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Association between Modified Frailty Index and Surgical Outcomes in Intradural Skull Base Surgery

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Abstract

The objective of this study is to evaluate the impact of preoperative frailty on short-term outcomes following intradural resection of skull base lesions. The 2005-2017 ACS-NSQIP database was queried for 30-day post-operative outcomes of patients undergoing intradural resection of the skull base, extracted by CPT codes 61601, 61606, 61608, and 61616. Five-item modified frailty index (mFI) was calculated based on the history of diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, chronic hypertension, and functional status. A total of 701 patients (58.8% female, 72.0% white) were included with a mean age of 51.8 ± 14.7 years. Compared to patients with mFI=0 (n=403), patients with mFI ≥1 (n=298) were more likely to have higher rates of reoperation (13.4% vs. 8.7%, p=0.045), medical complications (20.5% vs. 9.2%, p<0.001), surgical complications (13.8% vs. 8.4%, p=0.024), discharge to non-home facility (DNHF) (24.8% vs. 13.3%, p<0.001), and prolonged length of hospitalization (7.3 ± 6.8 days vs. 5.6 ± 5.0, p=0.003). Moreover, mFI=1-3 was also associated with higher BMI, non-white race, high ASA, and older age (all p<0.05). Upon adjusting for age, BMI, race, ASA score, and surgical site, multivariate regression analysis demonstrated that higher mFI (treated as a continuous variable) was associated with higher odds of medical complications (OR=1.630, CI=1.153-2.308, p=0.006), surgical complications (OR=1.594, CI=1.042-2.438, p<0.031), and LOS ≥10 days (OR=1.609, CI=1.176-2.208, p=0.003). In conclusion, the 5-item mFI can be an independent predictor of several important short-term surgical outcomes following intradural resection of skull base lesions, warranting further investigations into its clinical utility.

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Keywords

Frailty; modified frailty index; morbidity; NSQIP; skull base

Introduction

Deciding on whether a patient can tolerate surgery, or if optimizing certain clinical parameters can help improve their postoperative outcomes, are important considerations for the operating surgeon. Despite this, the aforementioned judgments are often subjective and stem from the experience of the providers rather than from objective measures. Although age has been an important predictor of patients' resilience and ability to tolerate surgeries, several recent studies have suggested that frailty is a stronger prognosticator of surgical outcomes.[1–3] Frailty can be described as an individual's decreased physiological reserve and diminished ability to tolerate stressful events.[4, 5] Namely, physiologic changes as a result of comorbidities, malnourishment, inactivity, and stress, and not just natural aging, can lead to a reduced capacity to maintain normal homeostasis under stressful conditions.[6, 7] Because traditional frailty models (e.g., physical phenotype and cumulating deficits)[8, 9] can be too comprehensive and difficult to use for prompt surgical risk assessment, there have been recent efforts to establish various modified frailty indexes (mFI) which are more clinically interpretable.[10, 11]

The recent literature has validated the existing relationship between patients' 5-item mFI and various postoperative outcomes in spine surgery,[12, 13] head and neck surgery,[14, 15] and general surgery.[16, 17] This has important implications, as this metric can serve as an important prognostic tool to quickly evaluate patients' surgical risks or identify at-risk patients for better optimization of pre-, peri-, or postoperative parameters. Despite its important quality improvement implications, the influence of mFI on outcomes for intradural resection of skull base lesions has yet to be determined. Herein, this study utilized the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) to evaluate the effect of the 5-item mFI on short-term surgical outcomes following intradural resection of skull base lesions.

Methods

This study did not require Institutional Review Board approval due to the publicly accessible and de-identified nature of the data. Data was collected from the 2005-2017 ACS-NSQIP database, which acquires information from more than 600 hospitals.[18] The following Current Procedural Terminology (CPT) codes were utilized to extract patients undergoing excision of intradural skull base lesions: 61601 (intradural resection or excision of neoplastic, vascular or infectious lesion of base of anterior cranial fossa, including dural repair, with or without graft), 61606 (intradural resection or excision of neoplastic, vascular or infectious lesion of infratemporal fossa, parapharyngeal space, petrous apex), 61608 (intradural resection or excision of neoplastic, vascular or infectious lesion of parasellar area, cavernous sinus, clivus or midline skull base), and 61616 (intradural resection or excision of neoplastic, vascular or infectious lesion of base of posterior cranial fossa, jugular foramen, foramen magnum, or C1-C3 vertebral bodies). The CPT codes that characterize the procedures within this database are standardized 5-digit codes that offer surgeons healthcare professionals a uniform language for coding specific medical procedures with the intent of streamlining reporting, communicating with insurance or billing departments, and promoting efficiency/accuracy. The codes selected for analysis in the current study specify procedures upon the skull base involving the anterior, middle, and/or posterior cranial fossae. Patients' demographic information, pre- and peri-operative clinical data, and 30-day post-operative outcomes were collected, and those with incomplete 30-day outcome information were excluded. The "readmission" variable was the only exception: Since this outcome was added to NSQIP in 2012, patients recorded prior to this year do not have this information, thus the reported percentages reflect the sub-cohort with available readmission information. Lastly, this study's references to "short-term" outcomes refer to the 30-day postoperative timeline that patients are followed within the NSQIP database.

For each patient, we calculated a 5-item mFI based on five NSQIP variables: dependent functional status, diabetes mellitus, history of chronic obstructive pulmonary disease (COPD), history of congestive heart failure (CHF), and hypertension requiring medication. This specific scoring system was previously validated in a study by Subramaniam *et al.* and has been shown to be strongly correlated with the 11-question mFI.[11] The reported American Society of Anesthesiologists (ASA) score was categorized as low (class 1-2) versus high (class 3-4) ASA. Discharge to non-home facility (DNHF) included patients that were discharged to skilled care or unskilled facilities, separate acute care centers, or rehabilitation centers. Postoperative complications were categorized as surgical or medical complications in accordance with previous NSQIP studies.[19–21] Specifically, medical complications included pneumonia, unplanned reintubation, >48 hours ventilator use, deep vein thrombosis, pulmonary embolism, urinary tract infection, renal insufficiency, acute renal failure, cerebrovascular accident with neurological deficit, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, sepsis, or septic shock. Surgical complications included blood transfusion <72 hours postoperatively, wound disruption, superficial surgical site infection (SSI), deep SSI, or organ/space SSI. The mortality variable in ACS- NSQIP refers to 30-day all-cause mortality even if it was not directly due to the surgery.

PASW Statistics 18.0 software (SPSS Inc., Chicago, IL) was used for statistical analyses, with p-values <0.05 considered statistically significant. Two-tailed unpaired t-tests and chi-squared tests of independence were utilized for continuous and categorical variables, respectively. one-way analysis of variance with Tukey honest significant differences was performed to evaluate the difference among means of more than two groups. Odd ratios (OR) and regression coefficients (β), along with their corresponding 95% confidence intervals (CI), were obtained from logistic and linear regressions, respectively, to evaluate various independent relationships while accounting for potential confounders.

Results

A total of 701 patients met the inclusion criteria, consisting of 58.8% female and 72.0% white patients. The cohort's average age was 51.8 ± 14.7 years (range=18-89 years). The cohort consisted of intradural resections of 123 (17.5%) anterior cranial fossa (ACF; CPT 31601), 265 (37.8%) middle cranial fossa (MCF; CPT 61606/61608), and 313 (44.7%) posterior cranial fossa (PCF; CPT 61616) lesions. Table 1 compares patients according to these three skull base subcohorts, demonstrating older age (p=0.001) and shorter operation times (p<0.001) among ACF cohorts, and fewer surgical complications (p<0.001) among PCF cases.

The patients' mFI score breakdowns (mean 0.53 ± 0.69) with the associated comorbidities are demonstrated in Table 2. The surgical outcomes of patients with mFI=0 (n=403) and mFI=1-3 (n=298) were compared as listed in Table 3, demonstrating that the latter group was more likely to undergo reoperations (13.4% vs. 8.7%, p=0.045), surgical complications (13.8% vs. 8.4%, p=0.024), medical complications (20.5% vs. 9.2%, p<0.001), prolonged length of hospitalization (7.3 ± 6.8 days vs. 5.6 ± 5.0, p=0.003), and DNHF (24.8% vs. 13.3%, p<0.001). This also demonstrated that, besides being associated with older age and high ASA score (both p<0.001), mFI=1-3 was also associated with higher BMI (p<0.001) and non-white race (p=0.011). On multivariate logistical regression analysis after adjusting for age, sex, race, BMI, ASA score, surgical site, and operative time as important clinical confounders, patients with mFI ≥1 had significantly higher likelihood of surgical complications (OR=1.972, 95% CI=1.026-3.864, p=0.043), medical complications (OR=1.887, 95% CI=1.140-3.161, p=0.015), and LOS ≥10 days (OR=2.012, 95% CI=1.178-3.483, p=0.011). These multivariate logistic regression results, which account for confounders and elucidate the independent relationship between mFI and outcomes, are summarized in Table 4.

To further elucidate the effects of higher mFI, patients with mFI=0-1 (n=627) were compared to those with mFI=2-3 (n=74) as listed in Table 5. This demonstrated that mFIs of 2-3 were associated with higher rates of reoperation (17.6% vs. 9.9%, p=0.043), medical complications (28.4% vs. 12.3%, p<0.001), DNHF (27.4% vs. 17.0%, p=0.044), and prolonged hospitalization (10.2 ± 12.6 vs. 6.3 ± 7.1, p=0.010). Additionally, upon adjusting for age, sex, race, BMI, ASA score, surgical site, and operative time as important clinical confounders, multivariate regression analysis demonstrated that higher mFI (treated as a continuous variable) was associated with greater medical (OR=1.586, CI=1.114-2.265, p=0.011) and surgical (OR=1.607, CI=1.029-2.511, p=0.036) complications. Moreover, increased frailty was not only associated with longer lengths of hospitalization (β=1.994, CI=0.735-3.252, p=0.002), but also with LOS ≥10 days (OR=1.957, CI=1.370-2.814, p<0.001). These multivariate logistic regression results, which account for confounders and elucidate the independent relationship between mFI and outcomes, are summarized in Table 4.

Discussion

In this study, we demonstrated the important prognostic value of the modified frailty index in patients undergoing intradural resections of skull base lesions. Despite a wide variability in how frailty indices are formulated, the mFI's association with morbidity and mortality has been established in multiple surgical populations.[12–17] Due to its simplicity, the mFI can be easily calculated for most patients in the clinic or at the bedside using information obtained from routine histories and physical examinations. Even in this study's patient population which had low frailty scores on average, we were still able to demonstrate strong associations between mFI and several postoperative parameters or adverse events. This information is important for preoperative patient selection and for counseling patients on the possible scenarios for recovery following these proposed procedures. Although studies have previously evaluated the role of preoperative frailty in head and neck surgeries,[14, 22, 23] this is the first to investigate the influence of mFI on surgical outcomes in skull base surgery.

Overall, we found that a fairly high percentage of patients in this study (20.2%) suffered from at least one medical or surgical complication, which, in the context of how complex skull base surgeries are, is consistent with earlier reports in the literature. These postoperative complications impose a significant financial and emotional burden on patients and their families.[24] Therefore, there is great clinical value in utilizing mFI as a presurgical index for identifying high-risk surgical candidates or optimizing certain pre or per-operative parameters. Evaluation of frailty can provide new insights on the patient's operative risk, thereby enabling surgeons to better tailor their interventions, which may sometimes include providing preoperative therapies that mitigate the impact of frailty. In fact, through implementation of multifaceted preventive therapy programs, studies have demonstrated the ability to effectively reduce frailty in elderly patients.[25, 26] At the least, an objective measure of frailty can enhance surgeons' awareness of possible adverse outcomes and prompt increased postoperative monitoring for patients who are considered to be more frail.

Our analyses demonstrated significant associations between increasing frailty and higher rates of reoperation, medical complications, and surgical complications. Furthermore, frailty was determined to be a strong predictor of prolonged hospitalization and DNHF. Even after adjusting for age, sex, race, BMI, ASA score, surgical site, and operative time, multivariate analysis continued to demonstrate increased adverse events among patients with higher mFI scores. This is consistent with previous studies that demonstrated the presence of medical comorbidity as a risk factor for postoperative complications in skull base tumor resections.[27–29] Several otolaryngologic studies have even shown mFI to be a stronger predictor of postoperative complications than age and ASA score, both of which are factors that have been classically used in evaluating surgical risk. [30–32] This is particularly important, as focusing on a patient's health status by using frailty instead of age can help to alleviate age discrimination in preoperative assessments.[33, 34] Multivariate regression further demonstrated that prolonged hospitalization was significantly associated with higher mFI scores. This was likely a consequence of the greater incidence of postoperative complications among frail patients. In fact, studies have shown that postoperative complications can increase LOS to almost three times the average length of hospitalization for common head and neck operations.[35, 36] Additionally, hospitalization stays might have been further augmented at higher mFIs due to greater care needs that had to be addressed prior to discharge or delays in patients returning to baseline function.

In our analysis of the frail population, we found chronic hypertension and diabetes mellitus to be the most common comorbidities contributing to patient frailty. This finding was similar to the observations reported in a large-population retrospective study of elective and emergency general surgery cases.[37] Furthermore, as poorly-controlled diabetes and hypertension can commonly lead to chronic kidney disease,[38] these two conditions have been found to be morbidity synergistic and associated with significantly greater increases in frailty risk.[39] Therefore, physicians should be aware of the prevalence of these comorbidities and actively recognize their associated risks to guide preoperative counseling and optimize patient outcomes. Our investigation further revealed that older age, non-white race, higher ASA score, and higher BMI were more common at higher frailty scores. Population-based studies investigating the relationship between comorbid conditions and frailty have uncovered similar associations.[40–42] However, a large-population prospective study by Cawthon *et al.* not only demonstrated increased frailty in older ages and non-white races, but also demonstrated higher mortality risk in frailer patients.[43] While we did not find similar associations between mortality and mFI, the statistical power of our analysis may have been limited by the relatively low mortality rate in our patient population.

Many of the limitations in our study were a consequence of the inherent drawbacks associated with a large administrative database. Since the outcomes reported in NSQIP are restricted to 30 days, we were unable to analyze the long-term effects of frailty on postoperative morbidity and mortality. Moreover, information regarding patient readmission, discharge site, and elective surgical admissions were missing for a large number of our patients due to lack of a complete data set. This significantly reduced the sample size of some our univariate analyses, which could have introduced Type II errors. Additionally, the rate of medical complications may have been underestimated, since the NSQIP does not include several adverse outcomes, such as postoperative depression, anxiety, and cognitive decline, that are commonly observed in elderly patients after surgery.[44] Similarly, NSQIP does not report specific surgical complications which are unique to skull base surgery (e.g., intracranial hemorrhage, pneumocephalus, cerebrospinal fluid leak). NSQIP also does not report whether such surgeries were performed via traditional open approaches or via endoscopic approaches given limitations inherent to skull base procedural coding, and it also does not report the specific pathology (e.g., meningioma vs. glioma) which may result in different short-term outcomes. Furthermore, comparing these findings to our institutional patients was beyond the scope of the study, but future studies are encouraged to investigate the association between mFI and outcomes of intradural surgeries using institutional patients. Finally, since only 2 of our patients had mFI ≥3, we could not assess the full predictive range of the mFI in the context of skull base surgeries. In light of the retrospective nature of our study, future investigations focused on prospective validation and analysis of the mFI in this patient population are warranted.

Conclusion

In this study, we demonstrated the clinical value of incorporating the modified frailty index as a routine presurgical index for identifying high-risk surgical candidates for intradural skull base tumor resections. By evaluating the impact of preoperative mFI on acute postoperative outcomes, we demonstrated strong associations between increasing mFI and higher rates of medical and surgical complications and lengthier hospitalization. The mFI is a simple, but effective tool that can enable physicians to objectively evaluate patients based on their functional status. Therefore, this data-driven predictive tool can assist surgeons in guiding presurgical counseling and enhancing the informed consent process.

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Table 1.

Comparison of patient outcomes between intradural resection of anterior, middle, and posterior skull base lesions. Values in parentheses reflect percentages.

Variables	ACF resection (n=123)	MCF resection (n=265)	PCF resection (n=313)	*p*-value
Age, yr	56.3 ± 14.2	51.4 ± 14.9	50.5 ± 14.6	**0.001** [a]
Operation Time, min	338.2 ± 170.8	385.6 ± 189.4	419.1 ± 193.4	**<0.001** [b]
LOS, days	6.6 ± 5.8	6.4 ± 6.0	6.2 ± 5.8	0.861
Reoperation	13 (10.6)	28 (10.6)	34 (10.9)	0.992
Readmission [*]	18/99 (18.2)	22/212 (10.4)	27/244 (11.1)	0.108
Surgical Complications	20 (16.3)	37 (14.0)	18 (5.8)	**<0.001** [c]
Medical Complications	19 (15.4)	40 (15.1)	39 (12.5)	0.578
Mortality	1 (0.8)	4 (1.5)	3 (1.0)	0.768
DNHF [*]	23/110 (20.9)	42/231 (18.2)	47/279 (16.8)	0.643

mFI = modified frailty index, ACF = anterior cranial fossa, MCF = middle cranial fossa, PCF = middle cranial fossa, DNHF = discharge to non-home facility

[a] ACF cases were associated with older ages than MCF (p=0.007) or PCF (p=0.001) cases.

[b] ACF cases were associated with shorter operation times than MCF (p=0.05) or PCF (p<0.001).

[c] PCF cases were associated with fewer surgical complications than MCF (p=0.004) or ACF (p<0.001) cases.

[*] Variable contains missing values, so the % represent the corrected denominator of the available values.

Table 2.

Prevalence of 5-item mFI patient categories as well as the individual clinical components that make up this index. Values in parentheses reflect percentages.

mFI Subgroups (cohort n=701)		mFI Clinical Components (cohort n=701)	
mFI: 0	403 (57.5)	**Chronic hypertension**	260 (37.1)
		Diabetes mellitus	84 (12.0)
mFI: 1	224 (32.0)	**Dependent functional status**	18 (2.6)
mFI: 2	72 (10.3)	**Chronic obstructive pulmonary disease**	11 (1.6)
mFI: 3	2 (0.3)	**Congestive heart failure**	1 (0.1)

No patients with mFI 4 or 5 existed in this database.

Table 3.

Comparison of baseline presentation and surgical outcomes between patients with mFI=0 and those with mFI=1-3.

Variables	mFI = 0 (n=403)	mFI = 1-3 (n=298)	*P*-value
Gender: Female	242 (60.0)	170 (57.0)	0.425
Race: Non-white *	52/346 (15.0)	57/268 (21.3)	**0.011**
Age	46.8 ± 14.3	58.7 ± 12.3	**<0.001**
BMI	28.1 ± 5.9	31.4 ± 7.4	**<0.001**
More recent operation (2014-17)	237 (58.8)	167 (56.0)	0.463
Non-elective surgery *	52/361 (14.4)	45/264 (17.0)	0.368
ASA: High	186 (46.2)	224 (75.2)	**<0.001**
Length of operation, minutes	396.9 ± 187.0	385.9 ± 194.3	0.452
Reoperation	35 (8.7)	40 (13.4)	**0.045**
Readmission *	40/316 (12.7)	27/238 (11.3)	0.639
Surgical complication	34 (8.4)	41 (13.8)	**0.024**
Medical complication	37 (9.2)	61 (20.5)	**<0.001**
Mortality	3 (0.7)	5 (1.7)	0.250
Length of hospitalization, days	5.6 ± 5.0	7.3 ± 6.8	**0.003**
LOS >10 days	44 (10.9)	62 (20.8)	**<0.001**
Disposition: DNHF *	48/362 (13.3)	64/258 (24.8)	**<0.001**

* Variable contains missing values, so the % represent the corrected denominator of the available values.

Table 4.

Multivariate regression of surgical outcomes according to mFI in skull base surgery patients while adjusting for the confounding effects of age, sex, race, BMI, ASA score, surgical site, and operation time.

Variables	Binary mFI (0, ≥1)		Continuous mFI	
	Coefficient (95% CI)	*P*-value	Coefficient (95% CI)	*P*-value
Reoperation *	1.372 (0.911-2.058)	0.127	1.226 (0.677-2.231)	0.501
Readmission *	0.764 (0.477-1.196)	0.250	0.710 (0.376-1.327)	0.285
Surgical complication *	1.607 (1.029-2.511)	**0.036**	1.972 (1.026-3.864)	**0.043**
Medical complication *	1.586 (1.114-2.265)	**0.011**	1.887 (1.140-3.161)	**0.015**
Length of hospitalization, days †	1.994 (0.735-3.252)	**0.002**	1.292 (−0.489-3.074)	0.156
LOS ≥10 days *	1.957 (1.370-2.814)	**<0.001**	2.012 (1.178-3.483)	**0.011**
Disposition: DNHF *	1.205 (0.848-1.706)	0.296	1.272 (0.769-2.108)	0.349

mFI: Modified Frailty Index; DNHF: Discharge to Non-Home Facility; LOS: Length of Stay

*Analyzed via logistic regression with resulting Odds ratio

†Analyzed via linear regression with resulting beta coefficient

Table 5.

Comparison of baseline presentation and surgical outcomes between patients with mFI=0-1 and those with mFI=2-3.

Variables	mFI = 0-1 (627)	mFI = 2-3 (74)	*P*-value
Gender: Female	372 (59.3)	40 (54.1)	0.383
Race: Non-white *	88/543 (16.2)	21/71 (29.6)	**0.009**
Age	50.9 ± 14.8	60.0 ± 11.4	**<0.001**
BMI	29.0 ± 6.4	33.3 ± 8.7	**<0.001**
More recent operation (2014-17)	365 (58.2)	39 (52.7)	0.364
Non-elective surgery *	85 (13.6)	12 (16.2)	0.415
ASA: High	343 (54.7)	68 (91.9)	**<0.001**
Length of operation, minutes	391.0 ± 186.3	402.1 ± 221.0	0.635
Reoperation	62 (9.9)	13 (17.6)	**0.043**
Readmission *	61/497 (12.3)	6/57 (10.5)	0.702
Surgical complication	63 (10.0)	12 (16.2)	0.104
Medical complication	77 (12.3)	21 (28.4)	**<0.001**
Mortality	6 (1.0)	2 (2.7)	0.181
Length of hospitalization, days	6.3 ± 7.1	10.2 ± 12.6	**0.010**
LOS >10 days	81 (12.9)	25 (33.8)	**<0.001**
Disposition: DNHF *	95/558 (17.0)	17/62 (27.4)	**0.044**

* Contain missing values, so the % represent the corrected denominator of the available values.