Adapting the 5-factor modified frailty index for prediction of postprocedural outcome in patients with unruptured aneurysms

James Feghali, MD, Abhishek Gami, BS, Sarah Rapaport, BS, Jaimin Patel, BS, Adham M. Khalafallah, MD, Sakibul Huq, BS, Debraj Mukherjee, MD, MPH, Rafael J. Tamargo, MD, and Judy Huang, MD

Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

OBJECTIVE The 5-factor modified frailty index (mFI-5) is a practical tool that can be used to estimate frailty by measuring five accessible factors: functional status, history of diabetes, chronic obstructive pulmonary disease, congestive heart failure, and hypertension. The authors aimed to validate the utility of mFI-5 for predicting endovascular and microsurgical treatment outcomes in patients with unruptured aneurysms.

METHODS A prospectively maintained database of consecutive patients with unruptured aneurysm who were treated with clip placement or endovascular therapy was used. Because patient age is an important predictor of treatment outcomes in patients with unruptured aneurysm, mFI-5 was supplemented with age to create the age-supplemented mFI-5 (AmFI-5). Associations of scores on these indices with major complications (symptomatic ischemic or hemorrhagic stroke, pulmonary embolism, pneumonia, or surgical site infection requiring reoperation) were evaluated. Validation was carried out with the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database (2006–2017).

RESULTS The institutional database included 275 patients (88 underwent clip placement, and 187 underwent endovascular treatment). Multivariable analysis of the surgical cohort showed that major complication was significantly associated with mFI-5 (OR 2.0, p = 0.046) and AmFI-5 (OR 1.9, p = 0.028) scores. Significant predictive accuracy for major complications was provided by mFI-5 (c-statistic = 0.709, p = 0.011) and Am FI-5 (c-statistic = 0.720, p = 0.008). The American Society of Anesthesiologists Physical Status Classification System (ASA) provided poor discrimination (area under the curve = 0.541, p = 0.618) that was significantly less than that of mFI-5 (p = 0.023) and AmFI-5 (p = 0.014). Optimal relative fit was achieved with AmFI-5, which had the lowest Akaike information criterion value. Similar results were obtained after equivalent analysis of the endovascular cohort, with additional significant associations between index scores and length of stay (β = 0.6 and p = 0.009 for mFI-5; β = 0.5 and p = 0.003 for AmFI-5). In 1047 patients who underwent clip placement and were included in the NSQIP database, mFI-5 (p = 0.001) and AmFI-5 (p < 0.001) scores were significantly associated with severe postoperative adverse events and provided greater discrimination (c-statistic = 0.600 and p < 0.001 for mFI-5; c-statistic = 0.610 and p < 0.001 for AmFI-5) than ASA score (c-statistic = 0.580 and p = 0.003).

CONCLUSIONS mFI-5 and AmFI-5 represent potential predictors of procedure-related complications in unruptured aneurysm patients. After further validation, integration of these tools into clinical workflows may optimize patients for intervention.

https://thejns.org/doi/abs/10.3171/2021.2.JNS204420

KEYWORDS intracranial aneurysms; frailty; complications; length of stay; vascular disorders

Frailty is commonly described as a state of deteriorated physiological capacity and susceptibility to environmental insults. Surgery represents one example of such insults, and associations between surgical outcome and frailty have been explored. The 11-factor modified frailty index (mFI-11) and Charlson Comorbidity Index are two examples of stratification tools that determine a patient’s frailty. mFI-11, which is composed

ABBREVIATIONS AIC = Akaike information criterion; AmFI-5 = age-supplemented 5-factor modified frailty index; ASA = American Society of Anesthesiologists Physical Status Classification System; AUC = area under the curve; MCA = middle cerebral artery; mFI-5 = 5-factor modified frailty index; mFI-11 = 11-factor modified frailty index; NIS = National Inpatient Sample; NSQIP = National Surgical Quality Improvement Program.


INCLUDE WHEN CITING Published online August 13, 2021; DOI: 10.3171/2021.2.JNS204420.

©AANS 2022, except where prohibited by US copyright law
of a set of 11 medical history items, was created on the basis of the Canadian Study of Health and Aging frailty index to predict postoperative morbidity and mortality. The Charlson Comorbidity Index is a tool that predicts mortality within 1 year of hospital admission on the basis of 20 variably weighted medical history items and has been used as a standardized measure of comorbidity burden. Although these measures have demonstrated predictive value in relation to morbidity and mortality, they have been deemed clinically impractical to determine owing to the large number of variables surveyed. In addition, mFI-11 can no longer be used in national databases owing to changes in included variables over time. Consequently, the streamlined 5-factor modified frailty index (mFI-5) was created. This measure assesses five accessible factors: functional status, history of diabetes, chronic obstructive pulmonary disease, congestive heart failure, and hypertension. It has been validated for its efficacy in predicting outcomes of orthopedic and neurosurgical oncology procedures.

The applicability of mFI-5 with respect to outcome prediction for patients with unruptured aneurysm has not been explored. Unruptured aneurysm patients may have a high burden of vascular risk factors, which are well represented in mFI-5; therefore, the index may be well suited for this population. This study attempted to validate mFI-5 as an outcome predictor of endovascular and microsurgical treatment of unruptured aneurysms, with the aim of indicating the measure’s utility for optimizing the care of patients considering preventative treatment of a potentially injurious pathology.

Methods

Patients

A prospectively maintained, IRB-approved database of consecutive patients with unruptured aneurysm who were treated with clip placement or endovascular therapy between January 2017 and December 2018 was used for this study. Patient consent was waived due to the absence of patient contact or intervention resulting from the study. We excluded patients with polycystic kidney disease, pediatric patients (age < 18 years), and patients with previously treated, fusiform, or mycotic aneurysm. At our institution, recommendations for unruptured aneurysm treatment incorporate findings of assessments of aneurysm morphology and characteristics, patient risk factors and preferences, and surgeon appraisal of procedural risks.

Variables

Aneurysms were diagnosed with digital subtraction angiography, which was utilized to ascertain aneurysm size and location. mFI-5 was calculated on the basis of the definitions used in the original paper by Subramaniam et al. Scores on the American Society of Anesthesiologists Physical Status Classification System (ASA), a commonly used comorbidity scale, were also calculated for every patient. The primary outcome of interest was the occurrence of major postprocedural complications, including symptomatic ischemic or hemorrhagic stroke (diagnosed on the basis of imaging evidence with attributable symptoms that reflected worsening functional status, as measured with the modified Rankin Scale), pulmonary embolism, pneumonia, or surgical site infection requiring reoperation. Other outcomes included length of hospital stay after surgery and minor complications, such as self-limited cerebellar sag hemorrhage (as described by Friedman et al.), transient ischemic attack, deep venous thrombosis, groin hematoma, urinary tract infection, epidural hematoma, seizure, and contained intraprocedural aneurysm rupture with no sequelae (e.g., stroke or neurological deficit).

Statistical Analysis

Analysis was carried out using SPSS version 25.0 (IBM Corp.), with statistical significance set at p < 0.05. Subgroup analysis was performed using treatment subgroups that received clip placement or endovascular therapy. Univariable comparisons between patients with and without major complication were performed using the chi-square and Fisher exact tests for categorical variables and the independent-samples t-test for continuous variables. Because all patients had independent functional status, this component of mFI-5 was deemed less relevant for patients with unruptured intracranial aneurysm. mFI-5 was supplemented with patient age to create age-supplemented mFI-5 (AmFI-5), a combined index of age and frailty meant to optimize prediction of postprocedural complications in this patient population. Utilizing the Youden index, we identified an optimal cutoff age of 50 years or older as most predictive of major complications in both cohorts. Table 1 describes the components of mFI-5 and AmFI-5.

Receiver operating curve analysis with area under the curve (AUC) was used to determine the predictive accuracies of both indices and ASA for major complications. DeLong’s test was used to check for significant differences in AUC due to the inclusion of age (mFI-5 vs AmFI-5) and to compare the predictive accuracies of the frailty indices with that of ASA. Optimal relative fit of the mFI-5, AmFI-5, and ASA models was additionally assessed using Akaike information criterion (AIC), which indicates better fit and decreased complexity with lower values. Calibration was assessed using the Hosmer-Lemeshow test. Multivariable logistic regression that incorporated variables with p < 0.2 on univariable analysis was used to evaluate the frailty indices as potential independent predictors of outcome. Associations of scores on these indices with any complication (major or minor) and with length of stay were secondarily evaluated.

Validation of the frailty indices was performed with the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) data set (2006–2017). The algorithm published by Dasenbrock et al. was utilized to identify the population of patients with unruptured aneurysm who underwent elective clip placement. Associations between frailty indices and development of serious adverse postoperative events, as defined with previously published NSQIP criteria, were evaluated and compared.
TABLE 1. Factors included in mFI-5, AmFI-5, and ASA

<table>
<thead>
<tr>
<th>Index</th>
<th>Included Factors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>mFI-5*</td>
<td>Dependent functional status, diabetes (insulin or noninsulin), chronic obstructive pulmonary disease,† congestive heart failure, &amp; hypertension (requiring medication)</td>
</tr>
<tr>
<td>AmFI-5</td>
<td>Age ≥50 yrs, diabetes (insulin or noninsulin), chronic obstructive pulmonary disease,† congestive heart failure, &amp; hypertension (requiring medication)</td>
</tr>
<tr>
<td>ASA†</td>
<td>Healthy</td>
</tr>
<tr>
<td>II</td>
<td>Mild systemic disease (no substantive limitations)‡</td>
</tr>
<tr>
<td>III</td>
<td>Severe systemic disease§</td>
</tr>
<tr>
<td>IV</td>
<td>Severe systemic disease w/ constant threat to life</td>
</tr>
<tr>
<td>V</td>
<td>Moribund &amp; not expected to survive w/o procedure</td>
</tr>
</tbody>
</table>

* Each factor in the frailty indices is worth 1 point.
† Emphysema or chronic bronchitis resulting in any of the following: functional disability, hospitalization, chronic bronchodilator therapy, or abnormal results on pulmonary function testing.
‡ Examples include active smoking, social alcohol drinking, pregnancy, obesity, and well-controlled diabetes or hypertension.
§ Examples include poorly controlled diabetes or hypertension, chronic obstructive pulmonary disease, morbid obesity, active hepatitis, alcohol dependence, end-stage renal disease, and remote history of myocardial infarction, stroke, or transient ischemic attack.

with the predictive accuracy of ASA, which is systematically used in NSQIP-based studies.

Results

Patient and Aneurysm Characteristics

The study population included a total of 275 patients who were treated for unruptured intracranial aneurysm: 88 (32%) underwent clipping placement, and 187 (68%) underwent endovascular therapy. The mean ± SD mFI-5 and AmFI-5 scores were 0.76 ± 0.82 and 1.52 ± 1.06, respectively. The mean age was 57.8 ± 12.5 years, and there were 234 (85%) females. In total, 34 (12%) aneurysms were located in the anterior communicating or anterior cerebral artery, 32 (12%) in the clinoidal internal carotid artery, 25 (9%) in the superior hypophyseal artery, 57 (21%) in the ophthalmic internal carotid artery, 24 (9%) in the posterior communicating artery, 5 (2%) in the anterior choroidal artery, 10 (4%) at the internal carotid artery termination, 49 (18%) in the middle cerebral artery (MCA), 23 (8%) in posterior circulation, and 16 (6%) in other/unspecified internal carotid artery locations. The mean aneurysm size was 6.1 ± 4.4 mm.

Outcome Analysis

Microsurgical Clip Placement

Institutional Cohort. All major (ischemic stroke, hemorrhagic stroke, pulmonary embolism, pneumonia, and surgical site infection requiring reoperation) and minor complications are summarized in Fig. 1. Among surgically treated patients, the major complication rate was 17% (15/88 patients). Results of univariable analysis are summarized in Table 2. The average mFI-5 score was significantly higher in patients with major complication (p = 0.008), as was the average AmFI-5 score (p = 0.005). ASA score was not associated with the occurrence of major complication (p = 0.895). Location in the MCA was significantly associated with major postoperative complication (p = 0.020). There was successively higher risk of major complication with every point increase in mFI-5 (Fig. 2) and AmFI-5 (Fig. 3). On multivariable analysis, major complication was significantly associated with mFI-5 (OR 2.3, 95% CI 1.3–4.0, p = 0.028) and AmFI-5 (OR 1.9, 95% CI 1.1–3.4, p = 0.028) score. Results of receiver operating curve analysis are summarized in Fig. 4. In the surgical cohort, significant predictive accuracy (AUC = 0.709, p = 0.011) for major complication was provided by mFI-5, with AmFI-5 demonstrating greater discrimination (AUC = 0.720, p = 0.008); however, the difference was nonsignificant (p = 0.653 determined with DeLong’s test). Both indices demonstrated goodness of fit, as indicated by the nonsignificant p values determined with the Hosmer-Lemeshow test. ASA provided poor discrimination (AUC = 0.541, p = 0.618) that was significantly less than that of mFI-5 (p = 0.023) and AmFI-5 (p = 0.014). Optimal relative fit was achieved with AmFI-5, which had the lowest AIC value. Combining MCA location with AmFI-5 score yielded a highly predictive model (AUC = 0.800, p < 0.001).

The occurrence of any postoperative complication was significantly associated with mFI-5 (OR 2.3, 95% CI 1.3–4.1, p = 0.004, AUC = 0.687) and AmFI-5 (OR 2.1, 95% CI 1.3–3.4, p = 0.002, AUC = 0.716) score. The mean ± SD length of stay was 7.0 ± 4.7 days, and no significant association between length of stay and frailty was identified in the surgical cohort.

NSQIP Cohort. The NSQIP cohort consisted of 1047 unruptured aneurysm patients who underwent clipping placement. Severe postoperative adverse event occurred in 136/1047 patients (13%) and was significantly associated with mFI-5 (p = 0.001) and AmFI-5 (p < 0.001) score. Increased risk of adverse event was encountered with higher mFI-5 and AmFI-5 scores (Fig. 5). Greater discrimination of severe adverse event was provided with mFI-5 (AUC = 0.600, p < 0.001) and AmFI-5 (AUC = 0.610, p < 0.001), compared with that of ASA (AUC = 0.580, p = 0.003). However, the difference was not statistically significant (p = 0.538 for mFI-5 vs ASA, and p = 0.294 for AmFI-5).
Feghali et al. vs ASA). Optimal relative fit was achieved with AmFI-5, which had the lowest AIC value.

**Endovascular Therapy**

Major and minor complications are illustrated in Fig. 1. The following treatment modalities were used: 26 (14%) patients were treated with coiling, 149 (80%) with flow diversion, and 12 (6%) with stent-assisted coiling. In the endovascular therapy cohort, the major complication rate was 6% (12/187 patients). There was no significant association between endovascular treatment modality and major complication (p = 0.865). Results of univariable analysis are summarized in Table 2. The average mFI-5 score of patients with major complication was significantly higher than that of patients without major complication (p = 0.028), as was the average AmFI-5 score (p = 0.009). Male sex was also significantly associated with major complication after endovascular treatment (p = 0.038). The major complication rate significantly increased with every 1-point increase in mFI-5 (Fig. 2) and AmFI-5 (Fig. 3) score. On multivariable analysis, major complication was significantly associated with mFI-5 (OR 4.0, 95% CI 2.1–7.4, p < 0.001, AUC = 0.768) and AmFI-5 (OR 3.9, 95% CI 2.1–7.1, p < 0.001, AUC = 0.792). The mean ± SD length of stay was 2.1 ± 2.5 days and was significantly associated with mFI-5 (β = 0.6, 95% CI 0.2–1.1, p = 0.009) and AmFI-5 (β = 0.5, 95% CI 0.2–0.9, p = 0.003) score.

**Discussion**

Our results validate the utility of mFI-5 for predicting outcomes after clip placement and endovascular therapy for unruptured aneurysm. Supplementing mFI-5 with age (AmFI-5) additionally improved predictive power. The applicability of these results in both an institutional database and NSQIP—determined with evaluations of two outcomes (major complications and severe adverse events) and two treatment modalities (clip placement and endovascular therapy)—confirmed the external validity and flexibility of these indices for predicting outcomes of patients with unruptured aneurysm.

**Predictors of Adverse Outcomes in Patients With Unruptured Aneurysm**

Previous efforts have identified characteristics associated with increased treatment risk in patients with unruptured aneurysm. Concerning the risk of clip placement, Dasenbrock et al. developed the NSQIP unruptured aneurysm scale using data sets from 2007 to 2014. The scale included 1 point for a bleeding disorder; 2 points for age

---

**FIG. 1.** Major and minor complications after endovascular therapy and clip placement for unruptured aneurysm. DVT = deep vein thrombosis; TIA = transient ischemic attack; UTI = urinary tract infection.
51–60 years, cardiac disease, diabetes, morbid obesity, anemia, and operative time between 240 and 330 minutes; 3 points for leukocytosis and operative time exceeding 330 minutes; and 4 points for age older than 60 years. This complex scoring system predicted several postoperative complications with an AUC of 0.7 for the NSQIP data set and 0.6 for the National Inpatient Sample (NIS). Given the number of included variables and complexity of this

### TABLE 2. Univariate analysis of baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Clip Placement</th>
<th>Endovascular Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Major Complication (n = 73)</td>
<td>Major Complication (n = 15)</td>
</tr>
<tr>
<td>mFI-5</td>
<td>0.70 ± 0.83</td>
<td>1.33 ± 0.82</td>
</tr>
<tr>
<td></td>
<td>37 (51)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>AmFI-5</td>
<td>1.37 ± 1.15</td>
<td>2.27 ± 0.88</td>
</tr>
<tr>
<td></td>
<td>22 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ASA</td>
<td>2.6 ± 0.6</td>
<td>2.7 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>54.4 ± 12.6</td>
<td>60.0 ± 7.6</td>
</tr>
<tr>
<td>Female sex</td>
<td>58 (79)</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Race</td>
<td>0.535</td>
<td>0.914</td>
</tr>
<tr>
<td>White</td>
<td>49 (67)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Black</td>
<td>16 (22)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (7)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Current tobacco smoking</td>
<td>23 (32)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Stroke or TIA history</td>
<td>6 (8)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Aneurysm Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AComA/ACA</td>
<td>21 (29)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>PComA</td>
<td>8 (11)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Non-PComA ICA</td>
<td>17 (23)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>MCA</td>
<td>24 (33)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>3 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Max diameter, mm</td>
<td>6.7 ± 5.8</td>
<td>5.9 ± 2.4</td>
</tr>
</tbody>
</table>

ACA = anterior cerebral artery; AComA = anterior communicating artery; ICA = internal carotid artery; PComA = posterior communicating artery; TIA = transient ischemic attack.
Categorical data are presented as number (percent) and continuous data are presented as mean ± SD.
* Statistically significant (p < 0.05).
scoring system, the scale is difficult to apply to everyday clinical practice; moreover, the inclusion of operative time and leukocytosis complicates utilization of this score for decision-making in the preoperative setting.

In our endovascular cohort, we identified a major complication rate of 6%, which is in line with the neurological complication rate of 5.5% reported by Ji et al. in their analysis of 1060 unruptured aneurysm patients who were treated endovascularly. It is worthwhile to note that the prevalence of major morbidity (ASA > II) in our endovascular cohort was 60%, reflecting a patient population that may have been more prone to procedural complications. With regard to risk prediction, Ji et al. developed a 3-point risk score for neurological complications based on size, core area, and cerebral ischemic comorbidity, with an AUC of 0.714. However, aneurysm size and ischemic comorbidity (stroke or transient ischemic attack) were not significant predictors of complications in our endovascular cohort. Supplementing this risk score with an age-supplemented frailty index may help achieve greater discrimination and external validity.

Newman et al. used NIS to develop a 20-item comorbidity scale that was predictive of poor outcome after clip placement or endovascular therapy for unruptured aneurysms. Computing a score with 20 variables that may vary between −5 and +55 limits the practicality of this risk-stratification scale. Furthermore, it is very difficult to ascertain whether the most highly weighted predictors (neurological deficit, renal failure, gastrointestinal hemorrhage, and electrolyte disturbance) were actual comorbidities or postoperative complications on the basis of the NIS-based ICD-9 codes, which limits the validity of this scale. It was also surprising that hypertension, diabetes, and congestive heart failure—comorbidities that have been identified as important factors associated with complications in a recent meta-analysis of 106,433 patients treated for unruptured aneurysms were not included in the scale. We identified MCA location as a predictor of major complications in the cohort that underwent clip placement. This is consistent with the findings of Grigorian et al., who reported that MCA location was associated with the second highest morbidity rate after vertebrobasilar aneurysm in a cohort of 312 patients with unruptured aneurysm who were treated with clip placement.

**FIG. 2.** Increase in major complications with increasing mFI-5 score, with linear trend lines (p = 0.024 for clip placement and p = 0.003 for endovascular therapy according to the Fisher exact test).

**FIG. 3.** Increase in major complications with increasing AmFI-5 score, with linear trend lines (p = 0.035 for clip placement and p = 0.005 for endovascular therapy according to the Fisher exact test).

**Applicability of mFI-5 in Neurosurgery**

mFI-5 score was recently investigated as a potential predictor of various outcomes after surgery for brain tumor. In a cohort of 234 patients who underwent endoscopic endonasal resection of pituitary adenoma, each 1-point increase in mFI-5 score increased length of stay by 0.64 days and total charges by $3954. In a larger cohort of 1692 surgical patients with brain tumor, including meningioma, high-grade glioma, low-grade glioma, pituitary tumor, and brain metastasis, each additional 1-point increase on mFI-5 translated to a 0.32-day increase in ICU length of stay and a 1.38-day increase in total length of stay. Additionally, higher mFI-5 score was independently associated with venous thromboembolism, physiological/metabolic derangement, respiratory failure, and sepsis, as well as increased total hospital charges. In a separate analysis, mFI-5 demonstrated predictive utility comparable to those of the Charlson Comorbidity Index and mFI-11 with respect to 90-day postoperative mortality after brain tumor surgery.

The findings of this study expand the applicability of mFI-5 to cerebrovascular neurosurgery, specifically to patients with unruptured aneurysm. Accurate prediction of treatment risk may have important implications regarding decision-making, patient counseling, and patient optimization prior to elective intervention. All components of mFI-5, which include hypertension, diabetes mellitus, and chronic obstructive pulmonary disease (a surrogate of clinically significant smoking burden), represent well-known vascular risk factors. This highlights the relevance of this frailty index to cerebrovascular pathology and may explain the favorable discrimination and calibration properties observed in this study. Outcome data emphasize the role of traditional vascular risk factors, such as hypertension and diabetes, for determining intervention risk. Parallel to their predictive utility, mFI-5 and AmFI-5 are also highly practical tools that may be easily integrated with everyday clinical practice and may be rapidly calculated in an early clinical encounter with excellent interrater agreement. When we combined frailty index scores with other characteristics, such as sex and aneurysm location, predictive accuracy approached an AUC of 0.8.

We postulate that frailty index scores can be further combined with other characteristics, such as morphology, neck width, and calcification, to maximize predictive accuracy. Because clip placement may subject patients to
higher risk of complications, frailty indices could be used to better select candidates for clip placement. Additional potential uses of frailty indices include guiding enhanced recovery after surgery protocols for elective craniotomy (e.g., preoperative medical optimization of frail patients and minimization of high-acuity intensive care for non-frail patients) and triaging patients according to need for intensive care monitoring after endovascular procedures. Furthermore, complications and increased length of stay in unruptured aneurysm patients are associated with greater hospital charges; therefore, improved patient selection and index-guided optimization have the potential to lower healthcare cost. Finally, the findings herein validate the use of mFI-5 and AmFI-5 as research tools that can effectively summarize risk according to the comorbidities reported in large database studies, with greater relevance than other metrics such as the ASA for patients with unruptured aneurysm.

Limitations
This study was primarily based on data from a single tertiary referral center with cerebrovascular expertise. We sought to confirm wider applicability by investigating the associations between index scores and outcomes in the NSQIP data set. The indices outperformed another comorbidity index, the ASA, which increases confidence in the potential utility and external validity of the findings. The number of patients with very high frailty (≥ 3 points on mFI-5 and ≥ 4 on AmFI-5) was relatively small, as would be expected for patients with unruptured aneurysm. Therefore, validation with larger cohorts may clarify the true complication rates in this subgroup of patients who were treated endovascularly and with clip placement.

Conclusions
mFI-5 and AmFI-5 represent potential predictors of procedure-related complications in unruptured aneurysm patients. Validation of the concept of frailty in larger cohorts of patients with unruptured aneurysm, as well as patients with other cerebrovascular diseases, remains warranted. With further validation, integration of these tools into existing clinical workflows may improve decision-making, counseling, and optimization of patients for intervention.

References

FIG. 4. Receiver operating curves. Predictive accuracies for major complications, with the AUCs of mFI-5, AmFI-5, and ASA shown for patients who underwent clip placement (left) and those who underwent endovascular therapy (right). Figure is available in color online only.


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Huang, Feghali, Mukherjee, Tamargo. Acquisition of data: Feghali, Gami, Rapaport, Patel, Khalafallah, Huq. Analysis and interpretation of data: Feghali. Drafting the article: Feghali, Khalafallah. Critically revising the article: all authors. Reviewed submitted version of manuscript: Huang, Feghali, Gami, Rapaport, Patel, Huq, Mukherjee, Tamargo. Approved the final version of the manuscript on behalf of all authors: Huang. Statistical analysis: Feghali. Study supervision: Huang.

Correspondence
Judy Huang: Johns Hopkins Hospital, Baltimore, MD. jhuang24@jhmi.edu.