Journal of Neuro-Oncology (2018) 136:197–206
https://doi.org/10.1007/s11060-017-2644-0

CLINICAL STUDY

The modified frailty index and 30-day adverse events in oncologic neurosurgery

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Received: 11 March 2017 / Accepted: 22 October 2017 / Published online: 14 November 2017

Abstract

The modified frailty index (mFI) is emerging as a leading measure for preoperative risk assessment using routinely available medical record data. Our objective was to determine if mFI predicts morbidity and mortality in the diverse national cohort of patients undergoing neurosurgery for intracranial neoplasms. We identified patients in the National Surgical Quality Improvement Program who underwent oncologic neurosurgery procedures between 2008 and 2012. The mFI, ranging from 0 to 1, was calculated as the proportion of 11 possible risk factors present. We assessed the associations between mFI and 30-day mortality, neurologic and medical complications, prolonged length of stay, and unfavorable discharge in univariate and multivariable analyses and compare the index to established risk stratification techniques. A total of 9149 patients were identified. Mortality, severe medical complications, prolonged length of stay, and unfavorable discharge increased incrementally with increasing levels of frailty. Severe neurologic complications were highest in those with low frailty. In multivariable logistic regression analysis, increased frailty increased the odds of all adverse outcomes, including neurologic complications. The mFI increased the ability to predict all outcomes beyond available indices and was the most reliable predictor of neurologic complications. The mFI can be calculated from routinely collected medical record data and is predictive of 30-day adverse outcomes in a wide variety of neurosurgical oncology patients. The index may be a useful component of preoperative risk assessment with implications for shared decision-making, perioperative planning, and risk adjusted outcomes measurement in national quality registries.

Keywords Frailty · Neurosurgery · Oncology · Risk assessment · Quality measurement · Complications

Introduction

As the population ages and neuro-oncologic treatment options expand, older and higher comorbidity patients with brain tumors are increasingly presenting as neurosurgical candidates [1, 2]. Surgical decision-making in this population is complex. In addition to balancing the risks and benefits of operating on a particular tumor, decision-makers must attempt to quantify the added risk that a patient's underlying health status contributes to the full episode of care. There are countless potential risk factors to consider and medical information may be incomplete. Existing clinical tools tend to be subjective, such as the American Society of

Electronic supplementary material The online version of this article (doi:10.1007/s11060-017-2644-0) contains supplementary material, which is available to authorized users.

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Anesthesiology (ASA) class, [1] or narrowly focused on a single outcome, such as cardiac risk assessment [3]. Multivariable predictive models, while useful in clinical research and quality measurement, may be unavailable or impractical for routine clinical use [1, 2, 4]. There is a pressing need for more reliable and transparent tools to quantify preoperative risk.

Based on a combination of functional status and comorbidities, measures of frailty attempt to convey information about a patient's overall physical function and physiologic reserves [5, 6]. Several studies have demonstrated that the modified frailty index (mFI), a composite score of 11 common comorbidities and function status, can be calculated from routinely collected medical record data and is associated with outcomes in surgical and oncologic populations [7–14]. There is reason to suspect that functional status would play an even larger role in predicting neurooncology outcomes than in other fields. Preoperative neurological deficits are associated with increased risk of adverse outcomes [4, 15] and poor baseline functional status may limit the ability to recover from new neurologic deficits [16]. However, the mFI has not been validated in the oncologic neurosurgery population and its importance relative to other available indices in predicting outcomes remains to be determined.

The objective of our study was to determine whether the mFI, calculated from routinely collected, chart abstracted data in the National Surgical Quality Improvement Program (NSQIP), predicts morbidity and mortality in oncologic neurosurgery. We examined the discriminatory ability of the mFI to predict adverse outcomes in patients undergoing multiple types of surgery for a variety of pathologies and compared predictive ability to available indices in NSQIP.

Methods

Data were obtained from the American College of Surgeons (ACS) NSQIP database [17]. NSQIP captures data from the time of the initial index admission and follows patients for 30 days after surgery. It is a nationwide sample collected from over 400 hospitals. Data are abstracted from the first 40 cases for a given procedure during 8-day sampling cycles and sampling is staggered throughout the year to reduce bias in case selection. Raters are regularly audited and their data excluded if they do not meet preset standards of validity [18].

We identified patients who underwent neurosurgical procedures for intracranial neoplasms between 2008 and 2012. As further shown in Table S1, patients were included if they had (1) a Current Procedural Terminology (CPT) procedure code representing a surgery classified as supratentorial brain (61510, 61545, 61546), supratentorial dural (61512), or infratentorial (61548, 62165); (2) an International Classification of Diseases and Related Conditions, Ninth Revision (ICD-9) diagnosis code representing a pathology classified as primary brain malignant or uncertain (191.x, 192.8, 192.9, 194.3, 194.4, 237.0, 237.1, 237.5, 239.6, 239.7), primary brain benign (225.0, 225.8, 225.9, 227.3, 227.4, 228.00, 228.02), primary dural malignant or uncertain (192.1, 237.6), primary dural benign (213.0, 225.2), primary cranial nerve malignant or benign (192.0, 225.1, 237.72, 237.73), or secondary malignant (198.3, 140.x, 141.x, 142.x, 143.x, 144.x, 145.x, 146.x, 147.x, 148.x, 149.x, 150.x, 151.x, 152.x, 153.x, 154.x, 155.x, 156.x, 156.x, 158.x, 159.x, 160.x, 161.x, 162.x, 163.x, 164.x, 165.x, 170.x, 171.x, 172.x, 173.x, 174.x, 175.x, 176.x, 179.x, 180.x, 181.x, 182.x, 183.x, 184.x, 185.x, 186.x, 187.x, 188.x, 189.x, 190.x, 192.2, 192.3, 193.x, 194.0, 194.1, 194.5, 194.6, 194.8, 194.9, 195.x, 196.x, 197.x, 198.x, 199.x, 200.x, 201.x, 202.x, 203.x, 204.x, 205.x, 206.x, 207.x, 208.x, 209.x, or NSQIP Code for "disseminated cancer"); and (3) were at least 18 years old.

The mFI was calculated using 11 variables from the Canadian Study of Health and Aging (CSHA) Frailty Index [19] that were matched to variables in NSQIP as we have previously described [12] (Table 1). Each variable was scored one point in the numerator for every condition present. The numerator was then divided by the number of variables recorded for that patient (the denominator). Missing data or variables coded as "unknown" were excluded from the calculation of mFI. The mFI thus ranges from 0 to 1 with higher scores representing increasing frailty.

Preoperative demographic and clinical variables included surgery category (supratentorial brain, supratentorial dural, infratentorial, or transsphenoidal), pathology category (primary brain malignant, primary brain benign, primary dural malignant, primary dural benign, primary cranial nerve, and secondary malignant), the risk indices being compared (age, ASA class, and mFI), and other variables not included in the modified frailty index (sex, race, body mass index (BMI), tobacco use, bleeding disorders, hemiplegia, ventilator dependence, sepsis, albumin level, weight loss, transfusion, corticosteroid use, chemotherapy in the past month, radiotherapy in the past 90 days, and emergency status of the case). ASA class is a subjective, overall measure of a patient's burden of disease prior to surgery. It is coded by the evaluating clinician and is scored from 1, a normal healthy patient, to 6, an organ donor meeting the criteria for brain death [1].

The outcomes measured were 30-day mortality, 30-day severe medical complications, 30-day severe neurologic complications, 30-day any complication, extended length of stay (LOS), and unfavorable disposition. Mortality was defined as death within 30 days of the index procedure. Severe medical complications were defined according to the Clavian class IV categorization, which includes septic

Table 1 Conditions included in the mFI

	Condition	NSQIP Coding	Frequency/ Reported[1]	%
1	Diabetes mellitus	Insulin-dependent diabetes mellitus Non-insulin-dependent diabetes mellitus	1082/9149	11.8%
2	Functional status	Partially dependent or total dependent	774/9105	8.5%
3	Respiratory problems	Chronic obstructive pulmonary disease Current pneumonia	451/9149	4.9%
4	Congestive heart failure	Congestive heart failure	32/9149	0.3%
5	Myocardial infarction	Previous myocardial infarction	10/4430	0.2%
6	Other cardiac problems	Previous percutaneous coronary intervention Previous coronary surgery Angina	264/4693	5.6%
7	Hypertension	Hypertension requiring medication	3684/9149	40.3%
8	Peripheral vascular disease	Peripheral vascular disease or resting pain	33/4430	0.7%
9	Impaired sensorium	Impaired sensorium	310/4430	7.0%
10	Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	79/4330	1.8%
11	Cerebrovascular disease with neurological deficit	Cerebrovascular disease with deficit	155/4430	3.5%

NSQIP – National Surgery Quality Improvement Project.
1. Variables missing or coded as "Unknown" were excluded from the denominator.

NSQIP National Surgery Quality Improvement Project

[a]Variables missing or coded as "Unknown" were excluded from the denominator

shock, cardiac arrest, myocardial infarction, pulmonary embolism, need for more than 48 h of ventilation, or unplanned re-intubation [9, 12, 20]. Coma and cerebrovascular accident or stroke with a new neurologic deficit were categorized as severe neurologic complications. Any complication included the occurrence of a severe medical or neurologic complication as defined above, or a wound complication (wound dehiscence, superficial, deep, or organ space infection), pneumonia, acute renal failure, urinary tract infection, deep vein thrombosis, or sepsis. Prolonged length of stay was defined as hospitalizations lasting longer than 7 days. Unfavorable disposition was defined as a discharge destination other than home or a facility with a higher level of care than before admission.

Distributions of the outcomes across mFI scores were compared using Chi square tests. Multivariable logistic regression models were then constructed for each outcome and model fit statistics were calculated to determine the strength of association between each outcome and mFI, ASA class, age, combined indices, and the full model. The *c*-statistic is a measure of concordance, or the ability of a model to predict the outcome of interest, and is calculated as the area under a receiver operating characteristic curve (ROC) evaluating true and false positive rates. A value of one corresponds to a perfectly predictive model whereas a value of 0.5 indicates that the model is no more reliable than chance. All analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Clinical and demographic characteristics of the cohort are presented in Table 2. A total of 9149 patients who underwent resection of intracranial neoplasms were identified from the NSQIP database. Fewer surgeries were performed at increasing levels of frailty. The majority of patients had no frailty (51.5%), while 21.3% had low, 21.5% intermediate, and 5.7% high frailty. Transsphenoidal surgery patients were more likely to have low preoperative frailty (35.1%) than the full cohort (21.3%). Patients with benign primary brain tumors and primary cranial nerve tumors were also less frail. Compared to the full cohort, patients were more likely to have intermediate or high frailty if they had secondary malignant brain tumors, older age, were Black compared to White, or had higher preoperative ASA class, obesity, bleeding disorders, dependent functional status, hemiplegia, ventilator dependence, sepsis, low albumin (< 3.5), weight loss, blood transfusion, corticosteroid use, chemotherapy in the past month, or radiotherapy in the past 90 days.

In the univariate analysis (Fig. 1), increased mFI was associated with stepwise increases in the rates of mortality, severe medical complications, prolonged length of stay, and unfavorable discharge. This trend held true in subgroup analyses (see Table S2 in Supplementary Material) of nearly all categories of surgery and pathology with minor exceptions between adjacent levels of frailty and

Table 2 Clinical and demographic characteristics of patients undergoing oncologic neurosurgery stratified by mFI

	Frequency	No frailty (mFI = 0)	Low frailty (mFI = 0.01–0.19)	Intermediate frailty (mFI = 0.2–0.29)	High frailty (mFI ≥ 0.3)
	n (%)	Row %	Row %	Row %	Row %
Frequency	9149 (100)	51.5	21.3	21.5	5.7
Surgery category					
Supratentorial brain	5272 (57.6)	52.2	19.9	21.3	6.6
Supratentorial dural	1581 (17.3)	48.5	22.7	23.7	5.1
Infratentorial	1632 (17.8)	52.8	18.9	23.3	5.0
Transsphenoidal	664 (7.3)	49.8	35.1	13.0	2.1
Pathology category					
Primary brain malignant	3372 (39.1)	56.2	19.1	20.0	4.7
Primary brain benign	892 (10.3)	56.4	26.9	14.0	2.7
Primary dural malignant	119 (1.4)	52.9	25.2	16.0	5.9
Primary dural benign	1723 (20.0)	49.7	21.5	24.8	3.9
Primary cranial nerve	258 (3.0)	60.1	16.3	19.8	3.9
Secondary malignant	2257 (26.2)	42.2	22.0	25.6	10.2
Age					
< 45	2070 (22.6)	82.6	9.4	7.4	0.5
45–54	1905 (20.8)	62.0	18.7	16.3	2.9
55–64	2420 (26.5)	45.5	25.2	24.1	5.2
≥ 65	2754 (30.1)	26.0	28.5	33.4	12.1
Sex					
Male	4310 (47.1)	48.9	22.3	22.3	6.5
Female	4839 (52.9)	53.8	20.4	20.8	5.1
Race					
White	6773 (88.0)	51.4	20.7	22.1	5.8
Black	606 (7.9)	34.0	30.5	27.4	8.1
Other	321 (4.2)	54.2	18.4	23.1	4.4
ASA class					
1 or 2	2757 (30.1)	71.7	13.5	13.7	1.1
3	5321 (58.2)	45.4	24.9	23.6	6.1
≥ 4	1027 (11.2)	28.7	23.4	31.6	16.3
BMI					
Normal	2775 (31.3)	61.1	15.9	17.5	5.5
Overweight	3079 (34.7)	52.5	21.8	21.0	4.7
Obese	3020 (34.0)	41.3	25.7	26.2	6.9
Tobacco use					
No	7338 (80.2)	51.4	21.2	22.0	5.4
Yes	1811 (19.8)	51.7	21.6	19.3	7.3
Bleeding disorders					
No	8903 (97.3)	52.2	21.0	21.4	5.4
Yes	246 (2.7)	26.8	30.9	25.6	16.7
Functional status					
Independent	8331 (91.1)	56.3	20.1	20.4	3.2
Partially dependent	656 (7.2)	0.0	36.7	32.3	30.9
Totally dependent	118 (1.3)	0.0	24.6	37.3	38.1
Preop hemiplegia					
No	4002 (90.3)	50.8	43.0	4.8	1.4
Yes	428 (9.7)	25.9	52.8	13.3	7.9
Preop ventilator dependence					
No	9048 (98.9)	51.8	21.3	21.4	5.6

Table 2 (continued)

	Frequency	No frailty (mFI = 0)	Low frailty (mFI = 0.01–0.19)	Intermediate frailty (mFI = 0.2–0.29)	High frailty (mFI ≥ 0.3)
	n (%)	Row %	Row %	Row %	Row %
Yes	101 (1.1)	25.7	23.8	32.7	17.8
Preop sepsis					
No	8723 (95.3)	52.3	20.9	21.4	5.5
Yes	426 (4.7)	35.4	29.3	24.4	10.8
Preop albumin					
< 3.5	811 (18.4)	34.4	23.3	27.0	15.3
≥ 3.5	3595 (81.6)	51.0	20.9	22.8	5.2
Preop weight loss					
No	8910 (97.4)	51.8	21.2	21.4	5.5
Yes	239 (2.6)	38.1	22.6	23.4	15.9
Preop transfusion					
No	9121 (99.7)	51.5	21.3	21.5	5.7
Yes	28 (0.3)	28.6	14.3	25.0	32.1
Preop corticosteroid use					
No	7540 (82.4)	52.7	20.7	21.4	5.2
Yes	1609 (17.6)	45.6	23.9	22.2	8.3
Chemotherapy in past month					
No	4214 (46.1)	48.4	43.9	5.6	2.1
Yes	4935 (53.9)	54.1	2.0	35.0	8.9
Radiotherapy in past 90 days					
No	4310 (47.1)	48.8	43.7	5.5	2.0
Yes	4839 (52.9)	53.9	1.3	35.7	9.1
Emergency case					
No	8679 (94.9)	51.6	21.2	21.6	5.6
Yes	470 (5.1)	48.5	23.0	20.4	8.1
Anesthesia time (mins)					
< 240	1723 (36.1)	47.8	38.6	9.9	3.7
≥ 240	3044 (63.9)	49.4	41.5	7.1	2.0
Operation time (mins)					
< 180	4629 (50.6)	48.7	20.9	23.3	7.1
≥ 180	4520 (49.4)	54.3	21.6	19.7	4.4

BMI body mass index, *ASA* American Society of Anesthesiologists

where there were small numbers of cases (i.e. mortality rates among benign tumors and most outcomes for transsphenoidal surgery).

The rate of severe neurologic complications was notably higher (15.8%) in the low frailty group than in those with intermediate or high frailty (5.6 and 12.4%, respectively). This inconsistency contributed to a similar trend in the rate of any complication, which was 24.9% in the low frailty group compared to 18.6% in the intermediate frailty group (although rates of any complication remained highest among the high frailty group at 32.9%).

In the multivariable models (Fig. 2; Table 3), increasing levels of frailty were consistently associated with stepwise increased odds of all adverse outcomes including severe neurologic complications and any complications. Of all adverse outcomes, frailty was most strongly predictive of severe neurologic complications. Compared to patients with no frailty, patients with low frailty (OR 2.005, 95% CI 1.608–2.500), intermediate frailty (OR 3.116, 95% CI 2.304–4.213), and high frailty (OR 5.826, 95% CI 3.983–8.522) were at increased risk of severe neurologic complications. Table S3 represents a sensitivity analysis showing the results of a multivariable model including only those patients for whom all 11 mFI variables were coded (n = 4419).

Table 3 also demonstrates the comparative predictive ability of frailty, ASA class, and age in the multivariable models of adverse outcomes. Increasing ASA class also reliably predicted stepwise increases of all adverse outcomes. Frailty and ASA class had similar predictive ability for mortality (*c*-statistics 0.673 vs. 0.704), any complication

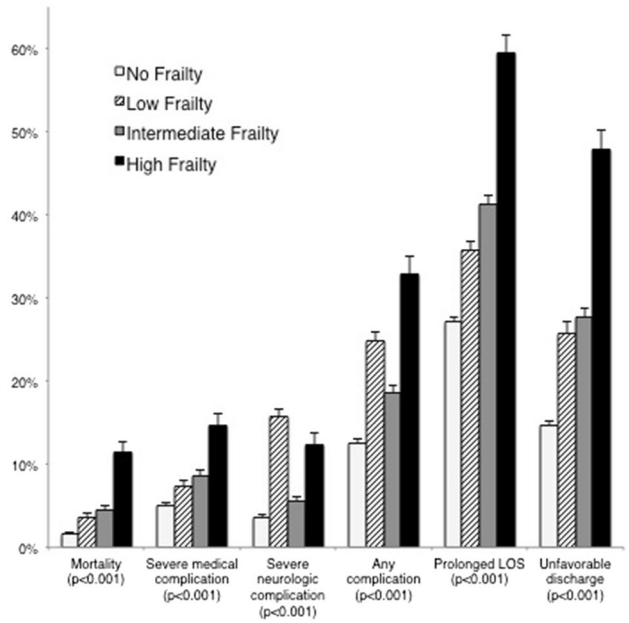

Fig. 1 Rate of adverse events by level of frailty. Error bars represent standard error of proportion. P-values represent global Chi square tests of proportions comparing the rates of adverse events between levels of frailty. *LOS* length of stay

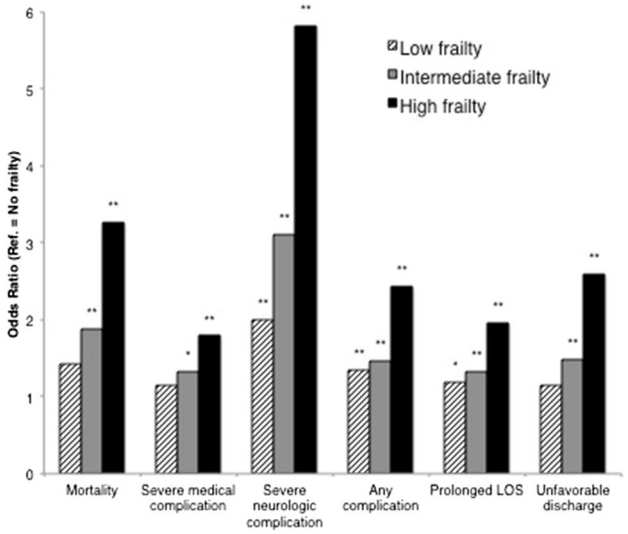

Fig. 2 Frailty as an independent predictor of outcomes in multivariable logistic regression models. Six multivariable models were constructed. Odds ratios reflect the odds of adverse events at each level of frailty with no frailty (mFI = 0) as the reference adjusted for all other predictors in the full models including age, ASA score, surgery category (supratentorial brain, supratentorial dural, infratentorial, or transsphenoidal), pathology category (primary brain malignant, primary brain benign, primary dural malignant, primary dural benign, primary cranial nerve, and secondary malignant), the risk indices being compared (age, ASA class, and mFI level), and other variables not included in the modified frailty index (sex, race, BMI), tobacco use, bleeding disorders, hemiplegia, ventilator dependence, sepsis, albumin level, weight loss, transfusion, corticosteroid use, chemotherapy in the past month, radiotherapy in the past 90 days, and emergency status of the case). *p < 0.05, **p < 0.001, *LOS* length of stay

(0.610 vs. 0.606), prolonged LOS (0.595 vs. 0.620), and unfavorable discharge (0.630 vs. 0.628). Frailty had greater predictive ability than ASA score for severe neurologic complications (0.681 vs. 0.609) whereas it was less predictive of severe medical complications (0.589 vs. 0.629). Both frailty and ASA class had greater predictive ability than age for all models. In fact, after adjustment for other risk factors in the models, only age ≥ 65 was reliably associated with increased odds of most adverse outcomes and the effect sizes (as measured by OR) were relatively small compared to those of ASA class and frailty. All models had improved predictive ability with the combination of frailty, ASA class, and age in the models.

Discussion

Our findings suggest that the modified frailty index, abstracted from routinely collected medical record data, is associated with adverse outcomes in a wide variety of patients undergoing resection of intracranial neoplasms. Incrementally higher levels of frailty independently predicted mortality, severe medical complications, severe neurologic complications, prolonged LOS, and unfavorable discharge. This relationship held true across multiple types of surgery and pathology and regardless of whether or not patients with missing (not coded) variables were included. The index improves the ability to predict adverse outcomes beyond existing preoperative risk indices in NSQIP but predictive ability is greatest when mFI, ASA class, and age are all included.

Surgeons routinely consider and report the surgical morbidity associated with various tumor pathologies, locations, and radiographic features. However, the ability to quantify the added risk that age, functional status, and multiple comorbidities contribute to a full episode of care remains limited and in practice is often a subjective process [4]. While most population-based studies suggest that advanced age increases postoperative risk, [21] single institution studies demonstrate that some elderly patients can tolerate surgery well [22, 23]. Many comorbidities have been associated with additional perioperative risk [4, 24] but it is not clear which ones are most important in the oncologic neurosurgery population and how best for surgeons to incorporate numerous potential risk factors into their preoperative risk assessment. There is reason to suspect that outcomes in neurosurgical oncology patients may also be more heavily dependent on preoperative functional status than in other surgical populations. Preoperative neurological deficits are associated with increased risk of adverse outcomes [4, 15]

Table 3 Select predictors from multivariable logistic regression models evaluating outcomes after oncologic neurosurgery

	OR	95% CI	p-value	*c*-statistic
Mortality[a]				
Frailty				0.673
None	Ref			
Low	1.435	(0.973–2.118)	0.069	
Intermediate	1.876	(1.321–2.664)	< 0.001	
High	3.262	(2.167–4.912)	< 0.001	
ASA score				0.704
1–2	Ref			
3	2.350	(1.452–3.804)	< 0.001	
≥ 4	5.509	(3.286–9.236)	< 0.001	
Age				0.645
< 45	Ref			
45–54	1.196	(0.701–2.039)	0.511	
55–64	1.636	(1.006–2.659)	0.047	
≥ 65	2.019	(1.249–3.264)	0.004	
Combined[b]				0.770
Full model[c]				0.810
Severe medical complication[a]				
Frailty				0.589
None	Ref			
Low	1.141	(0.883–1.476)	0.313	
Intermediate	1.329	(1.049–1.682)	0.018	
High	1.792	(1.301–2.469)	< 0.001	
ASA score				0.629
1–2	Ref			
3	1.609	(1.263–2.049)	< 0.001	
≥ 4	3.205	(2.381–4.315)	< 0.001	
Age				0.578
< 45	Ref			
45–54	1.191	(0.898–1.580)	0.2247	
55–64	0.886	(0.667–1.176)	0.4018	
≥ 65	1.312	(0.997–1.726)	0.0525	
Combined[b]				0.661
Full model[c]				0.690
Severe neurologic complication[a]				
Frailty				0.681
None	Ref			
Low	2.005	(1.608–2.500)	< 0.001	
Intermediate	3.116	(2.304–4.213)	< 0.001	
High	5.826	(3.983–8.522)	< 0.001	
ASA score				0.609
1–2	Ref			
3	1.561	(1.219–1.999)	< 0.001	
≥ 4	1.963	(1.424–2.705)	< 0.001	
Age				0.586
< 45	Ref			
45–54	1.032	(0.757–1.408)	0.8417	
55–64	1.304	(0.977–1.740)	0.0717	
≥ 65	1.216	(0.906–1.632)	0.1919	
Combined[b]				0.714
Full model[c]				0.813
Any complication[a]				
Frailty				0.610
None	Ref			
Low	1.350	(1.150–1.584)	< 0.001	
Intermediate	1.461	(1.235–1.728)	< 0.001	
High	2.433	(1.928–3.070)	< 0.001	
ASA Score				0.606
1–2	Ref			
3	1.497	(1.286–1.741)	< 0.001	
≥ 4	2.252	(1.834–2.766)	< 0.001	
Age				0.582
< 45	Ref			
45–54	1.050	(0.866–1.272)	0.6186	
55–64	1.150	(0.958–1.382)	0.1346	
≥ 65	1.431	(1.192–1.720)	< 0.001	
Combined[b]				0.654
Full model[c]				0.689
Prolonged LOS[a]				
Frailty				0.595
None	Ref			
Low	1.196	(1.030–1.388)	0.0188	
Intermediate	1.325	(1.157–1.518)	< 0.001	
High	1.959	(1.570–2.446)	< 0.001	
ASA score				0.620
1–2	Ref			
3	1.530	(1.356–1.726)	< 0.001	
≥ 4	2.158	(1.799–2.589)	< 0.001	
Age				0.582
< 45	Ref			
45–54	0.830	(0.710–0.969)	0.019	
55–64	0.970	(0.836–1.126)	0.690	
≥ 65	1.212	(1.041–1.412)	0.013	
Combined[b]				0.656
Full model[c]				0.752
Unfavorable discharge[a]				
Frailty				0.630
None	Ref			
Low	1.151	(0.937–1.414)	0.180	
Intermediate	1.493	(1.274–1.750)	< 0.001	
High	2.588	(2.039–3.285)	< 0.001	
ASA Score				0.628
1–2	Ref			
3	1.473	(1.244–1.745)	< 0.001	
≥ 4	2.328	(1.847–2.935)	< 0.001	
Age				0.648
< 45	Ref			
45–54	1.229	(0.973–1.554)	0.0839	
55–64	1.688	(1.357–2.099)	< 0.001	

Table 3 (continued)

	OR	95% CI	p-value	*c*-statistic
≥65	2.656	(2.136–3.302)	<0.001	
Combined[b]				0.699
Full model[c]				0.769

[a]N = 9105 for models of mortality, severe medical complications, severe neurologic complications, any complication, and prolonged LOS. 44 of 9149 patients were excluded due to missing data in ASA class. The model for unfavorable discharge included N = 6081 patients due to missing data in the outcome

[b]Combined preoperative indices include modified frailty index, age, and ASA class

[c]The full models included surgery category (supratentorial brain, supratentorial dural, infratentorial, or transsphenoidal), pathology category (primary brain malignant, primary brain benign, primary dural malignant, primary dural benign, primary cranial nerve, and secondary malignant), the risk indices being compared (age, ASA class, and mFI level), and other variables not included in the modified frailty index (sex, race, BMI, tobacco use, bleeding disorders, hemiplegia, ventilator dependence, sepsis, albumin level, weight loss, transfusion, corticosteroid use, chemotherapy in the past month, radiotherapy in the past 90 days, and emergency status of the case)

and poor baseline functional status may limit the ability to recover from new neurologic deficits [16]. The process of shared decision-making between surgeon and patient would benefit from a simplified tool that can take advantage of routinely collected clinical data to quantify the added risk of co-morbidities and functional status across a wide variety of oncologic neurosurgery patients.

Numerous preoperative risk assessment tools are available, but their usefulness may vary depending on the patient population, the surgical procedure under consideration, and the type of clinical data available [1, 2]. The Goldman Cardiac Risk Index [3] is widely used but is limited to predicting cardiac complications. There are several more comprehensive measures intended for use primarily on admission to an intensive care unit such as the Acute Physiology and Chronic Health Evaluation (APACHE-II), the Physiologic and Severity Score for the Enumeration of Mortality and Morbidity (POSSUM), and the Prognostic Nutritional Index, but these may be too cumbersome for routine preoperative evaluation and are not routinely available in registry data for validation in the neurosurgery population. The Elixhauser and Charlson/Deyo methods were developed to measure comorbidity in administrative claims data [25, 26] and do not easily translate to routine clinical use.

In oncologic neurosurgery practice, the most widely used preoperative risk assessment tools are Karnofsky Performance Score (KPS) and the ASA physical status classification system. KPS is widely used in oncology to classify patients into one of ten levels of functional impairment from disease. However, KPS may be more useful as an outcome measure than in risk assessment, where its reliability has been inconsistent [4, 27–29]. It has been criticized as subjective and unidimensional for its emphasis on functional status and failure to specific any particular co-morbidities [30]. It is not available in NSQIP's data and so comparison was beyond the scope of this study.

The ASA physical status classification system, one of the most widely used preoperative risk assessment tools, is a simple but subjective assessment that classifies patients into one of six levels of overall disease burden [1]. Similar to KPS, ASA is subjective, and does not specify comorbidities. In our study, frailty and ASA class had similar predictive ability for mortality, any complication, prolonged LOS, and unfavorable discharge. ASA had greater predictive ability for severe medical complications while mFI was more predictive of severe neurologic complications (coma or stroke with new deficit). The combination of ASA class and frailty substantially improved predictive ability for all outcomes, suggesting that both contribute additional information about risk.

The strong association between frailty and severe neurologic complications observed in our study warrants further attention. Prior population level neurosurgical studies have mirrored work in other fields and confirmed the ability of preoperative risk scores to predict postoperative medical complications and mortality, [4, 31, 32] treating neurosurgery patients as any other candidates for surgery. Given the relationship between neurologic deficits and performance status, [4, 15, 16] we anticipated our finding that the mFI, which takes into account functional status, would have greater predictive ability for neurologic outcomes. Frailty predicted neurologic deficits reliably after adjustment for surgery type and pathology category, suggesting it is a useful predictor of neurologic deficit for a wide range of oncologic neurosurgery patients. Of note, in the univariate analyses, low frailty patients were more likely to have severe postoperative neurologic complications than intermediate or high frailty patients. This risk may reflect higher rates of preoperative partial dependence and hemiplegia in the low frailty group (Table 2) compared to the intermediate and high frailty groups, suggesting surgeons were less apt to operate on patients with deficits if they were also medically ill. By mFI definition, patients with no frailty did not have impaired preoperative functional status. There were also notably low rates of preoperative chemotherapy and radiation in the low frailty group, consistent with the notion that these were otherwise healthy patients with preoperative deficits or tumors with high associated risk of deficit in need of surgery without delay for neoadjuvant treatments. These confounders were corrected for in the multivariable model. In this context, the ability to quantify frailty and its associated risks may further assist surgeons in the process of selecting appropriate surgical candidates.

The ability to calculate a simple frailty index in clinical practice and use the same variables in a national registry gives the mFI added value. Surgeons can easily calculate a risk assessment score in the clinical setting and those same variables can later be derived from registry data creating transparency and predictability in risk adjustment outcomes methodology. The persistence of the mFI's predictive ability in the presence of missing data adds to its practical utility. Findings in NSQIP are likely to be applicable to neurosurgery's national registry, the Quality Outcomes Database (QOD, formerly N^2QOD), [33] in the future. Both registries rely on similar methods of chart abstraction from routinely collected clinical data. The QOD may have the added benefit of capturing additional disease-specific variables relevant to risk prediction in neurosurgery. Ultimately, risk calculators that draw on large national cohorts and factor in numerous variables to provide patient-specific risk assessments will be useful but there remains a need for simple, widely applicable indices for the foreseeable future.

Limitations

We recognize several important limitations to our findings. First, as we have previously discussed, there are several limitations to NSQIP data in general [12]. Although NSQIP ensures that data abstractors are trained and employs methods of data validation, there remains the potential for bias in the record keeping and abstraction processes. While NSQIP captures patients from a large number of hospitals, the centers that participate may not be representative of all hospitals and patients undergoing surgery in the United States. Second, our study was conducted retrospectively, using data not specifically intended or validated for the measurement of frailty. The mFI is unable to measure specific phenotypes of frailty, such as weakness and decreased physical activity that have been captured in prospective studies validating frailty [11]. In NSQIP, abstractors can code a patient's functional status as independent, partially dependent, totally dependent, or unknown. These and other categorical variables, such as altered sensorium, may be subjective and do not capture more granular information about level of function. Fourth, while we have demonstrated an association between mFI and adverse outcomes in chart abstracted data it is not clear how use of the index would translate in routine clinical practice. Our sensitivity analysis suggests that the mFI predicts adverse outcomes whether or not patients with missing data are included in the cohort, however, the magnitude of the relationships may vary and predictive ability may suffer at the individual level. Measures that rely on the retrospective process of chart abstraction may be more useful for risk adjustment in quality measurement schemes than for Bayesian inference in individual cases of shared decision-making. Prospective validation would be needed. Finally, the scope of our study was limited to the prediction of 30-day adverse events. While this is an improvement over the discharge level data presented in many multi-center database studies, these near-term risks would nonetheless need to be weighed against the potential short and long-term benefits of achieving the surgical aims.

Conclusions

The mFI is a composite score of comorbidity and functional impairment that can be abstracted from routine medical record data. The mFI predicts adverse outcomes in a wide variety of neurosurgical oncology patients. Increased mFI was independently associated with increased mortality, severe medical and neurologic complications, increased LOS, and unfavorable discharge after adjusting for surgery and tumor type, age, ASA class, and other available variables. It improves the ability to predict adverse outcomes beyond age and ASA class and was the most reliable predictor of severe neurologic complications. Predictive ability is greatest when mFI, ASA class, and age, are combined. A frailty score, perhaps in combination with other risk factors, has potential use in preoperative shared decision-making and perioperative management. Frailty can also be calculated from registry data and may therefore have a complementary role in risk adjusted outcomes measurement. Further validation is needed in prospective studies and with variables more specific to neurosurgical oncology patients.

Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

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