Frailty as a Predictor of Morbidity and Mortality in Inpatient Head and Neck Surgery

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IMPORTANCE The increasing number of elderly and comorbid patients undergoing surgical procedures raises interest in better identifying patients at increased risk of morbidity and mortality, independent of age. Frailty has been identified as a predictor of surgical complications.

OBJECTIVE To establish the implications of frailty as a predictor of morbidity and mortality in inpatient otolaryngologic operations.

DESIGN Retrospective review of medical records.

SETTING National Surgical Quality Improvement Program (NSQIP) participating hospitals.

PATIENTS NSQIP participant use files were used to identify 6727 inpatients who underwent operations performed by surgeons specializing in otolaryngology between 2005 and 2010. The study sample was 50.3% male and 10.2% African American, with a mean (range) age of 54.7 (16-90) years.

MAIN OUTCOMES AND MEASURES A previously described modified frailty index (mFI) was calculated on the basis of NSQIP variables. The effect of increasing frailty on morbidity and mortality was evaluated using univariate analysis. Multivariate logistic regression was used to compare mFI with age, ASA, and wound classification.

RESULTS The mean (range) mFI was 0.07 (0-0.73). As the mFI increased from 0 (no frailty-associated variables) to 0.45 (5 of 11) or higher, mortality risk increased from 0.2% to 11.9%. The risk of Clavien-Dindo grade IV complications increased from 1.2% to 26.2%. The risk of all complications increased from 9.5% to 40.5%. All results were significant at \( P < .001 \).

In a multivariate logistic regression model to predict mortality or serious complication, mFI became the dominant significant predictor.

CONCLUSIONS AND RELEVANCE The mFI is significantly associated with morbidity and mortality in this retrospective survey. Additional study with prospective analysis and external validation is needed. The mFI may provide an improved understanding of preoperative risk, which would facilitate perioperative optimization, risk stratification, and counseling related to outcomes.
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The population of Americans older than 65 years is expected to double to 80 million from 2010 to 2040, and the prevalence of diabetes mellitus continues to increase. Patients typically accumulate functional and physiologic deficits as they age. All these factors lead to an increasing number of elderly and comorbid patients undergoing surgical procedures, raising interest in better identifying patients at increased risk of morbidity and mortality, independent of age. Piccirillo et al demonstrated markedly decreased survival in patients with laryngeal cancer with increased comorbidities as calculated using the Kaplan-Feinstein comorbidity index. Singh et al validated these findings using the simpler Charlson comorbidity index in 88 patients 45 years and younger. Frailty, which is defined as a decrease in the physiologic reserves, as well as multisystem impairments that are separate from the normal process of aging, has been identified as a predictor of surgical complications.

Frailty has been measured differently throughout the literature. There are 2 main operational definitions, the physical phenotype and the multidomain phenotype. The physical phenotype was described by Fried et al as the presence of unintentional weight loss, exhaustion, weakness (low grip strength), slow walking speed, and low level of physical activity. The multidomain phenotype is based on a comprehensive geriatric assessment, such as the Canadian Study of Health and Aging Frailty Index (CSHA-FI). This index consists of 70 variables that measure deficits in the physical, cognitive, functional, and social realms. It is referred to as a deficit accumulation index.

To our knowledge, a frailty index has not been applied in otolaryngology. A modified frailty index (mFI), created on the basis of the CSHA-FI, has proven effective in various surgical populations but not specifically in the head and neck surgery realm. Farhat et al showed the mFI to be highly associated with morbidity and mortality in elderly patients undergoing emergent surgical procedures. Karam et al found similar associations in vascular surgery. Obeid et al found that the rate of death or serious complication increased from 3.2% to 56.3% with increasing mFI in patients undergoing colectomy. The expansion of the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) has provided a vast database of otolaryngologic operations. We hypothesized that the mFI would be an accurate predictor of mortality, serious complications, and overall complications in inpatients undergoing head and neck surgery.

Methods

The NSQIP participant use files for the period 2005 through 2010 were used to identify inpatient head and neck surgical procedures performed by surgeons specializing in otolaryngology. Inpatients were selected because they have higher mean mFI scores than outpatients. The NSQIP is a national data set. At each participating site, a trained clinical nurse reviewer collects data on more than 136 variables including demographic characteristics, preoperative risk factors, intraoperative variables, and 30-day postoperative outcomes. The data were obtained in compliance with the NSQIP data use agreement under supervision of our institutional review board.

The mFI used in our study was created by Saxton and Velanovich by mapping 11 variables present in the CSHA-FI to 15 variables in the NSQIP data set. Previous reports had demonstrated the validity of the CSHA-FI with as few as 10 of its original 70 variables. An mFI score was calculated for each patient by dividing the number of variables present by the total number assessed (n/11). The 11 variables assessed were diabetes mellitus, functional status index of 2 or higher, chronic obstructive pulmonary disease or pneumonia, congestive heart failure, myocardial infarction, percutaneous coronary intervention and/or stenting or angina, hypertension requiring medication, peripheral vascular disease or ischemic rest pain, impaired sensorium, transient ischemic attack or cerebrovascular accident, and cerebrovascular accident with deficit. Functional status refers to the patient’s level of independence in performing activities of daily living (ADLs) in the 30 days prior to surgery, defined as bathing, feeding, dressing, using the toilet, and mobility. Functional status 1 is independent; the patient does not require any assistance from another person for any ADLs. Functional status 2 is partially dependent; the patient requires some assistance from another person. Functional status 3 is totally dependent. The variables were selected on the basis of availability in the NSQIP data set and correlation to the CSHA-FI. The variables are available in records of any routine history and physical examination, without any special testing. The CSHA-FI and our mFI are given in Figure 1 and Figure 2.

Patients with rare high mFI scores (>0.44) were grouped together into a high-frailty cohort to decrease the risk of poor cohort representation and unanticipated variability associated with small group sizes.

Thirty-day postoperative outcomes were identified in the NSQIP data set. Our primary outcomes were Clavien-Dindo grade IV complications and mortality. Additional outcomes were grouped as “any occurrence.” Any occurrence includes all tracked 30-day negative outcomes. These include incisional, deep space, and organ space infections; wound disruption; pneumonia; unplanned intubation; pulmonary embolism; need for mechanical ventilation for more than 48 hours; urinary tract infection; progressive renal insufficiency; acute renal failure; stroke and/or cerebrovascular accident; cardiac arrest; myocardial infarction; need for transfusion; vein thrombosis requiring therapy; sepsis; and septic shock. Clavien-Dindo grade IV complications are defined as life-threatening complications with organ dysfunction requiring intermediate care or intensive care unit management. For grade IV complications, we included postoperative septic shock, postoperative requirement of dialysis, pulmonary embolism, myocardial infarction, cardiac arrest, prolonged requirement of mechanical ventilation, and need for reintubation because these are the variables in NSQIP most consistent with organ dysfunction and need for intensive care unit management.

American Society of Anesthesiologists (ASA) class, wound class, and age are known to be highly predictive of adverse outcomes in the NSQIP database, so the effect of increasing ASA class, wound class, and age on grade IV complications or mortality was evaluated for comparison with mFI. The ASA clas-
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Original Investigation Research

Figure 1. The 70 Items of the Canadian Study on Health and Aging Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toiletting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of palomental reflex
- Other medical history

Figure 2. The 11 Items of the Modified Frailty Index

- History of diabetes mellitus
- Functional status 2 (not independent)
- History of chronic obstructive pulmonary disease or pneumonia
- History of congestive heart failure
- History of myocardial infarction
- History of percutaneous coronary intervention, stenting, or angiography
- History of hypertension requiring medication
- History of peripheral vascular disease or ischemic rest pain
- History of impaired sensorium
- History of transient ischemic attack or cerebrovascular accident
- History of cerebrovascular accident with neurological deficit

If 303 patients operated on by otolaryngologic surgeons during the 6-year study period, 6727 were identified as inpatients. The inpatient study sample was 50.3% male and 10.2% African American, with a mean (range; SD) age of 54.7 (16-90; 17.2) years. Figure 3 compares the distribution of mFI scores for the inpatients (mean [range; SD], 0.07 [0-0.73; 0.09]) with those of outpatients undergoing head and neck surgery, who were less frail (mean [range; SD], 0.04 [0-0.82; 0.07]) than the

Results

The rates of grade IV complications, death, and any occurrence were analyzed in comparison using univariate analysis with the χ2 test. Analysis was performed using SPSS, version 20, statistical software (IBM). The distribution of outcomes was compared with that of nonfrail patients (mFI = 0). The combined rate of grade IV complications or death by ASA class, wound class, age, and functional status was also evaluated using univariate analysis with the χ2 test, for comparison with the mFI.

Functional status was analyzed independently to evaluate the strength of its contribution to the mFI because it is the only available variable that is not a comorbidity. It was evaluated dichotomously as either independent or not independent to improve statistical accuracy. The Cochran-Mantel-Haenszel test for a 2 × 2 × 2 comparison was used to evaluate the association between functional status and grade IV complications or death while controlling for mFI. The association between age and grade IV complications or death was analyzed in the same fashion for comparison.

Multivariate logistic regression was used to compare mFI with ASA class, wound class, age, and functional status. Model development was done in a standard stepwise approach to multivariate analysis. All variables were first tested for significance with univariate analysis. Significant variables were included in the multivariate model. After the model was run, nonsignificant variables were removed and the model was rerun. Because we were concerned with both the relative value of functional status as a noncomorbidity variable and the overall value of the mFI as a predictive tool, the regression was performed twice: first with functional status separate from the mFI and then with functional status included in the mFI. Each ASA and wound class was represented individually because these variables are categorical. When categorical variables are added to the model, 1 class is assigned a reference odds ratio of 1. Regression was verified using subgroup and segmental analysis. P < .05 was considered significant.

Of 18 303 patients operated on by otolaryngologic surgeons during the 6-year study period, 6727 were identified as inpatients. The inpatient study sample was 50.3% male and 10.2% African American, with a mean (range; SD) age of 54.7 (16-90; 17.2) years. Figure 3 compares the distribution of mFI scores for the inpatients (mean [range; SD], 0.07 [0-0.73; 0.09]) with those of outpatients undergoing head and neck surgery, who were less frail (mean [range; SD], 0.04 [0-0.82; 0.07]) than the...
inpatients. Approximately half of the inpatients had a frailty score of 0, compared with nearly 70% of outpatients. The 10 most common procedures are shown in Table 1. Because only 10 patients had an mFI of 0.55, 2 of 0.64, and 2 of 0.73, these patients were grouped with the 28 patients who had an mFI of 0.45 to create the cohort mFI greater than 0.44. This avoids the statistical inaccuracy in approximation to the χ² distribution that occurs when expected frequencies are too low.

The proportions of evaluated complications are shown in Table 2. As the mFI increased from 0 (no frailty-associated variables) to 0.45 (5 out of 11) or higher, rates of mortality, serious complications, and all complications increased in a stepwise fashion. Mortality increased from 0.2% with mFI 0 to 11.9% with mFI greater than 0.44. The risk of grade IV complications increased from 1.2% to 26.2%, and the risk of all complications increased from 9.5% to 40.5%. This is depicted graphically in Figure 4. All results are significant at $P < .001$.

Rates of grade IV complications or death by wound class, ASA class, age 60 years and older, and functional status are shown in Table 3. The rate was 1.5% with wound class I, 5.1% with class II, 4.4% with class III, and 8.4% with class IV. Patients with ASA class 1 had an occurrence rate of 0.7%; class 2, 0.8%; class 3, 4.5%; class 4, 21.2%; and class 5, 57.1%. The results were significant with $P < .001$. Patients younger than 60 years had an occurrence rate of 2.1%, compared with 5.7% for those 60 years and older. Independent patients had an occurrence rate of 2.6%, whereas those who were not independent

![Figure 3. Frailty Distribution: Inpatient vs Outpatient](image)

![Figure 4. Complications With Increasing Modified Frailty Index](image)

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Patients, No. (%) (n = 6727)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60240</td>
<td>Thyroidectomy, total or complete</td>
<td>764 (11.4)</td>
</tr>
<tr>
<td>38724</td>
<td>Cervical lymphadenectomy, modified radical neck dissection</td>
<td>538 (8.0)</td>
</tr>
<tr>
<td>60220</td>
<td>Total thyroid lobectomy, unilateral, with or without isthmusectomy</td>
<td>403 (6.0)</td>
</tr>
<tr>
<td>42415</td>
<td>Excise parotid tumor and/or parotid gland, lateral, with dissection and preservation of facial nerve</td>
<td>352 (5.2)</td>
</tr>
<tr>
<td>60210</td>
<td>Partial thyroid lobectomy, unilateral, with or without isthmusectomy</td>
<td>235 (3.5)</td>
</tr>
<tr>
<td>42145</td>
<td>Palatopharyngoplasty</td>
<td>228 (3.4)</td>
</tr>
<tr>
<td>42826</td>
<td>Tonsillectomy, primary or secondary, age greater than 12 years</td>
<td>206 (3.1)</td>
</tr>
<tr>
<td>60500</td>
<td>Parathyroidectomy or explore parathyroid glands</td>
<td>203 (3.0)</td>
</tr>
<tr>
<td>60252</td>
<td>Thyroidectomy, total or subtotal, limited neck dissection</td>
<td>175 (2.6)</td>
</tr>
<tr>
<td>21501</td>
<td>Incision and drainage of deep abscess and/or hematoma, soft tissue of neck, and/or thorax</td>
<td>151 (2.2)</td>
</tr>
<tr>
<td>42420</td>
<td>Excise parotid tumor or parotid gland, total, with dissection and preservation of facial nerve</td>
<td>136 (2.0)</td>
</tr>
</tbody>
</table>

Table 2. Proportion of Complications With Increasing Modified Frailty Index

<table>
<thead>
<tr>
<th>Complication</th>
<th>Modified Frailty Index, Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 (n = 3353)</td>
</tr>
<tr>
<td>Any occurrence</td>
<td>9.5</td>
</tr>
<tr>
<td>CL4</td>
<td>1.2</td>
</tr>
<tr>
<td>Death</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Abbreviation: CL4, Clavien-Dindo grade IV.

Complications assessed included postoperative septic shock, postoperative requirement of dialysis, pulmonary embolism, myocardial infarction, cardiac arrest, prolonged requirement of mechanical ventilation, and reintubation.

Modified frailty index was calculated for each patient by dividing the number of variables present by the total number assessed (n/11).
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had a rate of 25.1%. All analyzed variables showed statistical significance with \( P \leq .001 \).

The Cochrane-Mantel-Haenszel test was used to evaluate the association between functional status and grade IV complications or death while controlling for mFI. This test showed a significant trend (\( \chi^2 = 64.492; P < .001 \)), suggesting that the functional status is significant independent of the overall frailty score. When the same test was run comparing age with grade IV complications or death while controlling for mFI, the trend was not significant (\( \chi^2 = 3.73; P = .20 \)), suggesting that mFI is more powerfully associated with grade IV complications or death than age is.

Multivariate logistic regression models were used to compare the relative strength of association between mFI, ASA class, wound class, and age, with the outcome grade IV complications or death. Model development was done in a standard stepwise approach to multivariate analysis. We started with all analyzed variables because they were all significant in univariate analysis. Wound class was not significant in the model, so it was removed to simplify the model. Odds ratios for ASA classes are in reference to ASA class 5, which was assigned a reference odds ratio of 1. We first tested a “modified” mFI without functional status and included functional status as a separate variable. In the model, the mFI was the dominant significant predictor, with a relative odds ratio of 11. Functional status was the second dominant predictor, with a relative odds ratio of 5. Age had a relative odds ratio of 1. All other ASA classes were protective relative to ASA class 5. In the model, ASA classes 1 and 2 had very similar relative odds ratios (0.019 and 0.018, respectively), but ASA classes 3 and 4 did not demonstrate statistical significance. This model is depicted in Table 4; all results were significant at \( P < .05 \), with the exception of ASA classes 3 and 4.

When the same model was run with functional status included in the mFI, the mFI became far more powerful, with a relative odds ratio of 109. In this model, ASA classes 1 through 4 were significant. The relative odds ratios of ASA classes 1 and 2 remained similar (0.012 and 0.012). The odds ratio for ASA class 3 was approximately 4 times that of ASA class 1 (0.046), and the odds ratio for ASA class 4 was approximately 14 times higher (0.175). Age again had a relative odds ratio of 1 but was no longer statistically significant (\( P = .20 \)). This model is depicted in Table 5; all results were significant at \( P < .05 \), with the exception of age.

Discussion

With an increasing elderly and comorbid surgical population, it is important to identify which patients are at increased risk. Despite wide variability in how frailty indices are constructed, they all seem to yield similar results, as long as the variables measured are related to health status. The mFI is a simple tool proven to be significantly associated with morbidity and mortality across multiple surgical populations. Variables included in the mFI are available in any routine history and physical, and the mFI score can be quickly calculated in a clinical or bedside setting. Compared with the mean (SD) mFI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified frailty index (minus functional status)</td>
<td>11.164 (2.558-48.723)</td>
<td>.001</td>
</tr>
<tr>
<td>Functional status: not independent</td>
<td>5.064 (3.613-7.098)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ASA class*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.019 (0.002-0.155)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td>0.018 (0.003-0.108)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3</td>
<td>0.073 (0.013-0.411)</td>
<td>.24</td>
</tr>
<tr>
<td>4</td>
<td>0.237 (0.041-1.355)</td>
<td>.11</td>
</tr>
<tr>
<td>Age ≥60 years</td>
<td>1.011 (1.001-1.020)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviation: ASA, American Society of Anesthesiologists.

* ASA class odds ratios are relative to ASA class 5.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified frailty index</td>
<td>109.087 (29.848-398.688)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ASA class*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.012 (0.002-0.087)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td>0.012 (0.002-0.060)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3</td>
<td>0.046 (0.009-0.226)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4</td>
<td>0.175 (0.035-0.877)</td>
<td>.03</td>
</tr>
<tr>
<td>Age ≥60 years</td>
<td>1.006 (0.997-1.016)</td>
<td>.20</td>
</tr>
</tbody>
</table>

Abbreviation: ASA, American Society of Anesthesiologists.

* ASA class odds ratios are relative to ASA class 5.
of patients undergoing colectomy\textsuperscript{13} (0.10 [0.11]), inpatients undergoing head and neck surgery are less frail, with a smaller standard deviation. Despite our otolaryngologic study population having low frailty, with a mean of less than 1 variable per patient, we have demonstrated the mFI to be more strongly associated with morbidity and mortality than wound class, ASA, and age.

Physicians are accustomed to thinking of age as an important predictor of complications, when in fact frailty is likely the strongest predictor. We demonstrated that inability to independently perform ADLs is highly associated with serious complications and death in this population. In multivariate analysis, functional status as an independent variable was more powerful than age and ASA, and when it was added to the mFI, the relative odds ratio of the index increased nearly 10-fold. Functional status is a critical component of the mFI. Although it does not have as high an odds ratio as the full mFI, as a single variable, functional status may serve as a simple surrogate for frailty when data-processing capacity is not available.

Our study was limited by retrospective analysis of prospectively collected data. Also, the NSQIP database collects postoperative data to only 30 days, and the database may not be a true national representation because only participating hospitals are included. Given the overall low frailty of patients undergoing head and neck surgery, we selected all inpatient otolaryngologic surgical procedures to better power our study and provide a broad data set; however, individual procedures are likely to vary widely in their rates of mortality and complications. Obeid et al\textsuperscript{13} found that the correlation between increasing frailty and morbidity and/or mortality holds true for patients undergoing colectomy, who have high numbers in the database. An additional limitation is the number of preoperative variables available for analysis. Previous literature has established precedence for modifying the CSHA-FI with as few as 10 variables,\textsuperscript{16} and we matched 15 NSQIP variables to 11 CSHA-FI variables. However, our variables are primarily medical comorbidities. The data set is not useful for measuring the physical phenotype of frailty\textsuperscript{9} because it does not track the presence of unintentional weight loss, exhaustion, weakness (low grip strength), slow walking speed, and low level of physical activity. Direct retrospective comparison to a comorbidity index such as Charlson or the Adult Comorbidity Evaluation\textsuperscript{27} also cannot be done because their variables are also not fully represented. Additional research is needed with comparison to various frailty and comorbidity indices, prospective analysis, and external validation.

Despite these limitations, the NSQIP data set provides a large representative sample of inpatient otolaryngologic operations, and our data suggest that procedures with overall low rates of morbidity and mortality may have significant risk in frail populations because we have demonstrated mortality increasing from 0.1% to 11.9% with increasing frailty. Frail patients may also have up to a 40.5% overall rate of complications and a 26.2% risk of Clavien-Dindo grade IV complications. The mFI may be useful for anticipating which patients are at increased risk of perioperative complications. This may be useful for risk stratification, perioperative counseling, and preoperative optimization.

\textbf{REFERENCES}

14. American College of Surgeons National Surgical Quality Improvement Program Semiannual Report:
Frailty as a Predictor of Morbidity and Mortality


