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ORIGINAL RESEARCH

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Frailty in middle cranial fossa approach for encephalocele or cerebrospinal fluid leak repair

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Abstract

Objective: The modified 5-item frailty index (mFI-5) is a concise, comorbidity-based risk stratification tool that can predict adverse outcomes after surgery. The goal of this study was to understand the frailty of patients undergoing surgery for temporal encephalocele or cerebrospinal fluid (CSF) leak and the utility of mFI-5 for predicting increased post-operative outcomes.

Methods: A retrospective review of adults with temporal encephalocele or CSF leak who underwent middle cranial fossa (MCF) approach craniotomies with or without mastoidectomy from January 2015 through August 2021 at a tertiary care academic medical center was performed. Patients who underwent additional surgeries or extended surgical approaches were excluded. The mFI-5 was calculated for all patients. Demographic and clinical data were obtained from the medical record.

Results: Thirty-six patients underwent 40 MCF approach craniotomies for temporal encephalocele or CSF leak, including three revision cases and one patient with sequential bilateral operations. Mean age was 54.1 ± 10.8 years, and 66.7% were female. In the univariable regression analysis, mFI-5 score, age, and procedure time use were significantly associated with increased hospital length of stay (LOS) but not increased intensive care unit (ICU) LOS. Anesthesia time and lumbar drain were significantly associated with increased hospital LOS and ICU LOS, and they remained significantly associated with increased hospital LOS in the multivariable model.

Conclusion: Frailty is associated with increased hospital LOS stay among patients undergoing MCF approach for CSF leak or encephalocele. Reducing anesthesia time and avoiding lumbar drain use are potentially modifiable risk factors that can reduce the LOS and associated costs.

Level of Evidence: 4.

KEYWORDS
frailty, length of stay, postoperative complications, skull base

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1 | INTRODUCTION

Spontaneous cerebrospinal fluid (CSF) leaks occur in the absence of trauma, surgery, or tumors and are associated with female sex, obesity, increased intracranial pressure, and obstructive sleep apnea.[1] In the lateral skull base, CSF leaks and encephaloceles occur along the tegmen tympani and tegmen mastoideum and can present as a middle ear effusion and aural fullness.[2,3]

The rates of craniotomy for spontaneous CSF leak repair are increasing.[4] Spontaneous CSF leaks have low rates of spontaneous resolution. Surgical repair of spontaneous leak repair by a middle cranial fossa (MCF) approach or combined approach with MCF and mastoidectomy (MCF-M) is generally an effective treatment with low morbidity.[5,6] Adverse outcomes after surgical repair for spontaneous CSF otorrhea have been associated with an abnormally thin tegmen,[7] and elevated intracranial pressure is associated with the need for revision surgery or shunt to resolve spontaneous CSF leaks.[8] Given the aging population and the need for risk stratification, the concept of frailty has been developed to describe a patient's physiologic, rather than chronologic age.[9]

Frailty has been used to quantify health status and predict surgical outcomes and complications. The modified frailty index (mFI) was developed using 11 factors in the National Surgical Quality Improvement Program (NSQIP) by the American College of Surgeons to assess morbidity and mortality across surgical specialties. The newer 5-item modified frailty index (mFI-5) was created in response to changes to NSQIP variables and removal of previously used factors. The mFI-5 has been shown to be predictive of postoperative complications.[10] It has been used to study complications in settings including thyroidectomy for multinodular goiter,[11] short-term surgical outcomes following complex head and neck surgery,[12] perioperative risk in head and neck microvascular reconstruction,[13] and postoperative complications after skull base surgery.[14] The objective of this study was to assess the rate of complications after middle fossa craniotomy for repair of spontaneous CSF leak or encephalocele and evaluate the ability of the mFI-5 to predict the risk of increased length of stay or added morbidity after surgery. We hypothesized that increased mFI-5 score would be associated with increased length of stay.

2 | MATERIALS AND METHODS

A retrospective review was performed for all adult patients with temporal encephalocele or CSF leak who underwent MCF approach craniotomies with or without mastoidectomy from January 2015 through August 2021 at the University of Nebraska Medical Center. Current Procedural Terminology (CPT) codes 61590 and 61591, and International Classification of Diseases, Tenth Revision (ICD-10) codes Q01.8 (encephalocele of other sites), Q01.9 (encephalocele, unspecified), and G96.0 (CSF leak) were used to identify patients from the electronic medical record.

Demographic and clinical data including sex, age, race, ethnicity, body mass index (BMI), beta-2 transferrin testing results, and surgical history were collected. The elements of the mFI-5 were collected and included: insulin-dependent or noninsulin-dependent diabetes mellitus, hypertension requiring medication, congestive heart failure (CHF) within 30 days before surgery, history of chronic obstructive pulmonary disease (COPD) or pneumonia, and non-independent functional health status (partially or totally dependent) at the time of surgery. Each variable was assigned 1 point and the mFI-5 score was calculated for each patient based on the sum of each of these five categories from 0 (no variables present) to 5 (all variables present). Frailty was subdivided based on mFI-5 score with mFI-5 $= 0$ classified as robust, mFI-5 $= 1$ as prefrail, and mfI-5 ≥ 2 as frail. Operative details including surgical indication and approach, anesthesia time (measured from time of induction to time of extubation), and procedure time were collected. Patients who underwent additional surgeries under the same anesthesia or extended surgical approaches were excluded.

Clinical outcomes and complications were defined a priori based on previous NSQIP studies as well as complications pertinent to MCF approach craniotomy. The primary endpoints were hospital length of stay (LOS) and intensive care unit (ICU) LOS. Secondary endpoints included intubation days, lumbar drain placement, duration of lumbar drain use, 30-day readmission, 30-day mortality, surgical site infection (SSI), central line-associated blood stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), pneumonia, pulmonary embolism (PE), renal insufficiency, acute renal failure (ARF), stroke/cerebrovascular accident (CVA) with neurologic deficit, cardiac arrest requiring (CPR), myocardial infarction (MI), bleeding requiring transfusion, deep vein thrombosis (DVT), sepsis, septic shock, and non-home discharge. Discharge to a non-home facility included discharge to an acute care facility, rehabilitation facility, or skilled or unskilled nursing facility.

Continuous variables were reported as mean and standard deviation (SD) if normally distributed or median and range if not normally distributed. Categorical variables were summarized as percentages and analyzed with Fisher's exact test. Analysis of continuous data was made with ANOVA with post-hoc Tukey tests. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to determine factors associated with prolonged hospital LOS, which was defined as at least 1 day more than the median hospital LOS. Multivariable linear regression was performed using hospital and ICU LOS as the dependent variables. Collinearity was defined as a variance inflation factor (VIF) of <1 or >10.

Statistical analysis was performed in R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). An $\alpha = .05$ was used to determine statistical significance for all statistical tests. Institutional review board approval was obtained from the University of Nebraska Medical Center (IRB# 412-19-EX).

3 | RESULTS

There were 36 patients identified who underwent 40 extradural MCF or combined MCF-M approaches for spontaneous CSF leak and/or

TABLE 1 Demographics and clinical characteristics

	Overall	Robust	Pre-frail	Frail	*p* value
Sex, *n* (%)					.15[a]
Male	14 (35.0)	2 (15.3)	3 (33.3)	9 (50.0)	
Female	26 (65.0)	11 (84.6)	6 (66.7)	9 (50.0)	
Age (mean ± SD)	54.9 ± 11.4	52.1 ± 10.5	49.5 ± 12.2	59.7 ± 10.3	**.046**[b]
BMI (median [IQR])	36.1 (29.8–42.0)	29.9 (29.5–34.4)	39.5 (29.8–48.6)	37.4 (35.8–41.7)	.15[b]
Race					.22[a]
White, *n* (%)	34 (85.0)	11 (84.6)	8 (88.9)	15 (83.3)	
Black, *n* (%)	4 (10.0)	0 (0.0)	1 (11.1)	3 (16.7)	
Other, *n* (%)	2 (5.0)	2 (15.4)	0 (0.0)	0 (0.0)	
Ethnicity, *n* (%)					.80[a]
Hispanic	4 (10.0)	2 (15.4)	1 (11.1)	1 (5.6)	
Non-hispanic	36 (90.0)	11 (84.6)	8 (88.9)	17 (94.4)	
mFI-5 factors, *n* (%)					**<.001**[a]
Insulin-dependent or noninsulin-dependent diabetes mellitus	15 (37.5)	0 (0.0)	2 (22.2)	13 (72.2)	
HTN requiring medication	25 (62.5)	0 (0.0)	7 (77.7)	18 (100.0)	
Partially dependent or totally dependent functional health status	3 (7.5)	0 (0.0)	0 (0.0)	3 (16.7)	
History of pneumonia or COPD	5 (12.5)	0 (0.0)	0 (0.0)	5 (27.8)	
Congestive heart failure within 30 days of surgery	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	
Surgical approach, *n* (%)					.29[a]
MCF alone	16 (40.0)	3 (23.8)	4 (44.4)	9 (50.0)	
MCF-mastoidectomy	24 (60.0)	10 (76.9)	5 (55.6)	9 (50.0)	
Mastoidectomy, *n* (%)					
Prior mastoidectomy	11 (27.5)	5 (38.5)	1 (11.1)	5 (27.8)	.44
New/revision mastoidectomy	20 (50.0)	6 (46.2)	5 (55.6)	9 (50.0)	>.99
Lumbar drain, *n* (%)					
Lumbar drain placed	8 (20.0)	2 (15.4)	1 (11.1)	5 (27.8)	.68

Note: Percentages are calculated out of column totals. Bold values denote statistical significance.
Abbreviations: COPD, chronic obstructive pulmonary disease; HTN, hypertension; IQR, interquartile range; MCF, middle cranial fossa; *n*, number; SD, standard deviation.
[a]Fisher exact test between robust, pre-frail, and frail groups.
[b]ANOVA between robust, pre-frail, and frail groups.

temporal encephalocele, including three revision cases and one patient with sequential bilateral operations. A combined MCF-M approach was used in 24 cases (60.0%). Nineteen (47.5%) cases had both CSF leak and encephalocele, 35.0% had encephalocele without CSF leak, and 22.5% had CSF leak without encephalocele.

The decision regarding which approach to use was made by the operating surgeons based on the size, location, and number of defects in the skull base. Among the 24 operations in which a mastoidectomy approach was used, 13 (54.2%) were for due to encephalocele on the ossicles or in the antrum, 6 (25.0%) were for evidence of mastoiditis, and 5 (20.8%) were for solely for inspection and repair from below. Operations were performed on the right side in 31 cases (77.5%, including the three revision cases) and on the left side in nine cases (22.5%). All repairs were performed with a multilayer technique using a combination of repair materials including fascia, cartilage, bone, fibrin glue, and collagen dura substitute.

The mean (SD) age at surgery was 54.9 (11.4) years and included operations on women in 26 (65.0%) cases and men in 14 (35.0%) cases. There were 13 patients with a mFI-5 of 0 (32.5%), 9 with mFI-5 of 1 (22.5%), 14 with mFI-5 of 2 (35.0%), and 4 with mFI-5 of 3 (10.0%). Median BMI was 36.1 kg/m^2 (interquartile range [IQR] 29.8–42.0 kg/m^2), and 27 patients (67.5%) were obese (BMI ≥30 kg/m^2), including 9 (22.5%) with class II obesity and 13 (32.5%) with class III obesity. Three (7.5%) operations were revisions for recurrent CSF leak a median of 13 months (range 6–22 months) after a prior repair. Table 1 shows the demographics and clinical characteristics.

TABLE 2 Hospital length of stay stratified by mFI-5 score

	Hospital LOS	
Number of comorbidities	Mean (SD)	Median (IQR)
0	2.9 (2.2)	2 (2–3)
1	3.0 (1.3)	3 (2–4)
2	3.6 (1.5)	3.5 (2–5)
3	7 (4.1)	5.5 (4.75–7.75)
Overall	3.6 (2.3)	3 (2–5)

Abbreviations: IQR, interquartile range; LOS, length of stay; SD, standard deviation.

TABLE 3 Perioperative events and complications

Outcome	Quantity
ICU LOS (median [IQR])	1 (1 to 1)
Hospital LOS (median [IQR])	3 (2 to 5)
Lumbar drain use	8 (20.0)
Lumbar drain days (mean ± SD)	4.25 ± 1.6
Surgical site infection	1 (2.5)
Renal insufficiency	1 (2.5)
Non-home discharge	3 (7.5)
30-day readmission	2 (5.0)

Note: There were no instances of intubation after surgery, central line-associated blood stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), pneumonia, pulmonary embolism, acute kidney injury, stroke/cerebrovascular accident (CVA) with neurologic deficit, cardiac arrest requiring (CPR), myocardial infarction, bleeding requiring transfusion, deep vein thrombosis, sepsis, or 30-day mortality. Categorical variables are reported by number, with values in parentheses representing percentages. Continuous variables are represented as mean ± SD or median (IQR).
Abbreviations: ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; *n*, number of patients; SD, standard deviation.

3.1 | Post-operative hospital course and complications

All patients were extubated after their operations and none required re-intubation. The decision to use a lumbar drain for CSF diversion was made by the neurosurgeon at the time of the operation. Eight (20.0%) of operations included lumbar drain placement for an average of 4.25 ± 1.6 days.

The median hospital length of stay was 3 days (IQR 2–5 days), with a mean (SD) of 3.6 (2.3) days. Median ICU LOS was 1 day (IQR 1 to 1 days, range 0–3 days). Table 2 shows the hospital LOS stratified by the number of mFI-5 comorbidities. There was a statistically significant difference between groups ($p = .01$), with post-hoc Tukey tests showing statistically significant differences between patients with three comorbidities compared to groups with fewer comorbidities, with adjustment for multiple comparisons (3 vs. 0 comorbidities, adjusted $p = .008$; 3 vs. 1, adjusted $p = .01$; 3 vs. 2, adjusted $p = .03$). Lumbar drain use was associated with a statistically significant increase in hospital LOS, with a median hospital LOS of 5.5 days (IQR 4.75–6.75 days) compared to a median hospital LOS of 2 days (IQR 2–4 days) among patients without lumbar drains ($p = .007$). Lumbar drain use had increased odds of prolonged hospital LOS (odds ratio [OR] 14.3, 95% CI 1.53–721.42, $p = .006$). Lumbar drain use was not associated with increased ICU LOS ($p = .10$). Combined MCF-M approach was not associated with increased hospital LOS ($p = .14$) or ICU LOS ($p = .42$).

Besides prolonged hospital stay for bedrest after intraoperative lumbar drain placement, patients were noted to have barriers to discharge including pain control ($n = 5$), working with physical therapy and/or occupational therapy ($n = 3$), and case management/insurance authorization for facility placement or home health care ($n = 3$). Three patients were discharged to a skilled nursing facility (SNF). One of these patients was living at a SNF prior to surgery, and the other two were discharged to a SNF for post-operative rehabilitation.

There were few post-operative complications (Table 3). There were no reported occurrences of CLABSI, CAUTI, pneumonia, PE, renal insufficiency, acute renal failure, stroke/CVA, cardiac arrest/MI, bleeding requiring transfusion, DVT, sepsis, or septic shock. Two patients had readmissions within 30-days after surgery. One patient was readmitted for treatment of a surgical site infection due to MRSA that required a wound washout. The other patient was admitted for post-operative treatment after a separate surgery. No patient had mortality within 30 days after surgery.

3.2 | Regression analysis

In the univariable regression analysis, mFI-5 score was significantly associated with increased hospital LOS ($p = .01$, $R^2 = 0.13$) but not increased ICU LOS ($p = .07$, $R^2 = 0.06$). Procedure time ($p = .02$, $R^2 = 0.10$) and anesthesia time ($r = 0.007$, $R^2 = 0.16$) were both associated with an increased hospital LOS. Anesthesia time ($p = .03$, $R^2 = 0.10$) but not surgery time ($p = .06$, $R^2 = 0.07$) was statistically significantly associated with increased ICU LOS. Age at time of surgery was associated with increased hospital LOS ($p = .02$, $R^2 = 0.11$) but not ICU LOS ($p = .45$, $R^2 = -0.01$). BMI was not statistically significantly associated with ICU LOS ($P = 0.07$) or hospital LOS ($p = .87$) (Table 4A). Age and mFI-5 score were positively correlated ($p = .02$, $r_s = 0.37$). There was not a significant correlation between anesthesia time and age ($p = .14$, $r_s = 0.24$) or between anesthesia time and BMI ($p = .95$, $r_s = 0.01$). Use of a lumbar drain was significantly associated with increased hospital ($p < .001$) and ICU LOS ($p = .03$).

Multiple regressions were performed to model hospital LOS using variables that were statistically significantly associated with hospital LOS in the univariable analysis. Anesthesia time and lumbar drain use remained statistically significant predictors of hospital LOS (Table 4B). The overall model predicted half of the variation in hospital LOS (adjusted $R^2 = 0.50$, $p < .001$). No factors were statistically significant predictors of ICU LOS. Anesthesia time and surgery time were highly

TABLE 4 Univariable and multivariable regression

(A) Univariable regression of anesthesia and procedure time						
	Hospital LOS			ICU LOS		
Factor	Coefficient (*B*)	Standard error	*p* value	Coefficient (*B*)	Standard error	*p* value
mFI-5 score	0.2017	0.0919	**.03**	0.1519	0.0803	.07
Age	0.0747	0.0307	**.02**	0.0057	0.0074	.45
BMI	0.0057	0.0360	.87	0.0146	0.0079	.07
Anesthesia time	0.0188	0.0065	**.007**	0.0035	0.0015	**.03**
Procedure time	0.0168	0.0070	**.02**	0.0033	0.0016	.06
Lumbar drain use	3.4687	0.7384	**<.001**	0.5000	0.1963	**.02**

(B) Multivariable regression of significant predictors on univariable analysis			
	Hospital LOS		
Factor	Coefficient (*B*)	Standard error	*p* value
mFI-5 comorbidities	0.4469	0.2857	.13
Age	0.0307	0.0255	.24
Anesthesia time	0.0346	0.0153	**.03**
Procedure time	−0.0309	0.0163	.07
Lumbar drain use	3.2222	0.7263	**<.001**

Note: Significant predictors on univariable analysis were used to calculate the multivariable regression. Units used to calculate regression coefficients: min (procedure and anesthesia time), kg/m^2 (BMI), years (age).
Abbreviations: ICU, intensive care unit; LOS, length of stay.

correlated for both the hospital and ICU LOS analysis (VIF between 9 and 10 for both). VIF for other factors was between 1 and 2.

4 | DISCUSSION

Frailty, age, and procedure time were associated with increased hospital LOS but not ICU LOS among patients undergoing MCF or MCF-M approach for the treatment of temporal encephalocele or spontaneous CSF leak, while anesthesia time and lumbar drain use were associated with both increased hospital and ICU LOS in the univariable analysis. Anesthesia time and lumbar drain use were the only factors that remained statistically significant in the multivariable analysis. The rate of post-operative complications was low, with most complications occurring 0 or 1 time, and with only 30-day readmission and non-home discharge occurring in two patients. Due to the low rates of these events, no analysis was performed to estimate the risk of these complications. The positive association between patients' mFI-5 scores and increases in hospital LOS has previously been reported after vestibular schwannoma resection,[15] head and neck microvascular reconstruction,[13] thyroidectomy,[11] and complex head and neck surgery.[12] In each of these studies, the mFI-5 score has been shown to be a better predictor for postoperative complications than patient age.

Defects in the tegmen and petromastoid segments of the temporal bone have been found in up to 34% of histologic temporal bone studies.[16,17] Multiple theories have been proposed to explain these skull base defects including aberrant arachnoid granulations into the middle ear or petrous air cells, atrophy of the tegmen caused by CSF pulsation, and excessive resorption of bone during pneumatization.[18] Spontaneous CSF leak and encephalocele are associated with increased BMI.[19,20] Patients with idiopathic intracranial hypertension (IIH) have similar demographics to those with spontaneous CSF leak or encephalocele, and IIH has been suggested as a potential cause or additional risk factor for spontaneous CSF leak or encephalocele.[21] Obesity was common in our sample, with 67.5% of patients being obese and 92.5% overweight or obese. Only three (7.5%) patients had a normal BMI, and none were underweight.

Operative repair of skull base dehiscences is generally recommended to avoid the increased risk of intracranial infection such as meningitis.[22] Multiple surgical approaches have been used including a transmastoid approach with tegmen reconstruction or middle ear/mastoid obliteration, middle fossa craniotomy, or a combined mastoid and middle fossa approach, with the choice of surgical approach determined by the size and location of skull base defect, patient health and hearing status, and surgeon preference.[5,22–25] The MCF approach has the advantage of being able to expose the entire floor of the MCF via an extradural dissection to identify bony dehiscences and any dural defects, affording less risk of surgical failure.[3,18,26,27] Rates of operative success in repairing the CSF fistula and closing the air-bone gap are high, with an average failure rate of 6.6% reported.[1,28]

Few post-operative complications or adverse outcomes were noted in the present study. Only one patient had a 30-day readmission for a surgical site infection requiring a return to the OR for wound washout. On review of the patient charts, the only other

30-day readmission was for a patient who was admitted following a separate, planned surgery. Of the three patients with non-home discharge, one returned to his previous living arrangement at a SNF. Three (7.5%) patients required revision surgery for recurrent CSF leak a median of 13 months (range 6–22 months) after their first repair.

Frailty on average increases with age as patient accumulate health deficits, however, frailty becomes more variable with age.[29–31] Thus, while age can be predictive of perioperative complications, age by itself can be less predictive of morbidity and mortality. Our data showed that increasing age predicted increased hospital LOS in the univariable analysis, but this relationship was no longer statistically significant in the multivariable analysis, and age was not predictive of perioperative adverse events.

Lumbar drain for CSF diversion was used in 20% of all operations in the present series, including one of three (33.3%) revision cases. Consistent with prior research, lumbar drain use was associated with increased hospital LOS.[6] Intraoperative lumbar drain placement aids temporal lobe relaxation but exposes patients to additional complications including headache, meningitis, pneumocephalus.[5,6] Anterior endoscopic skull base repair and MCF approach temporal bone repair for CSF leak without lumbar drain placement have been promoted to reduce the length of stay and cost of care, in light of the high success rate of surgical repair without the use of a lumbar drain.[1,6,32,33] Avoiding lumbar drain placement is a modifiable risk factor that can decrease LOS, however, lumbar drain use was not associated with adverse events in our series.

In cases of surgical failure due to recurrent CSF leak, evaluation and treatment of causes of elevated intracranial pressure have been recommended. Comorbid IIH may not become evident until after repair of a CSF fistula due to the egress of CSF decreasing intracranial pressure. Treatments with weight loss, acetazolamide, or ventriculoperitoneal shunting have been recommended in patients found to have IIH.[1,2,8,23] Additionally, obstructive sleep apnea (OSA) is more common among patients with spontaneous CSF leak, with transient spikes in intracranial pressure occurring during obstructive apnea episodes, making OSA a potential modifiable risk factor for CSF leak treatment failure.[34–36] Evaluation with magnetic resonance or computed venography (MRI or CTV) has been advocated to evaluate for bilateral transverse venous sinus stenosis (TVSS) as an independent risk factor for CSF leak recurrence.[37,38] Ultimately, due to the low rate of resolution of spontaneous CSF leak without operative repair, these patients generally undergo surgery, as did the three patients in the present study who had recurrent CSF leak.[22] Given the increasing rates of spontaneous CSF leak, there is a need to accurately risk stratifying these patients.[4]

5 | CONCLUSION

Operative repair of CSF leak or encephalocele using an MCF or combined MCF-M approach resulted in few perioperative complications. Frailty, as measured by the mFI-5 score, and age were associated with increased hospital LOS but not ICU LOS. The potentially modifiable risk factors anesthesia time and lumbar drain use were associated with an increase in both hospital and ICU LOS in the univariable analysis and were the only variables that remained statistically significantly associated with increased hospital LOS in the multivariable analysis.

CONFLICT OF INTEREST

None.

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