Anterior Skull Base Outcomes and Complications: A Propensity Score–Matched Evaluation of Age and Frailty as Measured by mFI-5 from the ACS-NSQIP Database

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Abstract

Background Frailty is increasingly recognized as a predictor of surgical outcomes; however, its utility in anterior cranial fossa (ACF) surgery remains unclear. We analyzed whether age and frailty are independent predictors of outcomes after ACF surgery using a retrospective cohort study.

Methods The American College of Surgeons National Surgical Quality Improvement Program database was queried, by Current Procedural Terminology codes, for ACF procedures in 2005 to 2020. Cases included open approaches, endoscopic approaches, and all tumor types except for pituitary adenoma. A propensity score–matched data set was analyzed via multiple logistic regression.

Results Unmatched multivariate analysis of ACF cases demonstrated that severe frailty (modified 5-item frailty index [mFI-5] ≥ 3) was independently associated with having any (odds ratio [OR] = 3.67) and minor (OR = 5.00) complications (both $p < 0.001$). Analysis of individual mFI-5 components demonstrated poor functional status was significantly associated with any (OR = 3.39), major (OR = 3.59), and minor (OR = 3.14) complications (all $p < 0.001$). After propensity score matching, only age was modestly impactful on minor complications (OR = 1.02) and extended length of stay (eLOS) (OR = 1.02) ($p < 0.001$). Frailty did not maintain its predictive ability after matching. Nonindependent functional status, as a subcomponent of mFI maintained

Keywords
- age
- anterior cranial fossa
- anterior skull base
- complications
- frailty
- mFI-5
- modified 5-item frailty index
- National Surgical Quality Improvement Program
- neurosurgery
- NSQIP
- propensity score matching

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significant predictive ability for any (OR = 4.94), major (OR = 4.68), and minor (OR = 4.80) complications and eLOS (OR = 2.92) (all $p < 0.001$).

Conclusion After propensity score matching, age demonstrated a greater ability to predict postoperative complications in ACF surgery than frailty. Rather than age or frailty, functional status served as a better outcome predictor and potential guide for patient counseling. Further validation of these findings in multicenter or disease-specific studies is warranted as well as aims to preoperatively improve functional status in ACF surgery.

Introduction

Anterior skull base pathology represents a rare but formidable territory because of the significant involvement of critical neurovascular structures.[1–3] Complications, readmissions, reoperations, and rehabilitation profoundly impact patient quality of life. Anterior cranial fossa (ACF) surgery involves a heterogeneous group of procedures for which it can be difficult to predict outcomes.[4,5] Identifying predisposing risk factors for adverse outcomes may be useful in avoiding complications and decreasing morbidity rates.[6–10] Previously proposed risk factors of complications after endoscopic skull base surgery include advanced age, size, history of prior surgery, preoperative radiation, elevated intracranial pressure, body mass index (BMI), blood urea nitrogen, and white blood cell counts.[1,11,12] Age-dependent differences in these factors yield unique patient risk profiles.[7,9] Identifying comprehensive, user-friendly metrics to predict postoperative outcomes will help neurosurgeons develop surgical treatment plans, improve outcomes, and optimize patient selection before surgical procedures.

The modified 5-item frailty index (mFI-5) informs medical providers assessing patients for morbidity, mortality, reoperation, and unplanned readmission risk.[13,14] The mFI-5 may demonstrate usefulness clinically as an objective measure of preoperative risk in skull base surgery[15,16]; however, the reported usefulness and predictive ability have varied within the literature.[15] Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, we compared the predictive ability of age and frailty, as measured by mFI-5. Further, to control for data and patient variation, we built a propensity score–matched data set from NSQIP data. We hypothesized that increasing frailty is predictive of postoperative complications and is a better predictor of postoperative complications in ACF surgery than age.

Methods

Data Source and Study Sample

The ACS-NSQIP database was used to identify patients who underwent ACF procedures in 2005 to 2020.[17,18] The source data are freely available to member institutions submitting to the NSQIP. The ACS-NSQIP and the hospitals participating in it are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors. This study did not require approval by an institutional review board because the data are deidentified.

Patients were included in this study if their records included Current Procedural Terminology (CPT) codes associated with ACF procedures (►**Fig. 1**), which included relevant approach or resection codes. These included open and endoscopic approaches. Patients who underwent pituitary adenoma surgery were excluded. If missing necessary data, quantitative variables were filled in with mean values. Categorical variables, particularly in relation to mFI-5 calculations, were treated as negative if values were not entered. The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were used for this study.

Study Variables

The mFI-5 calculation includes one point for each of the following variables: functional status, chronic obstructive pulmonary disease (COPD) or current pneumonia, hypertension requiring medication, diabetes mellitus, and congestive heart failure (CHF). These variables were collected, along with sex, age, BMI, race, smoking status, steroid use, bleeding disorders, American Society of Anesthesiologists (ASA) score, and presence of open wounds/infections. All operative characteristics and outcomes included in the NSQIP were included for analysis of complications.

Outcomes of interest were grouped into complication categories. Major complications were acute renal failure, cardiac arrest, deep surgical space infection, mortality, myocardial infarction, organ space infection, pulmonary embolism, reintubation, reoperation, sepsis, septic shock, stroke, ventilator dependence > 48 hours, and wound dehiscence. Minor complications were deep vein thrombosis (DVT), pneumonia, renal insufficiency, superficial surgical site infection, transfusion, and urinary tract infection (UTI). Other outcomes included reoperation, readmission, and extended length of stay (eLOS, characterized as hospital stays lasting ≥ 75th percentile of all cases).

Statistical Analysis

The analysis was performed using SPSS (V24.0; IBM, Armonk, New York, United States) and R (V4.2.1). Continuous

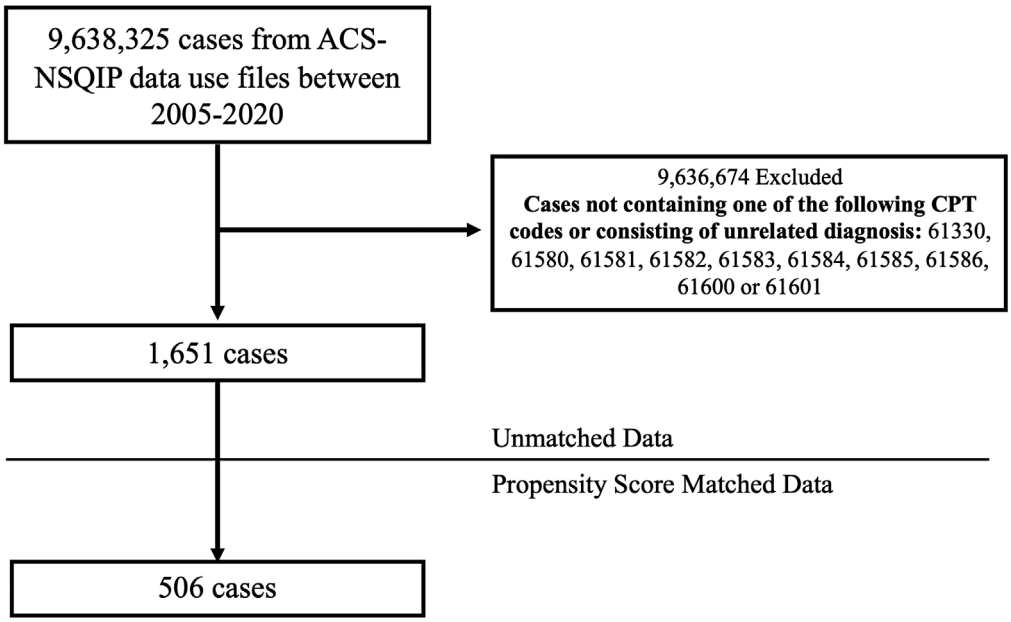

Fig. 1 Flow sheet of patients along with inclusion and exclusion criteria.

demographic and perioperative variables were evaluated using *t*-tests or one-way analyses of variance and categorical variables with chi-squared tests. Each patient's mFI-5 was calculated, and patients were categorized as nonfrail, prefrail, frail, and severely frail, for mFI-5 scores of 0, 1, 2, and 3+, respectively.

Clinically meaningful multivariate models were evaluated with multiple logistic regression adjusting for age, sex, BMI, relative value units, mFI-5, smoking status, chronic steroid use, bleeding disorders, open wound, and ASA score. A *p*-value of < 0.05 was considered statistically significant for all models.

A nearest-neighbor matching algorithm was performed to achieve more comparable data sets via the *MatchIt* R package. Matching was done with a 1:1 ratio, matching equal ratios of CPT codes, and by the length of operation. Length of operation was chosen as a proxy for case complexity, which could not be accounted for adequately with other NSQIP variables. To accommodate matching, cases were characterized into two groups, mFI-5 ≤ 1 ("nonfrail") or ≥ 2 ("frail").

Results

Unmatched Data Demographics and Comorbidities

The NSQIP contains 1,651 ACF procedures, with 51.8% nonfrail, 32.9% prefrail, 13.5% frail, and 1.8% severely frail (►**Table 1**). The mean age (49.5 ± 15.0, 60.6 ± 12.8, 64.3 ± 12.2, and 67.6 ± 12.5 years, respectively) differed significantly among groups ($p < 0.001$). The mean BMI did not differ significantly among frailty groups. All mFI-5 components differed significantly among groups (all $p < 0.001$). Nonindependent functional status (56.7%) and COPD (46.7%) occurred in approximately half of the severely frail patients. Hypertension was noticeably present in prefrail (84.3%), frail (96.4%), and severely frail (100%). Diabetes followed a similar trend, presenting in 81.6% of frail patients and 93.3% of severely frail patients. CHF cases were rare, with only three cases in these ACF patients. Smoking status did not significantly differ, but chronic steroid use ($p = 0.039$), presence of bleeding disorders ($p < 0.001$), and presence of open wounds or infections ($p = 0.002$) did.

Matched Data Demographics and Comorbidities

The matched ACF data set consisted of 506 cases, split equally as 253 nonfrail (mFI ≤ 1) and 253 frail (mFI ≥ 2) cases (►**Table 1**). As in the unmatched data, the mean age differed significantly (52.3 ± 15.7 vs. 64.7 ± 12.2 years, $p < 0.001$). The mean BMI was higher for the frail group (29.5 ± 7.1 vs. 32.4 ± 8.7, $p < 0.001$). Apart from CHF, with its small sample size, all mFI-5 components maintained significant differences among groups (all $p < 0.001$). Smoking status did not differ significantly; however, chronic steroid use differed (8.3% of nonfrail patients vs. 14.6% of frail patients, $p = 0.026$). Similarly, bleeding disorders differed significantly (1.6% of nonfrail patients vs. 5.9% of frail patients, $p = 0.01$).

Unmatched Operative Characteristics and Postoperative Outcomes

An eLOS was seen in 26.8% of nonfrail, 29.3% of prefrail, 33.6% of frail, and 55.2% of severely frail patients ($p = 0.003$) (►**Table 2**). Readmission rates did not differ significantly among groups. The rates of all complications were 24.6% of nonfrail, 28% of prefrail, 30.5% of frail, and 63.3% of severely frail patients ($p < 0.001$). Major complications differed significantly among groups ($p < 0.001$), particularly reintubation ($p < 0.001$), failure to wean from the ventilator in 48 hours ($p = 0.005$), sepsis development

Table 1 Demographics and comorbidities of ACF cases from NSQIP

	Unadjusted					Propensity-matched		
	Nonfrail $n = 855$ (51.8%)	Prefrail $n = 543$ (32.9%)	Frail $n = 223$ (13.5%)	Severely frail $n = 30$ (1.8%)	*p*-Value	mFI ≤ 1 $n = 253$ (50%)	mFI ≥ 2 $n = 253$ (50%)	*p*-Value
Demographics								
Male sex	417 (48.8)	297 (54.7)	118 (52.9)	15 (50.0)	0.176	115 (45.5)	133 (52.6)	0.109
Age $\geq$ 65 y	120 (14.0)	188 (34.6)	101 (45.3)	15 (50.0)	< **0.001**	56 (22.1)	133 (52.6)	< **0.001**
Mean age (y)	49.5 ± 15.0	60.6 ± 12.8	64.3 ± 12.2	67.6 ± 12.5	< **0.001**	52.3 ± 15.7	64.7 ± 12.2	< **0.001**
Mean BMI	28.5 ± 6.4	30.5 ± 7.4	32.0 ± 8.1	36.2 ± 11.7	0.467	29.5 ± 7.1	32.4 ± 8.7	< **0.001**
Race					**0.008**			0.687
White	554 (64.8)	355 (65.4)	150 (67.3)	16 (53.3)		167 (66.0)	166 (65.6)	
Black	108 (12.6)	98 (18.0)	36 (16.1)	8 (26.7)		37 (14.6)	44 (17.4)	
Asian/Pacific Islander	51 (6.0)	33 (6.1)	8 (3.6)	1 (3.3)		12 (4.7)	9 (3.6)	
Other	6 (0.7)	2 (0.4)	0	1 (3.3)		0	1 (0.4)	
Unknown	136 (15.9)	55 (10.1)	29 (13.0)	4 (13.3)		37 (14.6)	70 (27.7)	
Hispanic	54 (6.3)	32 (5.9)	29 (13.0)	1 (3.3)	**0.005**	18 (7.1)	30 (11.6)	0.189
Modified frailty index components								
Nonindependent functional status	0	22 (4.1)	26 (11.7)	17 (56.7)	< **0.001**	4 (1.6)	43 (17.0)	< **0.001**
COPD	0	14 (2.6)	22 (9.9)	14 (46.7)	< **0.001**	3 (1.2)	36 (14.2)	< **0.001**
Hypertension	0	458 (84.3)	215 (96.4)	30 (100)	< **0.001**	84 (33.2)	245 (96.8)	< **0.001**
Diabetes	0	49 (9.0)	182 (81.6)	27 (93.3)	< **0.001**	8 (3.2)	210 (84.2)	< **0.001**
CHF	0	0	1 (0.5)	2 (6.7)	< **0.001**	0	3(1.2)	0.082
Additional comorbidities								
Current smoker	184 (21.5)	105 (19.3)	36 (16.1)	8 (26.7)	0.237	58 (23.0)	44 (17.4)	0.121
Chronic steroid use	73 (8.5)	52 (9.6)	32 (14.3)	5 (16.7)	**0.039**	21 (8.3)	37 (14.6)	**0.026**
Bleeding disorders	9 (1.1)	122 (2.2)	13 (5.8)	2 (6.7)	< **0.001**	4 (1.6)	15 (5.9)	**0.01**
Open wound/infection	11 (1.3)	8 (1.5)	3 (1.3)	3 (10)	**0.002**	1 (0.4)	6 (2.4)	0.057

Abbreviations: ACF, anterior cranial fossa; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; mFI, modified frailty index; NSQIP, National Surgical Quality Improvement Program.
Note: Data are reported as *n* (%), mean ± standard deviation. Bold values highlight the statistically significant results.

($p < 0.001$), and septic shock ($p = 0.005$). Minor complications also differed significantly among groups ($p < 0.001$), with UTI ($p = 0.028$), pneumonia ($p < 0.001$), transfusion ($p < 0.001$), and DVT ($p = 0.009$) differing significantly.

Matched Operative Characteristics and Postoperative Outcomes

After propensity score matching, significant differences in both the mean LOS ($p = 0.007$) and eLOS ($p = 0.002$) remained between groups (►**Table 2**). The measure of any complications ($p = 0.002$) and major complications ($p = 0.023$) remained significant. Significantly differing major complications included reintubation ($p = 0.009$), pulmonary embolism ($p = 0.032$), failure to wean from the ventilator in 48 hours ($p = 0.023$), and sepsis ($p = 0.049$). Minor complications also differed significantly between groups ($p < 0.001$), with pneumonia ($p < 0.001$) and transfusion ($p = 0.001$) being statistically significantly different.

Multivariate Analysis of ACF Case Outcomes

Multivariate analysis of unmatched ACF cases suggested severe frailty predicts the occurrence of any complications and minor complications (odds ratio [OR] = 3.67 and 5.00, respectively) ($p < 0.05$) (►**Table 3**). Only age was predictive of eLOS (OR = 1.01) ($p < 0.05$). Analysis of individual mFI-5 components revealed that nonindependent functional status was a significant predictor for any complications (OR = 3.39), major complications (OR = 3.59), minor complications (OR = 3.14), and eLOS (OR = 3.93) ($p < 0.05$). Hypertension was also a significant predictor of eLOS (OR = 0.76) ($p < 0.05$).

After propensity score matching, the predictive ability of frailty was lost (►**Table 4**). Rather, increasing age became predictive of minor complications (OR = 1.02) and eLOS (OR = 1.02) ($p < 0.05$). Nonindependent functional status remained predictive of any complications (OR = 4.94), major complications (OR = 4.68), minor complications (OR = 4.80), and eLOS (OR = 2.92) ($p < 0.05$). Diabetes was

Table 2 Operative characteristics and postoperative outcomes for ACF cases from NSQIP

Variable	Unadjusted					Propensity-matched		
	Nonfrail $n = 855$ (51.8%)	Prefrail $n = 543$ (32.9%)	Frail $n = 223$ (13.5%)	Severely frail $n = 30$ (1.8%)	*p*-Value	mFI ≤ 1 $n = 253$ (50.0%)	mFI ≥ 2 $n = 253$ (50.0%)	*p*-Value
Mean operative time (min)[a]	347 ± 211	333 ± 210	318 ± 210	390 ± 213	0.516	322.3 ± 213.5	326.9 ± 211.5	0.809
Mean RVU	90.1 ± 47.8	93.0 ± 49.0	94.9 ± 54.5	101. ± 47.5	0.773	92.4 ± 49	95.6 ± 53.7	0.478
Mean ASA class	2.6 ± 0.6	2.9 ± 0.5	3.0 ± 0.5	3.3 ± 0.5	< **0.001**	2.63 ± 0.6	3.1 ± 0.5	< **0.001**
Mean LOS (days)[b]	6.1 ± 6.1	7.4 ± 9.0	7.8 ± 10.0	14.7 ± 19.2	< **0.001**	6.3 ± 7.2	8.6 ± 11.5	**0.007**
eLOS	228 (26.8)	158 (29.3)	74 (33.6)	16 (55.2)	**0.003**	59 (23.3)	90 (35.6)	**0.002**
Readmission	75 (8.8)	49 (9.0)	21 (9.4)	3 (10.0)	0.987	15 (5.9)	24 (9.5)	0.134
Discharge location					< **0.001**			< **0.001**
Home	720 (84.2)	426 (78.5)	163 (73.1)	17 (56.7)		210 (83)	180 (71.1)	
Nonroutine	75 (8.8)	85 (15.7)	45 (20.2)	10 (33.3)		24 (9.5)	55 (21.7)	
Unknown	60 (7.0)	32 (5.9)	15 (6.7)	3 (10.0)		19 (7.5)	18 (7.1)	
Any complications among cases	355 (24.6)	276 (28.0)	140 (30.5)	52 (63.3)	< **0.001**	92 (21.7)	192 (34.4)	**0.002**
Major complications among cases	194 (13.5)	153 (16.9)	72 (17.5)	28 (40.0)	< **0.001**	49 (12.6)	100 (20.2)	**0.023**
Reintubation	24 (2.8)	14 (2.6)	11 (4.9)	6 (20.0)	< **0.001**	5 (2.0)	17 (6.7)	**0.009**
Reoperation	64 (7.5)	46 (8.5)	21 (9.4)	6 (20.0)	0.089	19 (7.5)	27 (10.7)	0.216
Mortality	8 (0.9)	8 (1.5)	5 (2.2)	1 (3.3)	0.331	2 (0.8)	6 (2.4)	0.154
Stroke	16 (1.9)	15 (2.8)	5 (2.2)	0	0.590	4 (1.6)	5 (2.0)	0.737
Wound disruption	8 (0.9)	7 (1.3)	1 (0.4)	0	0.679	4 (1.6)	1 (0.4)	0.178
Acute renal failure	3 (0.4)	1 (0.2)	0	0	0.775	0	0	NA
Deep SSI	7 (0.8)	5 (0.9)	1 (0.4)	1 (3.3)	0.445	1 (0.4)	2 (0.8)	0.563
Organ space infection	9 (1.1)	9 (1.1)	3 (1.3)	2 (6.7)	0.070	3 (1.2)	5 (2.0)	0.476
Myocardial infarction	1 (0.1)	2 (0.4)	2 (0.9)	0	0.289	1 (0.4)	2 (0.8)	0.563
Cardiac arrest	1 (0.1)	2 (0.4)	0	0	0.637	0	0	NA
Pulmonary embolism	11 (1.3)	8 (1.5)	5 (2.2)	2 (6.7)	0.104	1 (0.4)	7 (2.8)	**0.032**
Fail to wean from ventilator > 48 h	31 (3.6)	21 (3.9)	10 (4.5)	5 (16.7)	**0.005**	5 (2.0)	15 (5.9)	**0.023**
Sepsis	11 (1.3)	12 (2.2)	6 (2.7)	4 (13.3)	< **0.001**	3 (1.2)	10 (4.0)	**0.049**
Septic shock	0	3 (0.6)	2 (0.9)	1 (3.3)	**0.005**	1 (0.4)	3 (1.2)	0.315
Minor complications	161 (17.2)	123 (18.8)	68 (24.2)	24 (56.7)	< **0.001**	43 (14.6)	92 (28.1)	< **0.001**
Superficial SSI	10 (1.2)	11 (2.0)	1 (0.4)	1 (3.3)	0.244	4 (1.6)	2 (0.8)	0.411
Urinary tract infection	10 (1.2)	8 (1.5)	7 (3.1)	2 (6.7)	**0.028**	5 (2.0)	9 (3.6)	0.278
Pneumonia	15 (1.8)	16 (2.9)	13 (5.8)	5 (16.7)	< **0.001**	3 (1.2)	18 (7.1)	< **0.001**
Transfusion	111 (13.0)	78 (14.4)	39 (17.5)	13 (43.3)	< **0.001**	26 (10.3)	52 (2.1)	**0.001**
Renal insufficiency	1 (0.1)	0	1 (0.4)	0	0.445	0	1 (0.4)	0.317
Deep vein thrombosis	14 (1.6)	10 (1.8)	7 (3.1)	3 (10.0)	**0.009**	5 (2.0)	10 (4.0)	0.190

Abbreviations: ACF, anterior cranial fossa; ASA, American Society of Anesthesiologists; eLOS, extended LOS; LOS, length of stay; mFI, modified frailty index; NSQIP, National Surgical Quality Improvement Program; RVU, relative value unit; SSI, surgical site infection.
Note: Data are reported as *n* (%), mean ± standard deviation, or as otherwise indicated.
[a]Values were missing for 2 patients; the mean was substituted.
[b]Values were missing for 10 patients; the mean was substituted.

Table 3 Multivariate analysis of complications and eLOS of unmatched patients

ACF cases odds ratio (95% confidence intervals)				
	Any complication	**Major complication**	**Minor complication**	**eLOS**
Not frail	Baseline			
Prefrail	1.03 (0.78–1.35)	1.09 (0.78–1.51)	0.99 (0.72–1.35)	0.89 (0.68–1.17)
Frail	1.02 (0.70–1.49)	0.98 (0.62–1.53)	1.21 (0.80–1.83)	0.93 (0.64–1.35)
Severely frail	**3.67 (1.60–8.44)**	2.30 (0.99–5.33)	**5.00 (2.18–11.49)**	1.76 (0.76–4.06)
Age	1.00 (0.99–1.01)	1.01 (0.99–1.02)	1.00 (0.99–1.01)	**1.01 (1.00–1.02)**
	Individual mFI-5 components			
Functional status	**3.39 (1.97–5.85)**	**3.59 (2.08–6.19)**	**3.14 (1.81–5.44)**	**3.93 (2.27–6.78)**
COPD	0.96 (0.50–1.83)	0.72 (0.32–1.61)	1.02 (0.50–2.07)	1.34 (0.72–2.49)
CHF	5.63 (0.42–74.72)	1.59 (0.10–24.59)	9.91 (0.76–128.68)	NA
Hypertension	0.93 (0.71–1.22)	0.96 (0.70–1.32)	0.99 (0.74–1.34)	**0.76 (0.59–0.99)**
Diabetes	1.08 (0.78–1.50)	0.90 (0.61–1.34)	1.23 (0.86–1.77)	1.27 (0.92–1.74)

Abbreviations: ACF, anterior cranial fossa; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; eLOS, extended length of stay; mFI, modified frailty index; NA, not available.
Note: Bold text signifies p-value < 0.05.

Table 4 Multivariate analysis of complications and eLOS of propensity score–matched patients

ACF cases odds ratio (95% confidence intervals)				
	Any complication	**Major complication**	**Minor complication**	**eLOS**
mFI ≤ 1	Baseline			
mFI > 1	1.27 (0.79–2.04)	1.07 (0.61–1.86)	1.55 (0.92–2.64)	1.08 (0.68–1.71)
Age	1.01 (0.99–1.03)	1.01 (0.99–1.02)	**1.02 (1.00–1.04)**	**1.02 (1.00–1.04)**
	Individual mFI-5 components			
Functional status	**4.94 (2.42–10.06)**	**4.68 (2.29–9.53)**	**4.80 (2.34–9.86)**	**2.92 (1.47–5.81)**
COPD	0.94 (0.42–2.11)	0.68 (0.26–1.83)	0.92 ((0.37–2.28)	1.07 (0.50–2.27)
CHF	6.27 (0.49–80.85)	1.33 (0.09–19.07)	11.50 (0.83–159.81)	NA
Hypertension	0.59 (0.33–1.06)	0.78 (0.40–1.55)	0.63 (0.33–1.24)	0.85 (0.49–1.49)
Diabetes	1.61 (0.96–2.71)	0.96 (0.54–1.72)	**1.20 (1.12–3.56)**	0.94 (0.58–1.54)

Abbreviations: ACF, anterior cranial fossa; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; eLOS, extended length of stay; mFI, modified frailty index; NA, not available.
Note: Bold text signifies p-value < 0.05.

also a significant predictor of minor complications (OR = 1.20) ($p < 0.05$).

Complication Rates and Length of Stay by Frailty, Stratified by Adult versus Elderly

A secondary analysis of complication rates in adult (18–64 years old) versus elderly ($\geq$ 65 years old) patients demonstrates benchmarks for complication rates using the NSQIP. ACF procedures in nonfrail adults experienced complications in 24% of procedures for nonfrail individuals and 27, 21, and 50% of prefrail, frail, and severely frail, respectively (►**Fig. 2**). Elderly groups experienced complications at 27, 30, 40, and 70%, respectively. LOS increased as frailty increased, with total LOS at 5.98, 7.23, 7.04, and 11 days for adults, and 6.71, 7.61, 8.58, and 16.2 days for elderly (nonfrail, prefrail, frail, and severely frail, respectively).

Discussion

Frailty and Age as Predictors of Negative Outcomes

The neurosurgical literature has demonstrated limited and mixed results in the utility of frailty as a predictor of outcomes for ACF surgery, with recent literature demonstrating frailty did not predict postoperative complications in some patients.[19] There are studies demonstrating the success of frailty in predicting negative outcomes in spinal surgery and brain tumors.[15,20–24] Henry et al[15] reported mFI-5 did not predict for complications when limited to ACF but was predictive in middle and posterior cranial fossa cases. Non-ACF studies have reported that a lack of patient frailty (i.e., lower frailty) demonstrated predictive ability within skull base cases, such as in transsphenoidal resection of pituitary tumors

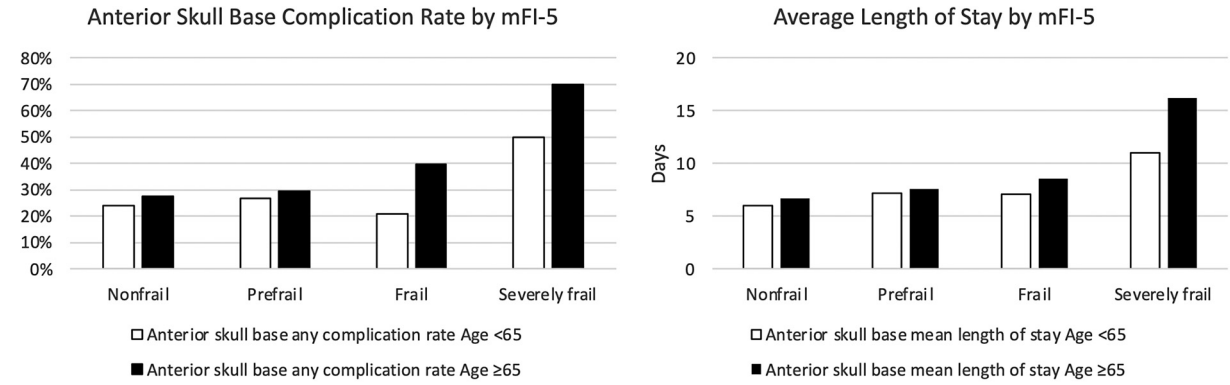

Fig. 2 Complication rates and length of stay by frailty, stratified by adult vs. elderly. (Left) Rates of any complication in adult and elderly patients; (Right) mean length of hospital stay in adult and elderly patients.

and for skull base meningiomas.[15,20,22] In comparison, other skull base studies demonstrated increased frailty associated with worse outcomes (e.g., vestibular schwannoma).[23]

Our preliminary multivariate analysis in this study showed that unmatched data suggested severe frailty has a significant predictive ability for any complications (OR = 3.67) and for minor ACF surgery complications (OR = 5.00) ($p < 0.05$). Age had a limited effect on eLOS. However, matched analysis demonstrated limited predictive ability for mFI and instead showed nonfunctional status was the most predictive of any complications, major complications, minor complications, and eLOS. These data reflect the real-world challenges of predicting outcomes in ACF surgery, and suggest functional status or some other measure of frailty is most helpful in counseling patients. To our knowledge, this is the only study that analyzed ACF procedures' outcomes using propensity score matching.

It may be possible to stratify higher-risk patients, who, according to this analysis, would consist of those with a nonindependent functional status or with more advanced age, to a higher level of care, with earlier mobilization and removal of lines/catheters and more aggressive medical therapy. This data may help guide the selection and optimization of higher-risk patients preoperatively, when applicable, and provides for patient-counseling regarding risks and outcomes.

Without accounting for, at a minimum, the same procedures and comparable case complexity, it is difficult to generalize results beyond the data set. ACF procedures are relatively rare, representing only 1,651 (0.02%) of the 9.6 million cases included in the NSQIP. This necessitates conservative use of propensity score matching, and as such our matching was limited to procedure and length of operation. Additional variables could serve to build a more comparable data set, but sufficient evidence and sample size were not available to select for these variables.

Limitations of Measuring Frailty

Although mFI-5 provides a snapshot of overall health, it is not comprehensive, and variation occurs outside the included variables. A more comprehensive frailty measure may be preferred, such as the modified 11-item frailty index (mFI-11), which builds on the mFI-5 to include a patient's history of transient ischemic attack or cerebrovascular accident, myocardial infarction, peripheral vascular disease, cerebrovascular accident with neurological deficit, angina, and impaired sensorium.[14,20] One study of the mFI-11 showed limited predictive ability in transsphenoidal pituitary tumor resection suggesting it may still be an incomplete measure of frailty in all patients.[20] The NSQIP database has not maintained records sufficient for an mFI-11 calculation beyond 2015, and because the case count for ACF was limited, it was not considered in this analysis. Lastly, the NSQIP database lacks the diagnostic codes and variables that would help clarify surgical approaches, tumor size, and surgical risk. Further validation of our findings will require additional studies.

Poor functional status is predictive of perioperative complications, particularly in meningioma resection, and our analysis underscored this significance.[9] Unmatched analysis revealed that a nonindependent functional status was predictive of the occurrence of any complications (OR = 3.39), major complications (OR = 3.59), minor complications (OR = 3.14), and eLOS (OR = 3.93) ($p < 0.05$). After propensity score matching, these results were even stronger, with ORs of 4.94, 4.68, and 4.80 for any, major, and minor complications, respectively. Identifying poor functional status may be a practical tool for surgeons evaluating patients preoperatively.

Complication Rates and Length of Stay in Adult versus Elderly

Complications after ACF procedures are not rare, and national benchmarks have not been established. An analysis in 1996 by Deschler et al[3] identified a 40% complication rate in a sample of 52 procedures, with infection and cerebrospinal fluid leaks being the most common. Another retrospective review of 115 patients identified a rate of major complications at 35%.[25] The NSQIP database, and this compilation of ACF cases, offered an opportunity to analyze these complication rates,

particularly in relation to this study, with adults defined as those under 65 years and elderly as those 65 years and older. Nonfrail adults demonstrated a 24% complication rate, compared with 27% in the nonfrail elderly population. Within the elderly population, these rates increased to 30, 40, and 70%, respectively, for prefrail, frail, and severely frail. LOS follows a similar trend, with adults having an average LOS of 5.98, 7.23, 7.04, and 11 days for nonfrail, prefrail, frail, and severely frail, respectively, while their respective counterparts in the elderly population were 6.71, 7.61, 8.58, and 16.2 days. As a comparatively large and diverse national database, this can help to establish baseline complication rates and LOS in ACF procedures.

Limitations

Although the strengths of this study include the multicenter collection of data, institutions may vary in how they code cases, and data from NSQIP can only aggregate broad categories of patients. Therefore, this analysis consists of all tumor types identified within ACF cases in the NSQIP, as well as all approaches that would be appropriate for procedures of the ACF. Patients with more severe disease may be recommended for more conservative approaches, and identification of these cases is limited in the use of the NSQIP data set. It is possible this could bias the statistical results. Additionally, errors in data entry can skew results. An audit of participating sites in the database demonstrated a disagreement rate of approximately 2%.[17] Additionally, the NSQIP is limited to the 30-day postoperative period, so outcomes outside this period are not considered. There is also the possibility of significant regional variation in this data, which cannot be accounted for by the present data set. Finally, the NSQIP data represented a relatively small number of patients in the higher age and frailty groups, limiting which data analysis was possible and necessitating the consolidation of higher frailty into a single category, mFI-5 of 3 or greater.

Conclusion

Our results suggest increased frailty, as measured by mFI-5 may not be predictive of outcome in ACF procedures after adjusting for surgical risk. Moreover, patient functional status was more useful in predicting complications and LOS. Patient guidance for ACF procedures certainly relies on significant clinical judgment and this data may aid in that decision-making. Further study is necessary to validate these findings in specific clinical scenarios.

Conflict of Interest
None declared.

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References

1 Horowitz PM, DiNapoli V, Su SY, Raza SM. Complication avoidance in endoscopic skull base surgery. Otolaryngol Clin North Am 2016;49(01):227–235
2 Wagenmann M, Scheckenbach K, Kraus B, Stenin I. Complications of anterior skull base surgery [in German]. HNO 2018;66(06): 438–446
3 Deschler DG, Gutin PH, Mamelak AN, McDermott MW, Kaplan MJ. Complications of anterior skull base surgery. Skull Base Surg 1996;6(02):113–118
4 Kuan EC, Badran KW, Yoo F, et al. Predictors of short-term morbidity and mortality in open anterior skull base surgery. Laryngoscope 2019;129(06):1407–1412
5 Almeida JP, de Albuquerque LA, Dal Fabbro M, et al. Endoscopic skull base surgery: evaluation of current clinical outcomes. J Neurosurg Sci 2019;63(01):88–95
6 Rezende GL, Neto ORM, Kückelhaus SAS. Morbidity in the postoperative follow-up of endoscopic anterior skull base surgery. Rev Bras Otorrinolaringol (Engl Ed) 2021;87(06): 689–694
7 Güldner C, Zimmermann AP, Diogo I, Werner JA, Teymoortash A. Age-dependent differences of the anterior skull base. Int J Pediatr Otorhinolaryngol 2012;76(06):822–828
8 Lawrence LA, Baker AB, Nguyen SA, Karnezis TT, Soler ZM, Schlosser RJ. Predictors of 30-day morbidity and mortality in transnasal microscopic pituitary tumor excision. Int Forum Allergy Rhinol 2016;6(02):206–213
9 Przybylowski CJ, Shaftel KA, Hendricks BK, et al. Perioperative complication profile of skull base meningioma resection in older versus younger adult patients. J Neurol Surg B Skull Base 2021;83 (04):411–417
10 Rizvi ZH, Ferrandino R, Luu Q, Suh JD, Wang MB. Nationwide analysis of unplanned 30-day readmissions after transsphenoidal pituitary surgery. Int Forum Allergy Rhinol 2019;9(03):322–329
11 Boling CC, Karnezis TT, Baker AB, et al. Multi-institutional study of risk factors for perioperative morbidity following transnasal endoscopic pituitary adenoma surgery. Int Forum Allergy Rhinol 2016;6(01):101–107
12 Hunsaker J, Khan M, Makarenko S, Evans J, Couldwell W, Karsy M. Prediction of readmission and complications after pituitary adenoma resection via the National Surgical Quality Improvement Program (NSQIP) database. Cureus 2021;13(05): e14809
13 Leven DM, Lee NJ, Kim JS, et al. Frailty is predictive of adverse postoperative events in patients undergoing lumbar fusion. Global Spine J 2017;7(06):529–535
14 Subramaniam S, Aalberg JJ, Soriano RP, Divino CM. New 5-factor modified frailty index using American College of Surgeons NSQIP data. J Am Coll Surg 2018;226(02):173–181.e8
15 Henry RK, Reeves RA, Wackym PA, Ahmed OH, Hanft SJ, Kwong KM. Frailty as a predictor of postoperative complications following skull base surgery. Laryngoscope 2021;131(09): 1977–1984
16 Goshtasbi K, Abiri A, Lehrich BM, et al. Association between modified frailty index and surgical outcomes in intradural skull base surgery. J Clin Neurosci 2021;91:255–259
17 ACS NSQIP Participant Use Data File. 2022. Accessed February 16, 2022 at: http://www.facs.org/quality-programs/acs-nsqip/participant-use
18 Khuri SF. The NSQIP: a new frontier in surgery. Surgery 2005;138 (05):837–843
19 Castle-Kirszbaum M, Wang YY, King J, Goldschlager T. Frailty does not preclude surgical success after endoscopic transsphenoidal surgery for pituitary adenomas. Pituitary 2021;24(06):922–929
20 Nguyen S, Kim RB, Cox P, et al. Impact of modified Frailty Index-11 (mFI-11) on postoperative complications in patients

undergoing transsphenoidal resection of pituitary tumors: analysis of 2006-2014 ACS-NSQIP database. J Clin Neurosci 2021;92:22–26

21 Harland TA, Wang M, Gunaydin D, et al. Frailty as a predictor of neurosurgical outcomes in brain tumor patients. World Neurosurg 2020;133:e813–e818

22 Kolakshyapati M, Ikawa F, Abiko M, et al; Alumni Association Group of the Department of Neurosurgery at Hiroshima University. Multivariate risk factor analysis and literature review of postoperative deterioration in Karnofsky Performance Scale score in elderly patients with skull base meningioma. Neurosurg Focus 2018;44(04):E14

23 Tang OY, Bajaj AI, Zhao K, et al. Association of patient frailty with vestibular schwannoma resection outcomes and machine learning development of a vestibular schwannoma risk stratification score. Neurosurgery 2022;91(02):312–321

24 Shahrestani S, Brown NJ, Nasrollahi TS, et al. Evaluating the predictive value of comorbidity indices in pituitary surgery: a mixed-effects modeling study using the Nationwide Readmissions Database. J Neurosurg 2022;•••:1–9

25 Shah JP, Kraus DH, Bilsky MH, Gutin PH, Harrison LH, Strong EW. Craniofacial resection for malignant tumors involving the anterior skull base. Arch Otolaryngol Head Neck Surg 1997;123 (12):1312–1317