Received 28 January 2023; Accepted 20 February 2024
Available online 2 March 2024

Abbreviations

Risk Analysis Index (RAI)
Modified Frailty Index (mFI-5)
Central Nervous System (CNS)
Extended Length of Stay (eLOS)
American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP)
Clavien-Dindo (CD)
Skilled Nursing Facility (SNF)
Receiver Operating Characteristic (ROC)
Area Under the Curve (AUC)
Confidence Intervals (CI)
Odds Ratios (OR)
Congestive Heart Failure (CHF)

some postoperative occurrences, such as nausea, vomiting, and pain, are anticipated and considered to be minor,[4] other occurrences are classified as major or life threatening, and result in increased healthcare utilization, extended length of stay (eLOS), or death.[6,7]

Frailty can be a key risk factor for postoperative complications.[8–11] Frailty is a state of physiological decline, manifesting as a depletion of functional reserve.[11–14] It is commonly seen in individuals with multiple comorbidities and is associated with worse outcomes across multiple surgical specialties.[8–10,13,15] Frail patients have increased rates of mortality, postoperative complications, and are more likely to be discharged to facilities with capacity for providing higher-level of care.[8,9,16] While a plethora of information about perioperative risk assessment exists,[8–10,13,17,18] and there is agreement about the presence of frailty as a syndrome, divergence of opinion still exists regarding its domains and the most appropriate strategy for accurately identifying and risk stratifying patients.[18,19]

The 5-factor modified frailty index (mFI-5) is one of the earlier tools that was developed and validated to objectively quantify an individual's physiologic deficits across two frailty domains i.e. health and functional domains.[20,21] The mFI-5, has been used extensively in neurosurgical literature as a frailty metric, and demonstrated to be an accurate predictor of adverse outcomes.[20,21] Nonetheless, its utility is limited because it stratifies patients based on only two frailty domains.[18,22] This approach may be underestimating, or otherwise excluding pertinent information. The risk analysis index (RAI) is an 11-variable weighted metric that was designed to better elucidate preoperative risk strata.[11,13,23] It was found to have excellent internal validity and has since been studied and disseminated across numerous surgical specialties.[10,13,23–25]

To our knowledge, no studies has been completed to assess whether RAI is effective in predicting worse postoperative outcomes in a subset of neurosurgery patients who experienced major complications. In this subset of patients, we hypothesized that RAI would be a reliable predictor of 30-day mortality. Furthermore, we anticipate that the RAI would demonstrate superior discrimination compared to the mFI-5 and increasing patient age. Therefore, we intend to investigate the predictive thresholds and compare the discriminatory capacity of RAI, mFI-5, and increasing patient age. In addition, we will compare their independent relationship to 30-day mortality.

2. Methods

2.1. Study population

We examined the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) participant use files for relevant information meeting our inclusion criteria. The ACS-NSQIP has been extensively described in the literature.[26,27] Briefly, this surgical registry is an aggregate of verified prospective patient samples, clinical characteristics, and 30-day postoperative outcomes. Our query yielded results for 19,096 patients undergoing neurosurgery between 2012 and 2020 who experienced a major postoperative complication.

The Clavien-Dindo (CD) surgical complication classification system was used to categorize the occurrence of complications by increasing severity into grades I-IV.[6] Briefly, the CD classification system is a widely used and validated surgical complication categorization tool that considers the acuity of care required to address the complication and the impact of the complication on the patient's quality of life.[7] CD Grade III complications require surgical, endoscopic, or radiological intervention. While CD Grade IV complications are described as life threatening, with failure in 1 or more vital organs, and requiring intermediate care or intensive care unit management e.g., sepsis or septic shock, acute cerebrovascular accident or stroke with neurological deficit, acute renal failure, pulmonary embolism, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, ventilator use greater than 48 h, and unplanned reintubation. The patients who had a CD III and/or CD IV were considered to have major complications. The University of New Mexico Institutional Review Board [IRB-21-315] evaluated, considered exempt (due to the deidentified nature of the ACS-NSQIP database), and approved this study protocol. Nonetheless, study procedures were established in conformity with the ACS-NSQIP data user agreement.

3. Risk assessment Metrices

3.1. The risk analysis index

The RAI was developed with robust methodology calibrated to predict mortality up to one year after surgery[13,23,25] Using data from the ACS-NSQIP, the RAI provides efficient risk stratification, as has been shown across a variety of specialties and subspecialties. Considerations such as patient demographics (sex, patient age with and without a relevant cancer diagnosis], place of residence [home, rehab facility, skilled nursing facility (SNF)], cognitive status, functional independence [ability to perform activities of daily living without assistance]) and clinical factors (recent unintentional weight loss >10 lbs., renal failure requiring dialysis, chronic heart failure, loss of appetite) contribute to the determination of a patient's risk (Table 1). Each variable is awarded the corresponding weighted score, to achieve a total score between 0 and 81, which is then stratified into frailty risk tiers: 0–20 (Robust), 21–30 (Pre-frail), 31–40 (Frail), and ≥41 (Very Frail) (Table 1).

3.1.1. The modified frailty Index-5 (mFI-5)

The mFI-5 it is based on five criteria that have undergone rigorous testing and are recorded in the ACS-NSQIP database. The mFI-5 includes the presence of congestive heart failure, chronic obstructive pulmonary disease, hypertension, and diabetes requiring medication. In addition, the final scored variable is functional independence, defined as the ability to perform activities of daily living without assistance. For each variable, a score of 0 represents the absence of the variable evaluated, while a value of 1 is given in its presence. When assessing each patient, the maximum possible mFI-5 score is applied (5). Similar to the RAI, the final score ranges from 0 (Robust), 1 (Pre-frail), 2 (Frail), and 3–5 (Very Frail) (Table 1).

3.1.2. Postoperative outcomes

The primary outcome in this study is the 30-day mortality rate for various neurosurgery procedural patient cohorts who experienced major complications. The total number of postoperative deaths for this group of patients was calculated by integrating the results of three different variables. To begin, the variable "year of death" defines the current calendar year in which the patient died, with corresponding date within 30 days of surgery. Second, patients who die during their postoperative hospitalization period are assigned "expired" as the discharge

Table 1
Variable weights and frailty screening cutoffs for risk analysis index and modified frailty index 5.

30-day Mortality

RAI	Sensitivity	Specificity	Correctly Classified	Positive Likelihood	Negative Likelihood
2	100.00%	0.00%	12.49%	1.00	
3	94.01%	16.94%	26.57%	1.13	0.35
4	92.33%	19.87%	28.92%	1.15	0.39
5	90.78%	22.07%	30.66%	1.16	0.42
6	89.52%	23.23%	31.51%	1.17	0.45
7	88.64%	23.77%	31.88%	1.16	0.48
8	79.17%	43.78%	48.20%	1.41	0.48
9	76.70%	47.78%	51.39%	1.47	0.49
10	73.93%	50.79%	53.68%	1.50	0.51
11	68.06%	57.47%	58.80%	1.60	0.56
12	64.46%	59.53%	60.15%	1.59	0.60
13	63.20%	60.45%	60.80%	1.60	0.61
14	61.90%	61.23%	61.32%	1.60	0.62
15	60.52%	61.65%	61.51%	1.58	0.64
16	53.77%	68.43%	66.60%	1.70	0.68
17	50.34%	70.16%	67.68%	1.69	0.71
18	48.53%	71.59%	68.71%	1.71	0.72
19	45.60%	73.27%	69.81%	1.71	0.74
20	42.37%	74.79%	70.74%	1.68	0.77
21	37.13%	80.14%	74.76%	1.87	0.78
22	35.67%	80.51%	74.91%	1.83	0.80
23	34.24%	81.01%	75.17%	1.80	0.81
24	31.39%	82.67%	76.26%	1.81	0.83
25	28.83%	84.03%	77.14%	1.81	0.85
26	21.84%	91.42%	82.73%	2.55	0.86
27	20.49%	91.87%	82.95%	2.52	0.87
28	19.07%	92.29%	83.14%	2.47	0.88
29	16.05%	94.12%	84.36%	2.73	0.89
30	15.09%	94.45%	84.54%	2.72	0.90
31	14.50%	94.63%	84.61%	2.70	0.90
32	12.70%	95.07%	84.78%	2.58	0.92
33	10.98%	95.65%	85.07%	2.52	0.93
34	5.83%	98.35%	86.79%	3.53	0.96
35	4.95%	98.67%	86.96%	3.71	0.96
36	4.57%	98.75%	86.98%	3.65	0.97
37	3.77%	98.99%	87.10%	3.75	0.97
38	3.52%	99.13%	87.19%	4.06	0.97
39	3.31%	99.16%	87.19%	3.95	0.98
40	2.89%	99.28%	87.23%	3.99	0.98
41	2.39%	99.37%	87.25%	3.80	0.98
42	1.55%	99.68%	87.42%	4.89	0.99
44	0.75%	99.82%	87.44%	4.20	0.99
45	0.63%	99.85%	87.45%	4.20	1.00
46	0.59%	99.87%	87.47%	4.67	1.00
47	0.59%	99.88%	87.47%	4.90	1.00
48	0.59%	99.89%	87.48%	5.45	1.00
49	0.50%	99.90%	87.48%	4.94	1.00
50	0.38%	99.93%	87.49%	5.25	1.00
51	0.21%	99.97%	87.51%	7.00	1.00
53	0.17%	99.98%	87.51%	7.00	1.00
54	0.13%	99.99%	87.51%	10.50	1.00
55	0.08%	99.99%	87.51%	14.01	1.00
58	0.04%	99.99%	87.51%	7.01	1.00

mFI-5	Sensitivity	Specificity	Correctly Classified	Positive Likelihood	Negative Likelihood
0	100.00%	0.00%	12.49%	1.00	
1	74.94%	34.74%	39.76%	1.15	0.72
2	36.34%	73.25%	68.64%	1.36	0.87
3	9.14%	94.93%	84.21%	1.80	0.96
4	1.38%	99.47%	87.21%	2.60	0.99
5	0.13%	99.98%	87.50%	5.25	1.00

Variable Weights for Frailty Assessment Tools

Modified Frailty Index-5:
Total=5:
0 - "Robust"
1 - "Typical"
2 - "Frail"
≥3 - "Very Frail"

Chronic Obstructive Pulmonary Disease (+1)
Congestive Heart Failure (+1)
Diabetes Mellitus (on oral medication or insulin) (+1)
Hypertension (on oral medication) (+1)
Partial and Total Functional Dependence (+1)

Risk Analysis Index:
Total=81:
≤20 - "Robust"
21-30 - "Typical"
31-40 - "Frail"
≥41 - "Very Frail"

Age:
With Cancer: 65-69 (20), 70-74 (19), 75-79 (18), 80-84 (17), 85-89 (16)
Without Cancer: 65-69 (2), 70-74 (3), 75-79 (4), 80-84 (5), 85-89 (6)
Sex: Male (+5)

Diagnosed Cancer (+1)
Chronic Kidney Disease (End-stage and/or Dialysis) (+6)
Congestive Heart Failure (+4)
Dyspnea (+8)

Poor Appetite (+4)
Unintentional Weight Loss >10lbs within 6 months (+5)

Decrease Reserve (High-level of Care Facility Resident) (+8)
Require Support to Complete Activities of Daily Living (without cognitive evaluation):
Partially Dependent (+8)
Totally Dependent (+16)

Typical = Pre-frail

disposition. The final variable, "end of life/care withdrawal," relates to the need for postoperative care coordination, which may include providing comfort measures or palliative care.

3.1.2.1. Statistical analysis. We estimated medians and their related interquartile ranges to define continuous data (IQRs). Dichotomous or categorical variables were assigned frequencies and percentages. The Chi-squared test, Fisher's exact test (for dichotomous or categorical data), the nonparametric Mann Whitney *U* test (for continuous data) were all used for comparisons. Using receiver operating characteristic (ROC) curve analysis, the sensitivity and specificity for predicting 30-day mortality were evaluated between RAI, mFI-5, and increasing patient age. The area under the curve (AUC) values and 95% confidence intervals (CI) are presented. The AUC is a measure of performance that averages across all possible levels of categorization; it can be thought of as the fraction of times a frail patient who had a major or life-threatening complication died or was ranked higher than another frail patient who did not experience mortality. Additionally, we performed ROC analysis stratified by procedure type (spine, cranial and others [vascular, functional, and non-tumor/spine procedures]). Similarly, multivariable regression was performed, with estimates presented as odds ratios (OR) and 95% CI. Statistical significance was assessed when the two-tailed *p*-value was less than or equal to 0.05.[28] For all statistical testing, STATA 17 was employed (StataCorp, LLP, College Station, TX).

4. Results

4.1. Study population characteristics

The population characteristics are delineated in Table 2. We identified 19,096 patients who had a neurosurgical procedure with subsequent CD III or IV complications. The median age of our data sample was 63 years old (IQR 53–72). Male patients accounted for 57.2% of the population. Race was unequally represented with a predominance of White individuals (68.3%), compared to Black (12.3%), Asian (3%), and Other (16.5%: American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and unreported) (Table 2). Only 6.6% of the population reported Hispanic ethnicity.

Overall, the median BMI was 29 (IQR 24.8–34.1) kg/m^3, and a cancer diagnosis was recorded in 24.9% of the population. The most common comorbidity was hypertension (58.4%), followed by diabetes (23.0%). The least common comorbidity was congestive heart failure (CHF), representing 1.7% of the study population (Table 2).

The median operative time was 167 min (IQR 108–257). Patients more frequently underwent a spine procedure 52.4%, compared to cranial 46.1%, and other non-spine/-cranial procedures 1.5%. Complications graded CD III were recorded in 56.6%, and life-threatening complications graded CD IV, in 43.4% of the population. The median LOS was 7 days (IQR 3–15). A smaller proportion of patients experienced eLOS 26.0% (≥75 percentile), and 35.5% of patients were discharged to a facility with higher level of care capacity. The 30-day readmission rate was 40.3%, and the 30-day morality rate was recorded in 12.5% of the population (Table 2).

Table 3 provides a detailed comparison of clinical and postoperative outcomes stratified by Clavien-Dindo (CD) III and CD IV categories. Generally, spine patients were seen to have a higher incidence of CD III complications, with a rate of 58.5% compared to CD IV complications, which was 44.4%. When focusing on patients who underwent cranial and other neurosurgical procedures, there was a higher rate of CD IV complications $P < 0.001$ (Table 3). In addition, CD IV complications were associated with higher rates of eLOS and higher mortality rates $P < 0.001$. On the other hand, patients with CD III complications exhibited higher rates of discharges to SNF and higher 30-day readmission rates $P < 0.001$ (Table 3).

4.1.1. Receiver operating characteristic analyses

The overall ROC analysis used to compare the predictive thresholds for RAI, mFI-5, and increasing patient age revealed superior discriminant validity threshold for RAI C-statistic 0.655 (95% CI: 0.644–0.666), compared to mFI-5 C-statistic 0.570 (95% CI 0.559–0.581), and increasing patient age C-statistic 0.607 (95% CI 0.595–0.619) DeLong p-value <0.001 (Fig. 1).

When the patient population was divided into various cohorts based on the different pathologies, the spine surgery group had the highest discriminant validity threshold for RAI (Fig. 2). A low RAI performance

Table 2
Characteristics of neurosurgery patients with major complications delineated by risk analysis index, and modified frailty Index-5 screening Tools.

		Risk Analysis Index$^{\alpha}$				Modified Frailty Index-5$^{\alpha}$			
Variables	**Total N=19096**	Robust N=14891	Pre-frail N=2961	Frail N=1054	Severely Frail N=190	Robust N=6403	Pre-frail N=7356	Frail N=4271	Severely Frail N=1066
Age, median (IQR), years	63.0 (53.0, 72.0)	63.0 (53.0, 72.0)	63.0 (52.0, 71.0)	64.0 (56.0, 72.0)	63.0 (55.0, 69.0)	55.0 (43.0, 65.0)	65.0 (56.0, 73.0)	67.0 (60.0, 74.0)	69.0 (61.0, 76.0)
Sex, n (%)									
Male	10930 (57.2%)	7527 (50.5%)	2297 (77.6%)	935 (88.7%)	171 (90.0%)	3533 (55.2%)	4242 (57.7%)	2538 (59.4%)	617 (57.9%)
Female	8166 (42.8%)	7364 (49.5%)	664 (22.4%)	119 (11.3%)	19 (10.0%)	2870 (44.8%)	3114 (42.3%)	1733 (40.6%)	449 (42.1%)
Race, n (%)									
White	13040 (68.3%)	10282 (69.0%)	1959 (66.2%)	678 (64.3%)	121 (63.7%)	4278 (66.8%)	5142 (69.9%)	2923 (68.4%)	697 (65.4%)
Black	2343 (12.3%)	1961 (13.2%)	261 (8.8%)	99 (9.4%)	22 (11.6%)	538 (8.4%)	964 (13.1%)	640 (15.0%)	201 (18.9%)
Asian	567 (3.0%)	412 (2.8%)	114 (3.9%)	34 (3.2%)	7 (3.7%)	187 (2.9%)	216 (2.9%)	130 (3.0%)	34 (3.2%)
Other*	3146 (16.5%)	2236 (15.0%)	627 (21.2%)	243 (23.1%)	40 (21.1%)	1400 (21.9%)	1034 (14.1%)	578 (13.5%)	134 (12.6%)
Ethnicity, n (%)									
Hispanic	1260 (6.6%)	990 (6.6%)	188 (6.3%)	69 (6.5%)	13 (6.8%)	449 (7.0%)	413 (5.6%)	314 (7.4%)	84 (7.9%)
BMI, median (IQR), kg/m^2	29.0 (24.8, 34.1)	29.4 (25.1, 34.7)	27.9 (24.0, 32.2)	26.9 (23.0, 31.6)	25.5 (21.8, 31.3)	27.5 (23.7, 32.0)	29.1 (25.1, 34.2)	30.9 (26.3, 36.0)	31.0 (25.8, 37.1)
ASA Score, n (%)									
I	183 (1.0%)	151 (1.0%)	22 (0.7%)	10 (0.9%)	0 (0.0%)	144 (2.2%)	24 (0.3%)	13 (0.3%)	2 (0.2%)
II	3491 (18.3%)	3085 (20.7%)	326 (11.0%)	76 (7.2%)	4 (2.1%)	1851 (28.9%)	1271 (17.3%)	347 (8.1%)	22 (2.1%)
III	10918 (57.2%)	8368 (56.2%)	1860 (62.8%)	598 (56.7%)	92 (48.4%)	3122 (48.8%)	4402 (59.8%)	2781 (65.1%)	613 (57.5%)
IV	4091 (21.4%)	2937 (19.7%)	705 (23.8%)	361 (34.3%)	88 (46.3%)	1143 (17.9%)	1487 (20.2%)	1060 (24.8%)	401 (37.6%)
V	413 (2.2%)	350 (2.4%)	48 (1.6%)	9 (0.9%)	6 (3.2%)	143 (2.2%)	172 (2.3%)	70 (1.6%)	28 (2.6%)
HTN, n (%)	11150 (58.4%)	8913 (59.9%)	1554 (52.5%)	579 (54.9%)	104 (54.7%)	0 (0.0%)	5995 (81.5%)	4103 (96.1%)	1052 (98.7%)
Diabetes, n (%)	4386 (23.0%)	3497 (23.5)	586 (19.8)	253 (24.0)	50 (26.3)	0 (0.0%)	528 (7.2%)	2951 (69.1%)	907 (85.1%)
COPD, n (%)	1463 (7.7%)	1082 (7.3%)	238 (8.0%)	115 (10.9%)	28 (14.7%)	0 (0.0%)	265 (3.6%)	673 (15.8%)	525 (49.2%)
CHF, n (%)	325 (1.7%)	195 (1.3%)	87 (2.9%)	31 (2.9%)	12 (6.3%)	0 (0.0%)	26 (0.4%)	112 (2.6%)	187 (17.5%)
Functional Status, n (%)									
Dependent	1901 (10.0%)	946 (6.4%)	549 (18.5%)	277 (26.3%)	129 (67.9%)	0 (0.0%)	542 (7.4%)	703 (16.5%)	656 (61.5%)
Cancer Diagnosis, n (%)	4749 (24.9%)	1231 (8.3%)	2351 (79.4%)	985 (93.5)	182 (95.8)	2083 (32.5)	1722 (23.4)	774 (18.1)	170 (16.0)
Operative time, median (IQR), mins	167.0 (108.0, 257.0)	162.0 (105.0, 251.0)	185.0 (122.0, 280.0)	180.0 (123.0, 260.0)	177.0 (121.0, 256.0)	175.0 (110.0, 276.0)	167.0 (109.0, 258.0)	160.0 (106.0, 242.0)	149.0 (101.0, 228.0)
Procedure Type, n (%)									
Spine	10010 (52.4%)	9116 (61.2%)	634 (21.4%)	212 (20.1%)	48 (25.3%)	2777 (43.4%)	3951 (53.7%)	2619 (61.3%)	663 (62.2%)
Cranial	8799 (46.1%)	5507 (37.0%)	2313 (78.1%)	839 (79.6%)	140 (73.7%)	3548 (55.4%)	3287 (44.7%)	1579 (37.0%)	385 (36.1%)
Others&	287 (1.5%)	268 (1.8%)	14 (0.5%)	3 (0.3%)	2 (1.1%)	78 (1.2%)	118 (1.6%)	73 (1.7%)	18 (1.7%)
Complications, n (%)$^{\Psi}$									
III	10800 (56.6%)	8506 (57.1%)	1608 (54.3%)	574 (54.5%)	112 (58.9%)	3771 (58.9%)	4184 (56.9%)	2303 (53.9%)	542 (50.8%)
IV	8296 (43.4%)	6385 (42.9%)	1353 (45.7%)	480 (45.5%)	78 (41.1%)	2632 (41.1%)	3172 (43.1%)	1968 (46.1%)	524 (49.2%)
LOS, median (IQR), days	7.0 (3.0, 15.0)	7.0 (3.0, 14.0)	8.0 (4.0, 17.0)	11.0 (7.0, 18.0)	13.0 (7.0, 23.0)	7.0 (3.0, 15.0)	7.0 (3.0, 14.0)	8.0 (3.0, 15.0)	10.0 (5.0, 18.0)
Extended LOS, n (%)*$^{\alpha}$	4966 (26.0%)	3581 (24.1%)	896 (30.3%)	400 (38.0%)	89 (46.8%)	1650 (25.8%)	1812 (24.6%)	1125 (26.3%)	379 (35.6%)
SNF, n (%)	6785 (35.5%)	5581 (37.5%)	968 (32.7%)	209 (19.8%)	27 (14.2%)	1887 (29.5%)	2677 (36.4%)	1770 (41.4%)	451 (42.3%)
30-day Readmission, n (%)	7682 (40.3%)	5980 (40.2%)	1237 (41.9%)	395 (37.5%)	70 (36.8%)	2518 (39.4%)	2986 (40.6%)	1759 (41.3%)	419 (39.3%)
30-day Mortality, n (%)	2386 (12.5%)	1500 (10.1%)	540 (18.2%)	277 (26.3%)	69 (36.3%)	598 (9.3%)	921 (12.5%)	649 (15.2%)	218 (20.5%)

BMI, body mass index, ASA, American Society of Anesthesiologists, HTN, hypertension, COPD, chronic obstructive pulmonary disease, CHF, congestive heart failure, LOS, Length of Hospital Stay, SNF, skilled nursing facility, Rehab, rehabilitation.
*αExtended LOS is defined as LOS ≥75 percentile.
$^{\alpha}$*P*-value computed using Fishers Chi Squared and exact tests for proportions. Nonparametric tests for medians.
$^{\alpha}$RAI comparisons, all significant (<0.01) except ethnicity, and readmissions.
$^{\alpha}$mFI-5 comparisons, all significant (<0.01) except readmissions.
Other: American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Unknown.
Other: Vascular, functional and non-tumor/spine procedures.
Complications, stratified by Claveín-Dindo classification; grades III-IV comprises of all life-threatening postoperative occurrences.

Table 3
Characteristics of neurosurgery patients with major complications delineated by Clavien-Dindo Complication grades.

Variables	Total $n = 19096$	CD III $n = 10800$	CD IV $n = 8296$	*P*-Value
Operative time, median (IQR), mins	167.0 (108.0, 257.0)	169.0 (109.0, 259.0)	165.0 (107.0, 255.0)	0.04
Procedure Type, n (%)				<0.001
Spine	10010 (52.4%)	6323 (58.5%)	3687 (44.4%)	
Cranial	8799 (46.1%)	4366 (40.4%)	4433 (53.4%)	
Others[a]	287 (1.5%)	111 (1.0%)	176 (2.1%)	
LOS, median (IQR), days	7.0 (3.0, 15.0)	7.0 (3.0, 14.0)	8.0 (3.0, 16.0)	<0.001
Extended LOS, n (%)[bα]	4966 (26.0%)	2562 (23.7%)	2404 (29.0%)	<0.001
SNF, n (%)	6785 (35.5%)	3563 (33.0%)	3222 (38.8%)	<0.001
30-day Readmission, n (%)	7682 (40.3%)	4872 (45.2%)	2810 (33.9%)	<0.001
30-day Mortality, n (%)	2386 (12.5%)	756 (7.0%)	1630 (19.6%)	<0.001

LOS, Length of Hospital Stay, SNF, skilled nursing facility, Rehab, rehabilitation. [α]*P*-value computed using Fishers Chi Squared and exact tests for proportions. Nonparametric tests for medians.
[a] Other: Vascular, functional and non-tumor/spine procedures.
[b] αExtended LOS is defined as LOS ≥75 percentile.

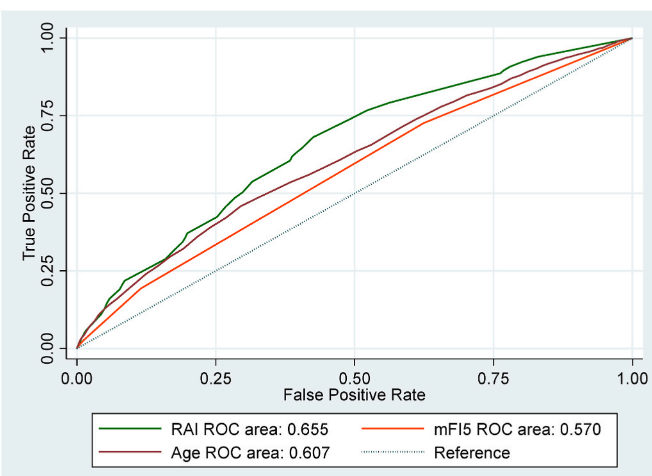

Fig. 1. Examining the discriminant validity threshold of frailty Screening tools and age on mortality in neurosurgery patients with life threatening complications.

was observed specifically in the subset of cranial procedures (Fig. 2).

4.1.2. Multivariable analysis

The RAI frailty classification system categorized 78% of the population as robust, 15.5% pre-frail, 5.5% frail, and 1% very frail. While the mFI-5 score distribution was 33.6% robust, 38.5% pre-frail, 22.4% frail, and 5.6% very frail (Table 2).

Multivariable regression analysis (adjusting for race, operative time, and BMI) revealed that RAI was independently associated with mortality compared to mFI-5 and increasing patient age (Table 4). Furthermore, there was a risk tier dose response relationship with mortality observed by RAI, normal patients OR 2.01 (95% CI 1.8, 2.24), frail patients OR of 3.14 (95% CI 2.71, 3.65), and very frail patients OR of 5.11 (95% CI 3.77, 6.92). While examining the mFI-5 categories, we found that for normal patients OR 1.45 (95% CI 1.30, 1.62), frail patients OR 1.85 (95% CI 1.64, 2.09), and Very Frail patients OR 2.65 (95% CI 2.23, 3.16), with mFI-5 again displaying a similar dose response. Age had the least descriptive ability, OR 1.03 (95% CI 1.02, 1.03) (Table 4).

In conducting a subgroup analysis based on the type of procedure i.e., spine, cranial, and other (vascular, functional, and non-tumor/spine procedures), a parallel trend was observed for the generated estimates. This trend mirrored those identified in the previously stated overall multivariable analyses (Table 4)

5. Discussion

In this ACS-NSQIP database study of 19,096 patients who experienced major complications after a neurosurgical procedure, we evaluated the discriminant validity threshold of two frailty risk assessment tools and the effect of increasing patient age on the primary outcome of 30-day mortality. Overall, in the context of predicting 30-day mortality, the RAI frailty scale outperformed the mFI-5 and increasing patient age. A higher RAI score prior to surgery was indicative of increased 30-day mortality risk. In the multivariable analyses, RAI demonstrated significantly larger effect sizes in comparison to mFI-5 and increasing patient age. This was also consistently noted in the stratified analysis by procedure type. Moreover, a clear dose–response relationship with mortality was identified, further reinforcing the findings. In our patient cohort, spine surgery was the most prevalent procedure. This prevalence enabled more robust comparative analysis due to the larger sample size.

Conventionally, it has been assumed that increasing patient age is a strong indicator of mortality risk. However, we observed that increasing patient age demonstrated only a modest predictive capacity and association with 30-day mortality. This is similar to what was observed in a systematic review by Kojima and colleagues, where they found that the average age of their cohorts did not play a significant role as a moderator between frailty and mortality.[29] While some older patients do not have the physiological reserve necessary to endure the impact of surgical procedures, subsequently resulting in poor postoperative occurrences, the subjectivity in surgical planning can be attributed to the limited knowledge of frailty or inadequate strategies for gauging preoperative risk.[30–32]

The RAI, which was used for this study, may be deployed with relative ease and requires only a small amount of time commitment, and can be done by medical aides.[13,33] Since the RAI's scoring range is more refined than that of the mFI-5, it can be used in a wide variety of patient populations, with cutoffs chosen based on factors such as the prevalence of frailty in a given population.[18,25] The RAI allows more room for risk stratification than the mFI-5, and therefore provides a more nuanced spectrum of possible scores, and the RAI has far superior discrimination when compared to the mFI-5.[18,25]

Incorporating the RAI into clinical workflows is feasible and can provide additional information for preoperative decision making, potentially shifting the conversation towards earlier care coordination measures, especially in the very frail patients. These strategies have been associated with improved mortality,[34] increased quality of life, decreased health care expenditures, and increased satisfaction with care.[31,32,35–37] Preoperatively, patients can receive improved risk assessment, thereby, expanding the pool of ideal surgical candidates beyond those who would have been excluded solely on the basis of increasing patient age.[31,32] Interestingly, increasing patient age has showed stronger discriminant validity thresholds in some instances,[38] this may provide support for the concept that patients' risk levels should be monitored continuously throughout the perioperative period.

When attempting to draw conclusions from this study, it is worth remembering the following limitations: first, there was no meaningful differentiation between the institutions regarding the total number of neurosurgical procedures carried out. The ACS-NSQIP is a deidentified database that does not allow for such granular analysis. We are unable to claim applicability of our findings to any center base on volume alone. Nonetheless, because of the vast number of centers that participate in the ACS-NSQIP, our study may be more generalizable than a single center study. Second, all retrospective studies are vulnerable to selection

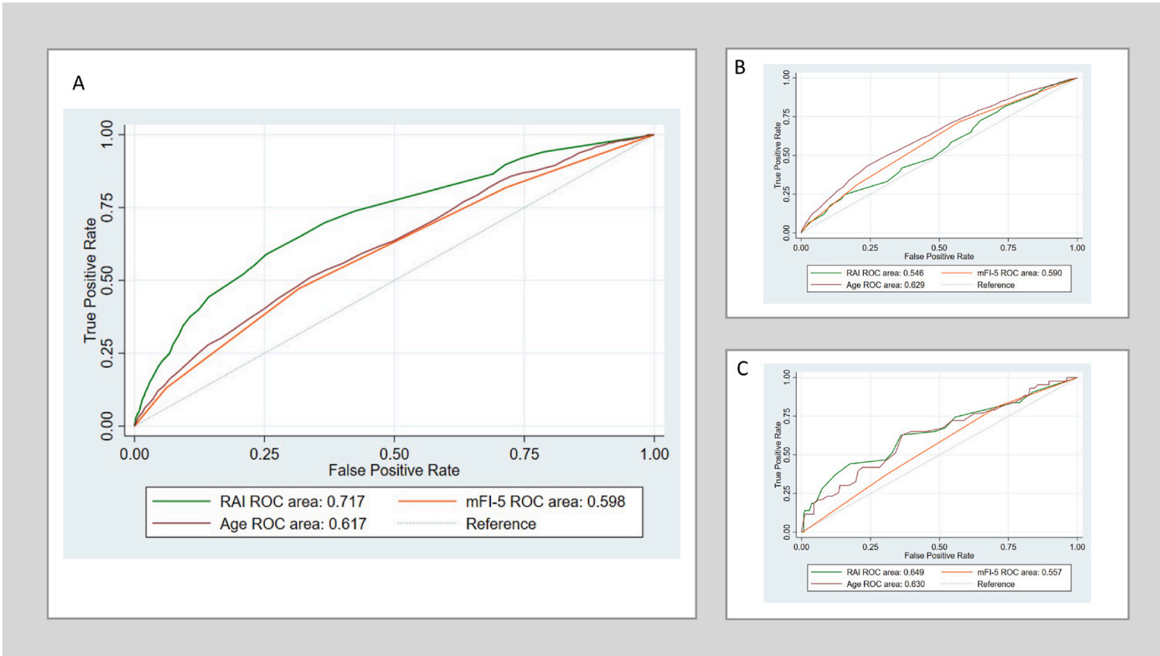

Fig. 2. Subgroup analysis examining the discriminant validity threshold of frailty Screening tools and age on mortality in neurosurgery patients with major complications stratified by procedure type.

Table 4
Examining the independent associations of frailty screening tools and age for mortality in neurosurgery patients with major complications.

Variables	Overall (n = 19096) 30-day Mortality OR (95% CI)	Spine (n = 10010) 30-day Mortality OR (95% CI)	Cranial (n = 8799) 30-day Mortality OR (95% CI)	Other (n = 287) 30-day Mortality OR (95% CI)
Robust (RAI = 0–20)	[REF]	[REF]	[REF]	[REF]
Pre-frail (RAI = 21–30)	2.01 (1.80, 2.24) *	3.94 (3.17, 4.89) *	1.11 (0.97, 1.26)	3.92 (1.19, 12.92) #
Frail (RAI = 31–40)	3.14 (2.71, 3.65) *	5.77 (4.18, 7.94) *	1.75 (1.47, 2.08) *	–*–
Very frail (RAI≥41)	5.11 (3.77, 6.92) *	13.60 (7.65, 24.20) *	2.51 (1.75, 3.61) *	–*–
Robust (mFI-5 = 0)	[REF]	[REF]	[REF]	[REF]
Pre-frail (mFI-5 = 1)	1.45 (1.30, 1.62) *	1.13 (0.90, 1.41)	1.31 (1.14, 1.50) *	1.23 (0.49, 3.11)
Frail (mFI-5 = 2)	1.85 (1.64, 2.09) *	1.71 (1.36, 2.15) *	1.58 (1.34, 1.86) *	1.34 (0.51, 3.53)
Very frail (mFI-5≥3)	2.65 (2.23, 3.16) *	2.66 (1.99, 3.57) *	2.07 (1.61, 2.66) *	1.31 (0.29, 5.86)
Age	1.03 (1.02, 1.03) *	1.03 (1.02, 1.04) *	1.02 (1.02, 1.03) *	1.03 (1.00, 1.07)

OR odds ratio; CI, confidence interval; RAI, risk analysis index; mFI-5, modified frailty index-5.
Regression models adjusted for race, BMI and operative time in multivariable models for RAI, mFI-5 (age variable included).
We followed strict variable selection to ensure no collinearity between variables.
**P*-value <0.001, #*P*-value ≤0.05.
–*–no data points to make meaningful comparisons.

bias and our study is no exception; however, care was taken when designing our statistical methods to reduce biases in our calculations wherever possible. A third limitation was the unequal representation of race. The breakdown for race differed from the most recent United States census data estimates.[39] Nonetheless, despite the aforementioned limitations, we are confident that our results can be extrapolated to other similar settings, as the ACS-NSQIP is representative of the patients receiving care across the United States. Fourth, while our study highlights distinct postoperative outcomes based on CD III and IV complications, for robust analyses, we combined these categories, preventing over-stratification of our data points, despite their differing clinical severity (even though both categories often requiring ICU transfer). This research underlines the need for further investigation into the subtle differences between these CD categories. A careful examination could provide invaluable insights for improved postoperative management. Independent analysis of these categories may refine our knowledge of their unique complexities, paving the way for more specific and successful postoperative care. Lastly, the ACS-NSQIP captures 30-day mortality data independent of inpatient status, therefore, this data may not be acquired uniformly across different institutions because of the differences in their operational capacity. Nonetheless, previous studies have extensively reported on the efficacy of RAI in predicting long-term mortality.[25]

6. Conclusion

When a major complication arises after neurosurgical procedures, frail patients have a higher likelihood of dying within 30 days than their non-frail counterparts. The RAI demonstrated a higher discriminant validity threshold than mFI-5 and increasing patient age, making it a more clinically relevant tool for identifying and stratifying patients by frailty risk tiers. Care coordination for these at-risk patients can be improved by identifying them preoperatively, and then tailoring multidisciplinary case management initiatives. These findings highlight the importance of initiatives geared toward enhancing the health of the frail patient, consequently mitigating long-term disability.

CRediT authorship contribution statement

Christopher C. Paiz: Project administration, Writing – original draft. **Oluwafemi P. Owodunni:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Evan N. Courville:** Project administration, Writing – review & editing. **Meic Schmidt:** Writing – review & editing. **Robert Alunday:** Writing – review & editing. **Christian A. Bowers:** Conceptualization, Investigation, Supervision, Writing – review & editing.

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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