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A comparative analysis of the Hospital Frailty Risk Score in predicting postoperative outcomes among intracranial tumor patients

Adrian E. Jimenez, BS,[1] Jiaqi Liu, BS,[2] Kyle V. Cicalese, BS, BA,[3] Miguel A. Jimenez, BS,[4] Jose L. Porras, MD,[1] Tej D. Azad, MD, MS,[1] Christopher Jackson, MD,[1] Gary L. Gallia, MD, PhD,[1] Chetan Bettegowda, MD, PhD,[1] Jon Weingart, MD,[1] and Debraj Mukherjee, MD, MPH[1]

[1]Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland; [2]Georgetown University School of Medicine, Washington, DC; [3]Virginia Commonwealth University School of Medicine, Richmond, Virginia; and [4]The University of Chicago Pritzker School of Medicine, Chicago, Illinois

OBJECTIVE In recent years, frailty indices such as the 11- and 5-factor modified frailty indices (mFI-11 and mFI-5), American Society of Anesthesiologists (ASA) physical status classification, and Charlson Comorbidity Index (CCI) have been shown to be effective predictors of various postoperative outcomes in neurosurgical patients. The Hospital Frailty Risk Score (HFRS) is a well-validated tool for assessing frailty; however, its utility has not been evaluated in intracranial tumor surgery. In the present study, the authors investigated the accuracy of the HFRS in predicting outcomes following intracranial tumor resection and compared its utility to those of other validated frailty indices.

METHODS A retrospective analysis was conducted using an intracranial tumor patient database at a single institution. Patients eligible for study inclusion were those who had undergone resection for an intracranial tumor between January 1, 2017, and December 31, 2019. ICD-10 codes were used to identify HFRS components and subsequently calculate risk scores. In addition to several postoperative variables, ASA class, CCI, and mFI-11 and mFI-5 scores were determined for each patient. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUROC), and the DeLong test was used to assess for significant differences between AUROCs. Multivariate models for continuous outcomes were constructed using linear regression, whereas logistic regression models were used for categorical outcomes.

RESULTS A total of 2518 intracranial tumor patients (mean age 55.3 ± 15.1 years, 53.4% female, 70.4% White) were included in this study. The HFRS had a statistically significant greater AUROC than ASA status, CCI, mFI-11, and mFI-5 for postoperative complications, high hospital charges, nonroutine discharge, and 90-day readmission. In the multivariate analysis, the HFRS was significantly and independently associated with postoperative complications (OR 1.14, $p < 0.0001$), hospital length of stay (coefficient = 0.50, $p < 0.0001$), high hospital charges (coefficient = 1917.49, $p < 0.0001$), nonroutine discharge (OR 1.14, $p < 0.0001$), and 90-day readmission (OR 1.06, $p < 0.0001$).

CONCLUSIONS The study findings suggest that the HFRS is an effective predictor of postoperative outcomes in intracranial tumor patients and more effectively predicts adverse outcomes than other frailty indices. The HFRS may serve as an important tool for reducing patient morbidity and mortality in intracranial tumor surgery.

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KEYWORDS frailty; neuro-oncology; outcomes; tumor

Despite advances in chemotherapy, immunotherapy, and radiation, resection remains the first-line treatment for most types of brain tumor.[1] While improvements in technology and surgical techniques have greatly enhanced the safety and clinical efficacy of these procedures, certain demographic and clinical characteristics have been shown to negatively impact the postoperative course of patients undergoing these treatments.[2–6] Thus, it is important for clinicians to investigate evidenced-based prognosticators of adverse outcomes in order to develop individualized care plans for patients.

In recent years, there has been increasing interest in

ABBREVIATIONS ASA = American Society of Anesthesiologists; AUROC = area under the receiver operating characteristic curve; CCI = Charlson Comorbidity Index; DVT = deep vein thrombosis; HFRS = Hospital Frailty Risk Score; LOS = length of stay; mFI-5 = 5-factor modified frailty index; mFI-11 = 11-factor modified frailty index; PE = pulmonary embolism.

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using quantitative frailty indices to predict surgical outcomes and assist with clinical decision-making.[7] Frailty indices such as the 11- and 5-factor modified frailty indices (mFI-11 and mFI-5) have demonstrated effectiveness in predicting adverse outcomes such as complications, mortality, and length of stay (LOS) in a variety of medical fields including neurosurgery.[7–11] In addition to frailty indices, scores quantifying baseline health status such as the American Society of Anesthesiologists (ASA) physical status classification and indices quantifying the medical comorbidity burden such as the Charlson Comorbidity Index (CCI) are also utilized in preoperative patient risk assessment.[12–14]

Developed by Gilbert et al. in 2018, the Hospital Frailty Risk Score (HFRS) is a novel index that quantifies frailty using ICD-10 codes.[15] Given that the HFRS can be calculated using only ICD-10 codes, the index is a promising tool for efficiently quantifying patient frailty in administrative data sets, thereby streamlining research efforts aimed at optimizing preoperative patient stratification.[16] The HFRS has been shown to accurately predict outcomes such as hospital LOS, nonroutine discharge, mortality, readmission, functional impairment, and hospital costs in a number of patient populations including arthroplasty, spine surgery, and vascular surgery cohorts.[16–18] However, a number of studies have stated that the HFRS may not identify some frail patients relative to other indices, and research has also suggested the HFRS may not accurately predict hospital readmission in elderly patient populations.[19–21] Further, the utility of the HFRS in predicting postoperative outcomes among intracranial tumor patients, as well as its performance relative to other frailty indices in this specific patient population, has not yet been established. Therefore, in this study we aimed to investigate the performance of the HFRS in prognosticating surgical outcomes among intracranial tumor patients while comparing its utility to other well-known metrics like the ASA physical status classification, CCI, mFI-5, and mFI-11. Validating the utility of the HFRS in intracranial tumor patients may provide neurosurgeons with an additional tool for optimizing clinical decision-making to reduce patient morbidity and mortality.

Methods

Patient Selection and Recorded Variables

We utilized demographic and clinical data from 2518 patients who had undergone resection for an intracranial tumor at a single institution between January 1, 2017, and December 31, 2019. Study data consisted entirely of retrospective patient data, which were obtained primarily through automated data retrieval from the Core for Clinical Research Data Acquisition (supported in part by the Johns Hopkins Institute for Clinical and Translational Research) using ICD-10 codes associated with patient electronic medical records. Retrieval of these data points was followed by a manual chart review by study investigators to verify accuracy. Brain tumor diagnoses were confirmed via manual chart review. The Johns Hopkins School of Public Health Institutional Review Board, acting as a Health Insurance Portability and Accountability Act Privacy Board, reviewed and approved the waiver of informed consent for this retrospective study.

For this study, ICD-10 codes were used to determine the HFRSs in our data set, as described by Gilbert et al.[15] Supplementary Table 1 describes the HFRS components and corresponding ICD-10 codes, along with their respective weights and the number of patients in our cohort with each component present. In line with the original study by Gilbert et al., patients were stratified into three groups based on their HFRS, with the low-frailty-risk cohort having scores < 5, the intermediate-risk cohort having scores of 5–15, and the high-risk cohort having scores > 15.[15]

The demographic and clinical data collected for each patient included the following variables: age, sex, race, ethnicity, marital status, insurance, intracranial tumor diagnosis, surgery number (i.e., first, second, or third/fourth surgery), ASA physical status classification, mFI score, hospital LOS, postoperative complications, discharge disposition, hospital charges (in $US 2019, when the financial data were collected), 90-day readmission status, and 90-day mortality. Patients were categorized as one of the four following races: White/Caucasian, Black/African American, Asian, or other. Ethnicity was recorded as either Hispanic/Latino or not Hispanic/Latino, and patient marital status was noted as married or not married. Insurance status consisted of the following three categories: private, Medicare, and Medicaid. We analyzed patients with the following intracranial tumor diagnoses: metastatic brain tumor, high-grade glioma, low-grade glioma, vestibular schwannoma, meningioma, pituitary tumor, or other tumor type. ASA classes ranged from 1 to 6 (in increments of 1), describing patients with localized disease that did not cause systemic disturbance (1) to patients with extreme systemic disorders and a poor physical state (6).[22] CCI scores were based on a 1- to 6-point scale and incorporated weighted indices of 19 separate, predefined comorbid conditions whereby certain conditions contributed to the overall composite risk score more than others (e.g., an AIDS diagnosis counted as 6 points, whereas dementia counted as 1 point), with a minimum score of 0 and a maximum score 37.[10,23] The mFI score was quantified using both the mFI-11 and mFI-5 whereby a patient received 1 point for the presence of each one of 11 or 5 various predefined comorbidities, respectively, as described previously.[24] The mFI-5, an abbreviated version of the mFI-11, incorporates the following conditions: history of diabetes, history of chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medication, and limited functional status requiring assistance with activities of daily living.[24] Total mFI-11 and mFI-5 scores ranging from 0 to 11 and 0 to 5 points, respectively, were then calculated.

Postoperative complications were defined in line with prior studies and included the following specific complications: pulmonary embolism (PE) or deep vein thrombosis (DVT), physiological or metabolic derangement, respiratory failure, or sepsis.[25] These were identified and noted during chart review based on their corresponding ICD-10 codes. Routine discharge disposition was defined as discharge to home (with either self-care or healthcare service assistance), and nonroutine discharge was defined as dis-

charge to a rehabilitation facility, skilled nursing facility, or hospice facility, as established by the prior literature.[26] Financial data used to calculate total hospital charges incurred by each patient were provided by our institution's Center for Clinical Data Analysis. Ninety-day readmission was defined as readmission to a hospital within 90 days of hospital discharge, and 90-day mortality was defined as death within 90 days of surgery.

Statistical Analysis

Data were collected using Microsoft Excel version 2016 (Microsoft Corp.) and analyzed using R statistical software version 4.0.2 (R Foundation for Statistical Computing). The Shapiro-Wilk test was used to test for normality. The Mann-Whitney U-test was used to determine nonrandom association of continuous variables (due to violation of the normality assumption), and Fisher's exact test was used to determine nonrandom association of categorical variables. Spearman's correlation coefficient was used to quantify the association between the HFRS and other frailty indices, and a test for association/correlation between paired samples was used to determine whether these associations attained statistical significance. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUROC), and the DeLong test was used to assess for significant differences between AUROCs. The R package pROC was used for ROC curve analysis and for determining optimal thresholds via maximization of Youden's J-statistic in order to calculate the sensitivity, specificity, positive predictive value, and negative predictive value of each frailty index (Supplementary Tables 2–6). To facilitate ROC curve analysis when comparing frailty indices, LOS and hospital charges were dichotomized at their respective 75th percentiles and analyzed as binary outcome variables, in line with prior studies.[27,28] Spiegelhalter's z-test was also used to assess for adequate calibration of the bivariate frailty models during comparative analysis, with $p < 0.05$ indicating inadequate calibration.[29] The R package rms was used to perform the Spiegelhalter z-test. The CalibrationCurves package was used to construct calibration curves and associated 95% confidence intervals for the frailty indices and each postoperative outcome. Multivariate models for continuous outcomes were constructed using linear regression, whereas logistic regression models were used for the multivariate analysis of categorical outcomes.

Results

Patient Demographics and Outcomes

Table 1 presents the demographic and clinical characteristics of the 2518 intracranial tumor patients in our cohort. The mean age of our cohort was 55.27 ± 15.14 years, and ages ranged from 18.35 to 90.84 years. Most of the patients were female (53.4%), White (70.4%), married (65.8%), and had private insurance (65.0%). The three most common tumor diagnoses were meningioma (24.5%), high-grade glioma (20.5%), and pituitary tumor (14.4%). Most patients (90.2%) were undergoing their first intracranial tumor resection, 210 patients (8.3%) their second surgery, and 37 patients (1.5%) their third or fourth surgery. The mean (± standard deviation) ASA class and CCI in our cohort were 2.64 ± 0.58 and 2.78 ± 2.08, respectively. The mean mFI-11 and mFI-5 scores were 0.97 ± 1.10 and 0.76 ± 0.82, respectively, whereas the mean HFRS was 4.94 ± 5.02.

The patients in our cohort had a mean hospital LOS of 5.49 ± 6.94 days. The majority of our patients (90.7%) did not experience postoperative complications, but the most common complications noted were PE or DVT in 6.6% of patients. The majority of our patients (84.0%) also had a routine discharge. The mean value of hospital charges was $44,364.49 ± $32,243.39. Finally, a total of 282 patients (11.2%) were readmitted to the hospital within 90 days of discharge, whereas 79 patients (3.1%) died within 90 days of surgery.

Comparative Analysis of Frailty Indices

Table 2 displays Spearman correlation coefficients (r_s) and significance test p values comparing the HFRS and other frailty indices. The HFRS had statistically significant, positive correlations with ASA ($r_s = 0.23$, $p < 0.0001$), CCI ($r_s = 0.45$, $p < 0.0001$), mFI-11 ($r_s = 0.43$, $p < 0.0001$), and mFI-5 ($r_s = 0.32$, $p < 0.0001$). Table 3 presents AUROC comparisons between the HFRS and other frailty indices. The HFRS had a statistically significantly greater AUROC than ASA class, CCI, mFI-11, and mFI-5 for postoperative complications, high hospital charges, nonroutine discharge, and 90-day readmission. Additionally, the HFRS had a statistically significantly greater AUROC than ASA class, CCI, and mFI-5 for prolonged hospital LOS. There were no statistically significant differences between the HFRS AUROC and the AUROCs for any other frailty index in predicting 90-day mortality. ROC curve plots for the HFRS and other frailty indices predicting postoperative outcomes are depicted in Fig. 1. All 30 models demonstrated adequate calibration via Spiegelhalter's z-test ($p > 0.05$), and calibration curves were created for the HFRS (Fig. 2) as well as for ASA class, CCI, mFI-11, and mFI-5 (Supplementary Figs. 1–4).

HFRS Subset Analysis

Table 4 presents the results of a subset analysis comparing intracranial tumor patients with a low HFRS risk to those with intermediate and high HFRS risks. When comparing intermediate- and low-frailty-risk cohorts, the former was significantly older ($p < 0.0001$), less likely to be Asian (OR 0.65, $p = 0.031$), more likely to be unmarried (OR 1.33, $p = 0.0021$), more likely to have Medicare (OR 2.26, $p < 0.0001$) or Medicaid (OR 1.64, $p = 0.0064$), and less likely to have a diagnosis of vestibular schwannoma (OR 0.61, $p = 0.011$), meningioma (OR 0.48, $p < 0.0001$), pituitary tumor (OR 0.53, $p < 0.0001$), low-grade glioma (OR 0.52, $p < 0.001$), or other intracranial tumor (OR 0.51, $p < 0.001$). Intermediate-risk patients were significantly more likely than low-risk patients to be undergoing their third or fourth intracranial tumor surgery (OR 2.32, $p = 0.018$). Furthermore, intermediate-risk patients were more likely to experience a prolonged hospital LOS ($p < 0.0001$), postoperative complications (OR 4.13, $p < 0.0001$), nonroutine discharge (OR 3.35, $p < 0.0001$), higher hospital

TABLE 1. Demographics, clinical characteristics, and outcomes in a cohort of 2518 surgical intracranial tumor patients

Characteristic	Value
Mean age in yrs	55.27 ± 15.14
Sex	
Male	1173 (46.6)
Female	1345 (53.4)
Race	
White/Caucasian	1772 (70.4)
Black/African American	419 (16.6)
Asian	147 (5.8)
Other	180 (7.1)
Marital status	
Married	1656 (65.8)
Not married	862 (34.2)
Insurance	
Private	1636 (65.0)
Medicare	715 (28.4)
Medicaid	167 (6.6)
Diagnosis	
Meningioma	616 (24.5)
High-grade glioma	515 (20.5)
Pituitary tumor	362 (14.4)
Metastatic brain tumor	346 (13.7)
Other	258 (10.2)
Low-grade glioma	226 (9.0)
Vestibular schwannoma	195 (7.7)
Surgery no.	
1st	2271 (90.2)
2nd	210 (8.3)
3rd or 4th	37 (1.5)
Mean ASA class	2.64 ± 0.58
Mean CCI	2.78 ± 2.08
Mean mFI-11 score	0.97 ± 1.10
Mean mFI-5 score	0.76 ± 0.82
Mean HFRS	4.94 ± 5.02
Mean hospital LOS in days	5.49 ± 6.94
Postop complication	
Yes	235 (9.3)
No	2283 (90.7)
Specific complications	
PE or DVT	166 (6.6)
Physiological or metabolic derangement	20 (0.8)
Respiratory failure	34 (1.4)
Sepsis	38 (1.5)
Discharge disposition	
Routine	2116 (84.0)
Nonroutine	402 (16.0)
Mean hospital charges in $US	44,364.49 ± 32,243.39
90-day readmission	
Yes	282 (11.2)
No	2236 (88.8)
90-day mortality	
Yes	79 (3.1)
No	2439 (96.9)

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TABLE 1. Demographics, clinical characteristics, and outcomes in a cohort of 2518 surgical intracranial tumor patients

Values are expressed as the mean ± standard deviation or number (%).

charges ($p < 0.0001$), 90-day readmission (OR 2.06, $p < 0.0001$), and 90-day mortality (OR 2.88, $p < 0.0001$) than were the low-risk patients. When comparing high- and low-HFRS-risk cohorts, the former was significantly older ($p < 0.0001$), more likely to be Black/African American (OR 1.85, $p = 0.0060$), more likely to be unmarried (OR 1.60, $p = 0.014$), more likely to have Medicare (OR 3.35, $p < 0.0001$) or Medicaid (OR 2.80, $p = 0.0030$), and less likely to be diagnosed with vestibular schwannoma (OR 0.17, $p < 0.001$), meningioma (OR 0.48, $p = 0.0058$), pituitary tumor (OR 0.087, $p < 0.0001$), low-grade glioma (OR 0.28, $p = 0.0012$), and other intracranial tumor (OR 0.31, $p = 0.0016$). High-frailty-risk patients were also significantly more likely to be undergoing their second tumor resection relative to low-risk patients (OR 1.91, $p = 0.025$). Finally, high-frailty-risk patients were also more likely to experience adverse postoperative outcomes such as prolonged hospital LOS ($p < 0.0001$), postoperative complications (OR 12.91, $p < 0.0001$), nonroutine discharge (OR 13.78, $p < 0.0001$), higher hospital charges ($p < 0.0001$), and 90-day readmission (OR 3.67, $p < 0.0001$) relative to low-frailty-risk patients.

Multivariate Analyses for Postoperative Outcomes

Table 5 presents the results of our multivariate analysis of the association between the HFRS and various postoperative outcomes when controlling for age, sex, race, marital status, insurance, tumor diagnosis, and surgery number. The HFRS remained significantly and independently associated with hospital LOS (coefficient = 0.50, $p < 0.0001$), postoperative complications (OR 1.14, $p < 0.0001$), nonroutine discharge (OR 1.14, $p < 0.0001$), high hospital charges (coefficient = 1917.49, $p < 0.0001$), and 90-day readmission (OR 1.06, $p < 0.0001$) in the multivariate analysis. There was no significant association between HFRS and 90-day mortality (OR 1.03, $p = 0.12$). Of note, a similar multivariate analysis of patient age and postoperative outcomes showed a significant and indepen-

TABLE 2. Comparative analysis of frailty indices

Statistic	ASA Status	CCI	mFI-11	mFI-5
r_s coefficient	0.23	0.45	0.43	0.32
p value*	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

* Reference is the HFRS. Boldface type indicates statistical significance.

TABLE 3. AUROC comparisons between the HFRS and other frailty indices

Outcome	HFRS AUROC	ASA		CCI		mFI-11		mFI-5	
		AUROC	p Value*	AUROC	p Value*	AUROC	p Value*	AUROC	p Value*
Prolonged LOS >6 days	0.68	0.61	**<0.0001**	0.62	**<0.0001**	0.65	0.051	0.64	**0.0046**
Postop complications	0.76	0.62	**<0.0001**	0.65	**<0.0001**	0.66	**<0.0001**	0.63	**<0.0001**
Nonroutine discharge disposition	0.72	0.62	**<0.0001**	0.68	**0.011**	0.67	**0.0018**	0.65	**<0.0001**
High hospital charges >$48,572.75	0.62	0.56	**<0.001**	0.52	**<0.0001**	0.59	**0.030**	0.58	**0.012**
90-day readmission	0.65	0.57	**<0.0001**	0.55	**<0.0001**	0.56	**<0.0001**	0.54	**<0.0001**
90-day mortality	0.65	0.64	0.75	0.67	0.51	0.63	0.51	0.60	0.21

* Reference is the HFRS AUROC. Boldface type indicates statistical significance.

dent association between age and hospital LOS (OR 0.04, $p < 0.0001$), nonroutine discharge (OR 1.04, $p < 0.0001$), and 90-day readmission (OR 1.06, $p = 0.01$).

Discussion

In the present study, we sought to quantify the effectiveness of the HFRS in predicting adverse outcomes for surgical intracranial tumor patients and to compare this metric to well-known health indices and frailty metrics, including the ASA classification, CCI, mFI-11, and mFI-5. Our comparative analysis demonstrated that the HFRS had significantly greater discriminative ability for predicting prolonged LOS, postoperative complications, nonroutine discharge disposition, high hospital charges, and 90-day readmission relative to these well-established health indices and frailty metrics. Additionally, when controlling for several demographic and clinical characteristics, the HFRS remained significantly and independently associated with hospital LOS (coefficient = 0.50, $p < 0.0001$), postoperative complications (OR 1.14, $p < 0.0001$), nonroutine discharge (OR 1.14, $p < 0.0001$), hospital charges (coefficient = 1917.49, $p < 0.0001$), and 90-day readmission (OR 1.06, $p < 0.0001$).

Prior Research

Recently, frailty emerged as an effective predictor of adverse outcomes in those undergoing surgery for intracranial tumor resection.[30–32] In a recent study, Torres-Perez et al. analyzed the clinical utility of frailty as a preoperative risk assessment tool in intracranial tumor patients by using several frailty instruments consisting of questionnaires based on frailty phenotype per the FRAIL scale, an acronymous metric that incorporates fatigue, resistance,

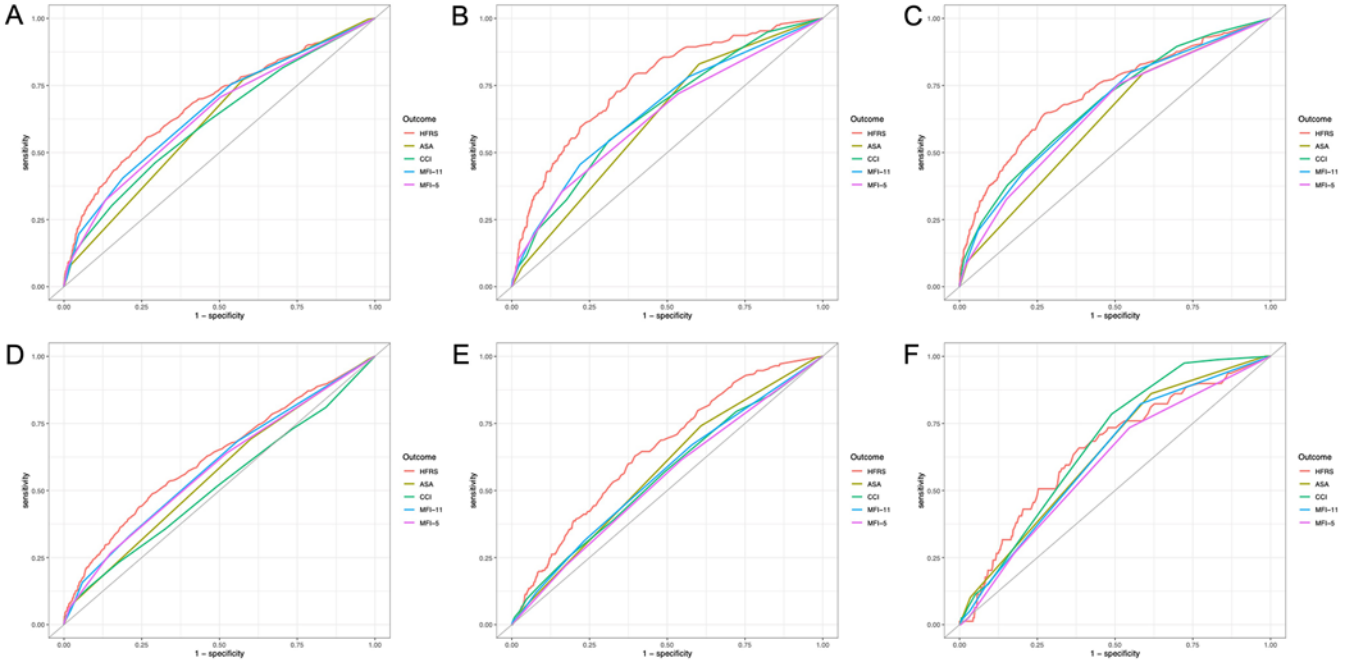

FIG. 1. Plots for the HFRS and other frailty indices demonstrate ROC curves for predicting a prolonged hospital LOS > 6 days (**A**), postoperative complications (**B**), discharge disposition (**C**), high hospital charges > $48,572.75 (**D**), 90-day readmission (**E**), and 90-day mortality (**F**). Figure is available in color online only.

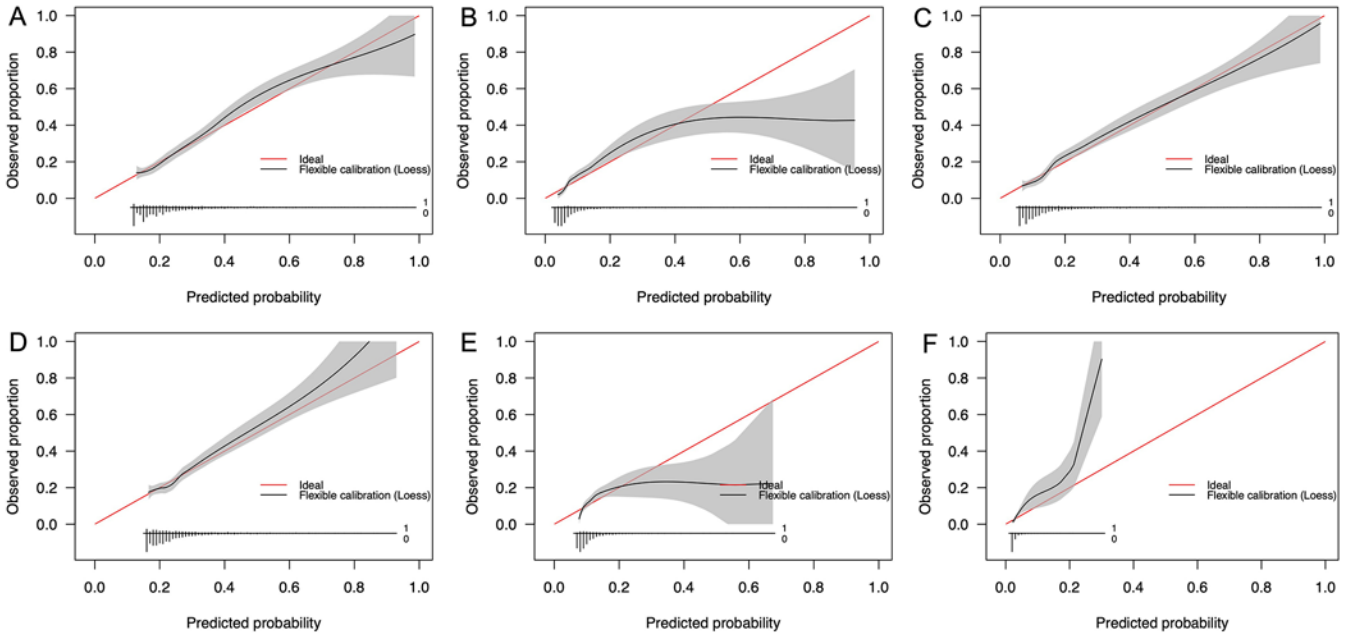

FIG. 2. Calibration curves and 95% confidence intervals for the HFRS and the postoperative outcomes of prolonged LOS > 6 days (**A**), postoperative complications (**B**), nonroutine discharge (**C**), high hospital charges > $48,572.75 (**D**), 90-day readmission (**E**), and 90-day mortality (**F**). Figure is available in color online only.

ambulation, illness, and loss of weight.[30] Additionally, patient frailty was evaluated through functional performance (gait speed) and a self-reported questionnaire that included variables related to the physical, cognitive, and psychosocial domains of frailty (Tilburg Frailty Indicator).[30] Patients preoperatively classified as frail or prefrail on the FRAIL scale became less autonomous according to routine functional performance scales, such as the Karnofsky Performance Status ($p = 0.037$) and Barthel Index ($p = 0.005$).[30] These findings highlight the link between frailty and postoperative complications and suggest that frailty-based preoperative stratification may be used to optimize patient outcomes.[30–32] Similarly, in a 2020 study, Harland and colleagues sought to determine whether frailty predicted neurosurgical complications via enhanced perioperative risk models among patients with intracranial tumors.[32] Utilizing a validated scale that assessed weakness, weight loss, exhaustion, low physical activity, and slowed walking speed, multivariate analysis revealed that preoperative frailty was associated with an increased risk of discharge to an acute rehabilitation center or skilled nursing facility instead of home ($p < 0.0001$), postoperative complications ($p = 0.035$), and a longer hospital stay ($p = 0.009$).[32]

In a 2020 study, Khalafallah and colleagues compared the utility of a recently developed, more streamlined mFI-5 to those of the CCI and the mFI-11 in predicting postoperative outcomes in intracranial tumor patients, with the results demonstrating that the adjusted mFI-5 model performed as well as the CCI and mFI-11.[10] Asemota and Gallia additionally examined the impact of frailty on the short-term outcomes of patients undergoing transsphenoidal pituitary surgery and found that the mortality rate was significantly higher among frail patients ($p < 0.001$).[33] Moreover, frail patients also demonstrated a greater likelihood of nonroutine discharges ($p < 0.001$), higher mean total charges ($p < 0.001$), and longer hospitalizations ($p < 0.001$).[33]

It has been well established that validated predictors of postsurgical outcomes among intracranial tumor patients may assist clinicians in determining treatment plans and counseling patients.[11,30–33] Recent studies have highlighted frailty as an important clinical entity and validated its utility as a preoperative risk assessment tool within neurosurgery. However, to our knowledge, the predictive utility of the HFRS and its comparative prognostic effectiveness relative to those of other frailty indices has not yet been investigated. Thus, we sought to be the first to investigate how the newly developed HFRS fares in predicting postsurgical outcomes among intracranial tumor patients and how it compares to the ASA classification, CCI, mFI-11, and mFI-5.

Present Study

Our analysis demonstrated that the HFRS may be more effective than other frailty indices in predicting postoperative outcomes within this patient population. AUROC comparisons between the HFRS and the other frailty indices demonstrated a significant difference in the predictive ability (as assessed by discrimination) of the HFRS tool compared with those of ASA classification, CCI, mFI-11, or mFI-5 (Table 3). These results demonstrated that the HFRS is more effective than the ASA system, CCI, mFI-11, and mFI-5 in predicting prolonged LOS, postoperative complications, discharge disposition, high hospital charges, and 90-day readmission in our sample

TABLE 4. Subset analysis of low-, intermediate-, and high-HFRS-risk cohorts of 2518 intracranial tumor patients

Characteristic	Low Frailty Risk (HFRS <5)	Intermediate Frailty Risk (HFRS 5–15)	p Value*	High Frailty Risk (HFRS >15)	p Value*
No. of patients	1595	796		127	
Mean age in yrs	53.56 ± 14.67	57.66 ± 15.60	**<0.0001**	61.79 ± 14.39	**<0.0001**
Sex					
Male	724 (45.4)	389 (48.9)	0.12	60 (47.2)	0.71
Female	871 (54.6)	407 (51.1)		67 (52.8)	
Race					
White/Caucasian	1128 (70.7)	561 (70.5)	Reference	83 (65.4)	Reference
Black/African American	242 (15.2)	144 (18.1)	0.14	33 (26.0)	**0.0060**
Asian	106 (6.6)	34 (4.3)	**0.031**	7 (5.5)	>0.99
Other	119 (7.5)	57 (7.2)	0.87	4 (3.1)	0.18
Marital status					
Married	1090 (68.3)	493 (61.9)		73 (57.5)	
Not married	505 (31.7)	303 (38.1)	**0.0021**	54 (42.5)	**0.014**
Insurance					
Private	1146 (71.8)	434 (54.5)	Reference	56 (44.1)	Reference
Medicare	354 (22.2)	303 (38.1)	**<0.0001**	58 (45.7)	**<0.0001**
Medicaid	95 (6.0)	59 (7.4)	**0.0064**	13 (10.2)	**0.0030**
Diagnosis					
Metastatic brain tumor	174 (10.9)	140 (17.6)	Reference	32 (25.2)	Reference
High-grade glioma	295 (18.5)	188 (23.6)	0.12	32 (25.2)	0.055
Vestibular schwannoma	128 (8.0)	63 (7.9)	**0.011**	4 (3.1)	**<0.001**
Meningioma	417 (26.1)	162 (20.4)	**<0.0001**	37 (29.1)	**0.0058**
Pituitary tumor	251 (15.7)	107 (13.4)	**<0.0001**	4 (3.1)	**<0.0001**
Low-grade glioma	154 (9.7)	64 (8.0)	**<0.001**	8 (6.3)	**0.0012**
Other	176 (11.0)	72 (9.0)	**<0.001**	10 (7.9)	**0.0016**
Surgery no.					
1st	1459 (91.5)	703 (88.3)	Reference	109 (85.8)	Reference
2nd	119 (7.5)	74 (9.3)	0.11	17 (13.4)	**0.025**
3rd or 4th	17 (1.1)	19 (2.4)	**0.018**	1 (0.8)	>0.99
Mean hospital LOS in days	4.25 ± 4.65	6.46 ± 6.25	**<0.0001**	15.07 ± 18.01	**<0.0001**
Postop complications					
Yes	67 (4.2)	122 (15.3)	**<0.0001**	46 (36.2)	**<0.0001**
No	1528 (95.8)	674 (84.7)		81 (63.8)	
Specific complications					
PE or DVT	56 (3.5)	79 (9.9)	—	31 (24.4)	—
Physiological or metabolic derangement	2 (0.1)	10 (1.3)	—	8 (6.3)	—
Respiratory failure	5 (0.3)	18 (2.3)	—	11 (8.7)	—
Sepsis	4 (0.3)	20 (2.5)	—	14 (11.0)	—
Discharge disposition					
Nonroutine	138 (8.7)	192 (24.1)	**<0.0001**	72 (56.7)	**<0.0001**
Routine	1457 (91.3)	604 (75.9)		55 (43.3)	
Mean hospital charges in $US	39,822.24 ± 24,498.41	48,101.86 ± 33,728.03	**<0.0001**	77,986.00 ± 67,148.64	**<0.0001**
90-day readmission					
Yes	129 (8.1)	122 (15.3)	**<0.0001**	31 (24.4)	**<0.0001**
No	1466 (91.9)	674 (84.7)		96 (75.6)	
90-day mortality					
Yes	31 (1.9)	43 (5.4)	**<0.0001**	5 (3.9)	0.18
No	1564 (98.1)	753 (94.6)		122 (96.1)	

Values are expressed as the mean ± standard deviation or number (%), unless indicated otherwise.
* Reference is the low-frailty-risk cohort. Boldface type indicates statistical significance.

TABLE 5. Multivariate analysis of HFRS and postoperative outcomes among 2518 surgical intracranial tumor patients

Outcome	OR	95% CI	p Value
Hospital LOS in days	0.50*	0.45–0.55	**<0.0001**
Postop complication	1.14	1.11–1.17	**<0.0001**
Nonroutine discharge	1.14	1.12–1.17	**<0.0001**
Hospital charges in $US	1917.49*	1677.23–2157.76	**<0.0001**
90-day readmission	1.06	1.04–1.09	**<0.0001**
90-day mortality	1.03	0.99–1.08	0.12

Multivariate analysis controlling for age, sex, race, marital status, insurance, tumor diagnosis, and surgery number. Boldface type indicates statistical significance.
* Coefficient rather than odds ratio.

of intracranial tumor patients. Following further prospective research efforts to better establish its utility in clinical workflows, the HFRS may prove to be an important tool for optimizing postoperative outcomes among intracranial tumor patients.

The superior predictive performance of the HFRS compared to the ASA, CCI, mFI-11, and mFI-5 may be explained by the medical comorbidities comprising each index, as well as the weighted calculation of the HFRS specifically. For example, the mFI-5, originally derived from Rockwood's Frailty Index, consists of only 5 variables—diabetes, high blood pressure, congestive heart failure, chronic obstructive pulmonary disease, and dependent functional status.[24,34] The HFRS, on the other hand, consists of 109 variables, many of which are weighed more or less than other factors when calculating a patient's final score.[15] A comparative study published by Meyer and colleagues in 2020 demonstrated that the HFRS outperformed the mFI-5 and other current risk stratification frailty-based models in predicting adverse events following primary hip and knee replacements.[35] Similarly, Hannah et al. found that the HFRS was a better predictor of LOS, ICU stay, and nonhome discharges relative to the ASA among spine neurosurgery patients.[16] Although the use of simpler metrics for risk assessment in clinical practice may initially seem easier and more feasible, the HFRS offers the opportunity to be calculated automatically since it is derived from routinely collected hospital administrative data.[35] In this manner, the proliferation of electronic health record systems makes the application of sophisticated risk-stratified frailty-based models such as the HFRS in clinical practice more feasible.[35,36]

Other major findings in our study include the significant and independent association of HFRS with several adverse postoperative outcomes. Regarding nonroutine discharge, it is likely that patients with high HFRSs experienced or were at risk for experiencing postoperative weakness and falls, necessitating rehabilitation in a specialized care facility.[16,32,34,37] Importantly, our observed association between the HFRS and discharge disposition is consistent with prior research findings in other surgical specialties. Specifically, the study by Hannah et al. noted a significant association between a high HFRS and nonroutine discharge among patients undergoing elective spine surgery (OR 16.7, $p < 0.0001$).[16] The association between frailty and increased hospital LOS, as well as between frailty and postoperative complications, has also been well established among intracranial tumor patients.[14,21,27,28] Because of their lower baseline health status relative to that of low-frailty-risk patients, the patients with high HFRSs likely more often experience complications after surgery, requiring additional treatment and subsequently increasing their hospital LOS.[10,30–32] Further, these additional treatments and prolonged LOSs likely also serve to drive up hospitalizations costs, validating our finding that greater frailty is significantly associated with higher hospital charges.[38] Similar to our results, a 2021 study by Meyer and colleagues, analyzing outcomes among 565 patients who underwent revision total hip arthroplasty and revision total knee arthroplasty, demonstrated that the HFRS was independently associated with surgical (OR 3.45, $p = 0.005$), medical (OR 7.29, $p = 0.007$), and other complications (OR 14.15, $p < 0.001$).[17]

Finally, our finding that higher HFRSs are independently associated with higher rates of 90-day readmissions suggests that many frail patients may be unable to attain a normal postoperative recovery or are more likely to experience deterioration, highlighting frailty as an important metric for informing discharge planning and patient counseling. Our results are also supported by findings in both the otolaryngology and cardiology literature. Voora et al., studying a cohort of 14,420 patients undergoing head and neck cancer surgery, found in a multivariate analysis that patients with an HFRS ≥ 5 were significantly more likely to experience a 30-day hospital readmission (OR 1.59, $p < 0.001$).[39] Wang et al., analyzing the outcomes of 21,878 patients who underwent left atrial appendage closure, found that an HFRS > 15 versus < 5 was significantly and independently associated with 30-day admission (OR 5.68, $p < 0.0001$).[40]

Concerning the diagnostic properties of the HFRS and postoperative outcomes, a false-negative prediction for postoperative complications, 90-day readmission, or 90-day mortality could be detrimental to patient care, as the tool would have failed to alert clinicians regarding an increased risk of these unfavorable outcomes. On the other hand, false-positive predictions regarding prolonged hospital LOS, nonroutine discharge, and high hospital charges would likely represent more of an inconvenience to patients, as clinicians may have requested unnecessary or expensive resources in anticipation of incorrectly predicted poor outcomes.

Overall, our results highlight the HFRS as an effective prognostication tool for postoperative outcomes among operative intracranial tumor patients. Our findings suggest that the HFRS has the potential to aid clinicians with preoperative assessment and stratification of high-risk patients, which may help to guide decisions regarding perioperative resource allocation. For instance, within the HFRS, a diagnosis of Alzheimer's disease is a nonmodifiable factor weighted relatively heavily within the scoring system and is independently associated with poor 90-day perioperative mortality. Such data points may help to guide patients and families toward surgical versus nonsurgical care in shared decision-making models.[41] Ad-

ditionally, select patients with a high HFRS who elect to undergo surgery may benefit from "prehabilitation" multimodal healthcare interventions designed to improve functional status and modifiable risk factors prior to surgery. While studies on the positive effect of prehabilitation on postoperative outcomes in neurosurgical patients are few, there is compelling evidence in the nonneurosurgical cancer literature that these interventions can improve postoperative outcomes, especially hospital LOS.[42–45] Future studies on the efficacy of prehabilitation in operative brain tumor patients are warranted.

Study Limitations

Several limitations are associated with the present study. Its retrospective nature limits any conclusions regarding causal relationships among the variables examined in our patient cohort. Given that the HFRS is derived from ICD-10 codes, over- and undercoding are potential sources of bias. Additionally, the HFRS itself includes several diagnoses that may only be accurately cataloged by specialized personnel including trained coders, leaving the score susceptible to under- and misreporting. We hope to pilot a prospective collaborative effort in concert with our trained coding staff to apply the HFRS to all surgical patients in the preoperative period. Another limitation of this study is that our entire cohort was surgically treated at a single institution, which could limit the generalizability of our study. Similarly, our results may not be valid for intracranial tumor patients undergoing radiotherapy or chemotherapy in lieu of surgery. While acknowledging these limitations, we believe that our work has provided the first comparative assessment on the utility of the HFRS and highlights a promising method for prognosticating postoperative outcomes among intracranial tumor patients.

Conclusions

The present study sought to quantify the effectiveness of the HFRS in predicting postoperative outcomes in intracranial tumor patients. The HFRS—as compared to indices such as the ASA classification, CCI, mFI-11, and mFI-5—had significantly higher AUROC values for predicting prolonged LOS, postoperative complications, nonroutine discharge dispositions, high hospital charges, and 90-day readmission. In a multivariate analysis, the HFRS remained significantly and independently associated with these outcomes. Collectively, these findings highlight the HFRS as a promising new tool for effectively prognosticating surgical outcomes among intracranial tumor patients.

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Disclosures

Dr. Bettegowda reports serving as a consultant for DePuy-Synthes, Bionaut Labs, Galen Therapeutics, Haystack Oncology, and Privo Technologies, as well as ownership in OrisDx.

Author Contributions

Conception and design: AE Jimenez, Liu. Acquisition of data: AE Jimenez. Analysis and interpretation of data: AE Jimenez. Drafting the article: AE Jimenez, Liu, Cicalese, MA Jimenez. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Mukherjee. Statistical analysis: AE Jimenez. Study supervision: Mukherjee.

Supplemental Information

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Correspondence

Debraj Mukherjee: Johns Hopkins University School of Medicine, Baltimore, MD. dmukher1@jhmi.edu.