A new comorbidities index for risk stratification for treatment of unruptured cerebral aneurysms

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OBJECTIVE Comorbidities have an impact on risk stratification for outcomes in analyses of large patient databases. Although the Charlson Comorbidity Index (CCI) and the Elixhauser Comorbidity Index (ECI) are the most commonly used comorbidity indexes, these have not been validated for patients with unruptured cerebral aneurysms; therefore, the authors created a comorbidity index specific to these patients.

METHODS The authors extracted all records involving unruptured cerebral aneurysms treated with clipping, coiling, or both from the Nationwide Inpatient Sample (2002–2010). They assessed the effect of 37 variables on poor outcome and used the results to create a risk score for these patients. The authors used a validation data set and bootstrapping to evaluate the new index and compared it to CCI and ECI in prediction of poor outcome, mortality, length of stay, and hospital charges.

RESULTS The index assigns integer values (–2 to 7) to 20 comorbidities: neurological disorder, renal insufficiency, gastrointestinal bleeding, paralysis, acute myocardial infarction, electrolyte disorder, weight loss, metastatic cancer, drug abuse, arrhythmia, coagulopathy, cerebrovascular accident, psychosis, alcoholism, perivascular disease, valvular disease, tobacco use, hypothyroidism, depression, and hypercholesterolemia. Values are summed to determine a patient's risk score. The new index was better at predicting poor outcome than CCI or ECI (area under the receiver operating characteristic curve [AUC] 0.814 [95% CI 0.798–0.830], vs 0.694 and 0.712, respectively, for the other indices), and it was also better at predicting mortality (AUC 0.775 [95% CI 0.754–0.792], vs 0.635 and 0.657, respectively, for CCI and ECI).

CONCLUSIONS This new comorbidity index outperforms the CCI and ECI in predicting poor outcome, mortality, length of stay, and total charges for patients with unruptured cerebral aneurysm. Reevaluation of other patient cohorts is warranted to determine the impact of more accurate patient stratification.

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KEY WORDS unruptured cerebral aneurysm; comorbidity index; coiling; clipping; vascular disorders

COMORBIDITIES impact patient stratification for outcome analyses in retrospective reviews in which large patient databases are used. For this reason, comorbidity stratification tools for outcome prediction are commonly used, such as the Charlson Comorbidity Index (CCI)⁴ and the Elixhauser Comorbidity Index (ECI).⁸ These tools have been applied to a broad range of diseases and fields, including end-stage renal disease,^{5,6,11} pancreatic cancer,²¹ orthopedic surgery,¹⁵ general surgery,¹⁶ and neurovascular disease.^{1,3,12,18} However, the broad range of diseases and fields to which these comorbidity indexes have been applied underscores their lack of specificity.

The CCI was designed for mortality analyses and derived from a small cohort of 604 patients with primary breast cancer at a single New York hospital.⁴ The ECI was derived from 438 acute-care hospitals in California, with a resultant set of 30 comorbidity measures with associated impacts on outcomes.⁸ Neither of these indexes was designed for use in unruptured cerebral aneurysms, but they have been applied to these patients.^{1,3,12,18} How accurately these indexes model the impact of disease burden in patients with unruptured cerebral aneurysms has not been studied.

Since the creation of the CCI in 1987, no studies have

ABBREVIATIONS AUC = area under the receiver operating characteristic curve; CCI = Charlson Comorbidity Index; CVA = cerebrovascular accident; ECI = Elixhauser Comorbidity Index; GEE = generalized estimating equations; GI = gastrointestinal; LOS = length of stay; MI = myocardial infarction; NIS = Nationwide Inpatient Sample; PHC4 = Pennsylvania Health Care Cost Containment Council.

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been done to validate this tool in the neurosurgical patient population. Similarly, no formal study has been done to validate the ECI. Given the numerous medical and surgical advances that have occurred since their creation, there is a significant possibility that these older indices may overestimate the impact of patient comorbidities, thus confounding the results of current retrospective reviews.

It was not until recently that attention has been paid to the impact of preprocedural comorbidities on patient outcomes for ruptured and unruptured cerebral aneurysms.² Using the Nationwide Inpatient Sample (NIS) database, Bekelis et al. were able to demonstrate the impact of 10 comorbidities on outcomes for ruptured and unruptured aneurysms undergoing clipping. However, their analysis did not take into account a full range of patient comorbidities and did not address the larger problem of designing a systematic way to incorporate these comorbidities into database analyses.

The NIS is a powerful database to study outcome data for cerebral aneurysms, and the question remains whether an index derived specifically from the disease population would outperform the CCI or ECI in mortality and morbidity prediction. Therefore, we set out to determine the impact of a wider range of comorbidities on patient outcomes for unruptured cerebral aneurysms undergoing treatment, and to use this information to create a comorbidity index applicable to this patient population. The implication of this study would be to propose an index more accurate than the CCI and ECI that should be used to analyze this patient population in all large patient databases.

Methods

The NIS database for the years 2002–2010 was obtained from the Agency for Healthcare Quality and Research's Healthcare Cost and Utilization Project (Rockville, MD). The NIS database is the largest all-payer hospital inpatient database in the US, comprising more than 7 million hospital stays and representing approximately 1000 hospitals each year. For each sampled hospital, all patient admissions for the year are recorded, allowing the calculation of annual hospital case volume. The years 2002–2010 were chosen because they represent the most up to date and

homogeneously encoded data set available from the NIS. More information regarding the NIS database is provided at <http://www.hcup-us.ahrq.gov/nisoverview.jsp>.

The NIS database was queried for all patients 18 years or older with *International Classification of Diseases, Ninth Revision* (ICD-9) codes for the diagnosis of unruptured cerebral aneurysm (437.3) and procedure codes for either clipping (39.51), coiling (39.79, 39.72, 39.52), or both (see Table 1 for patient demographic data). Patient comorbidities based on NIS or ICD-9 codes were then extracted for analysis (see Table 2 for comorbidity listings). Comorbidities were chosen based on a combination of the American Heart Association's perioperative cardiovascular risk factors⁹ and comorbid risk factors included in the CCI and ECI.

We used generalized estimating equations (GEE) to assess the effects of patient characteristics and comorbidities on the probability of poor outcome. Patients were classified as experiencing poor outcome if they died during admission or were discharged to hospice, to a skilled nursing, intermediate-care, or other long-term facility, or to a hospital-based Medicare-approved swing bed. Patients were classified as experiencing good outcome if they were discharged to home, to a short-term facility, or to an inpatient or outpatient rehabilitation facility, or if they left against medical advice. We assumed a binomial distribution for the outcome, and we included age, sex, and all comorbidities listed in Table 2 (excluding those associated with fewer than 5 cases of poor outcome) as potential predictors. To account for the clustering of observations on hospitals, we considered the hospital to be a repeated factor and assumed an exchangeable working correlation.

We assessed each model's predictive ability using the probability of concordance, or *c* statistic, which is equal to the area under the receiver operating characteristic curve (AUC).

To evaluate how well the models might predict outcomes for a new group of patients, we used 2 validation methods. 1) We created a prediction model based on 2002–2008 NIS data (11,693 observations with complete information on all predictors) and used it to predict outcomes for patients recorded in the NIS database in 2009–2010 (4039

TABLE 1. Demographic data in patients with unruptured cerebral aneurysms recorded in the NIS*

Characteristic	Overall (n = 18,423)	Treatment		
		Clip (n = 8,268)	Coil (n = 9,834)	Both (n = 321)
Mean age in yrs, $\pm$ SD (median)	55.4 $\pm$ 12.4 (56.0)	53.9 $\pm$ 11.6 (54.0)	56.7 $\pm$ 12.9 (57.0)	54.8 $\pm$ 10.9 (56.0)
Sex (% female) [†]	13,758 (75.0)	6,135 (74.5)	7,383 (75.5)	240 (74.8)
Race [†]				
White	9,741 (73.6)	4,332 (72.4)	5,267 (74.8)	142 (67.3)
Black	1,433 (10.8)	709 (11.8)	699 (9.9)	25 (11.8)
Hispanic	1,327 (10.0)	621 (10.4)	677 (9.6)	29 (13.7)
Asian/Pacific Islander	286 (2.2)	123 (2.1)	159 (2.3)	4 (1.9)
Native American	59 (0.4)	36 (0.6)	20 (0.3)	3 (1.4)
Other	386 (2.9)	163 (2.7)	215 (3.1)	8 (3.8)

* Except as otherwise noted, values are expressed as the number of patients (%).

[†] Eighty observations were missing information for sex, and 5191 observations were missing information for race.

TABLE 2. Comorbidities in patients with unruptured cerebral aneurysms

Comorbidity*	Overall (n = 18,423)	Treatment		
		Clip (n = 8268)	Coil (n = 9834)	Both (n = 321)
AIDS	22 (0.1%)	12 (0.1%)	NR	0 (0%)
Alcohol abuse	473 (2.6%)	253 (3.1%)	204 (2.1%)	16 (5.0%)
Anemic deficiency	1236 (6.7%)	608 (7.4%)	586 (6.0%)	42 (13.1%)
Arthritis	442 (2.4%)	205 (2.5%)	225 (2.3%)	12 (3.7%)
Blood loss	76 (0.4%)	32 (0.4%)	35 (0.4%)	NR
Chronic heart failure	389 (2.1%)	177 (2.1%)	208 (2.1%)	NR
Chronic respiratory disease	2966 (16.1%)	1356 (16.4%)	1560 (15.9%)	50 (15.6%)
Coagulopathy	313 (1.7%)	144 (1.7%)	160 (1.6%)	NR
Depression	1906 (10.4%)	886 (10.7%)	995 (10.1%)	25 (7.8%)
Diabetes w/o complications	1716 (9.3%)	739 (8.9%)	954 (9.7%)	23 (7.2%)
Diabetes w/ complications	99 (0.5%)	52 (0.6%)	44 (0.4%)	NR
Drug abuse	337 (1.8%)	167 (2.0%)	158 (1.6%)	12 (3.7%)
Hypertension	9993 (54.2%)	4495 (54.4%)	5314 (54.0%)	184 (57.3%)
Hypothyroidism	1585 (8.6%)	670 (8.1%)	886 (9.0%)	29 (9.0%)
Liver disease	218 (1.2%)	90 (1.1%)	123 (1.3%)	NR
Lymphoma	30 (0.2%)	12 (0.1%)	17 (0.2%)	NR
Electrolyte disorder	2185 (11.9%)	1210 (14.6%)	893 (9.1%)	82 (25.6%)
Metastatic cancer	40 (0.2%)	NR	32 (0.3%)	0 (0%)
Neurological disorder	243 (1.3%)	123 (1.5%)	103 (1.1%)	17 (5.3%)
Obesity	873 (4.7%)	399 (4.8%)	464 (4.7%)	NR
Paralysis	828 (4.5%)	484 (5.9%)	325 (3.3%)	19 (5.9%)
Perivascular disease	738 (4.0%)	256 (3.1%)	461 (4.7%)	21 (6.5%)
Psychosis	434 (2.4%)	223 (2.7%)	204 (2.1%)	NR
Pulmonary circulation disorder	86 (0.5%)	39 (0.5%)	46 (0.5%)	NR
Renal failure	326 (1.8%)	129 (1.6%)	191 (1.9%)	NR
Tumor w/o metastasis	127 (0.7%)	55 (0.7%)	69 (0.7%)	NR
Peptic ulcer	12 (0.1%)	NR	NR	0 (0%)
Valvular disease	474 (2.6%)	220 (2.7%)	241 (2.5%)	13 (4.1%)
Weight loss	193 (1.0%)	120 (1.5%)	59 (0.6%)	14 (4.4%)
Hypercholesterolemia	3737 (20.3%)	1559 (18.9%)	2128 (21.6%)	50 (15.6%)
Cardiomyopathy	119 (0.6%)	53 (0.6%)	64 (0.7%)	NR
Arrhythmia/dysrhythmia	1270 (6.9%)	596 (7.2%)	657 (6.7%)	27 (8.4%)
CVA/TIA	427 (2.3%)	209 (2.5%)	188 (1.9%)	30 (9.3%)
Angina pectoris	104 (0.6%)	52 (0.6%)	50 (0.5%)	NR
Acute MI	129 (0.7%)	66 (0.8%)	62 (0.6%)	NR
Old MI	489 (2.7%)	215 (2.6%)	269 (2.7%)	NR
Renal insufficiency/acute kidney failure	172 (0.9%)	79 (1.0%)	91 (0.9%)	NR
Chronic kidney disease	179 (1.0%)	58 (0.7%)	118 (1.2%)	NR
GI bleeding	26 (0.1%)	NR	17 (0.2%)	NR
Inflammatory bowel	82 (0.4%)	31 (0.4%)	51 (0.5%)	0 (0%)
Leukemia	14 (0.1%)	NR	NR	0 (0%)
Rheumatological	269 (1.5%)	128 (1.5%)	138 (1.4%)	NR
Tobacco use	4394 (23.9%)	2247 (27.2%)	2072 (21.1%)	75 (23.4%)

NR = small number not reported.

* AIDS, blood loss, lymphoma, tumor, ulcer, angina, inflammatory bowel, and leukemia were excluded from consideration because of low incidence. Age and sex were also included in the model, but not listed in the table.

complete observations). Although setting aside part of the original data as a validation data set generally results in less accurate prediction models,¹⁰ we included this step to evaluate how well a prediction model developed from NIS data might perform on a new data set. 2) We created a prediction model based on all available NIS data (2002–2010; 15,732 complete observations). To assess its likely predictive ability on a new data set, we bootstrapped the model 50 times, using the *c* statistic to gauge the model's predictive ability for each bootstrapped sample. We report the mean and 95% confidence interval of the bootstrapped *c* statistics to provide an indication of how much variability in predictive ability we would expect to encounter if the model were used to predict outcomes for new patients.

To reduce the number of predictors so that the model might be more clinically useful, we used a stepwise elimination method based on the Akaike Information Criterion (i.e., the stepAIC function in the R software package MASS). Because stepwise procedures are known to be somewhat unstable and vulnerable to the influence of extreme observations,¹⁰ we bootstrapped the stepwise routine 50 times and recorded the frequency with which each predictor was selected to remain in the final model. We considered a predictor selected in many bootstrap samples to be likely to perform better on a new data set than a predictor selected less often, and using this criterion, we took the top 20 predictors for poor outcome as our reduced model.

Finally, we used the coefficients of this model to create an integer-valued comorbidity index. We divided each coefficient by the absolute value of the smallest coefficient and rounded to the nearest integer. This established a point score for each comorbidity that varied between –2 (for hypercholesterolemia) to +7 (for neurological disorder). Our proposed comorbidity index is the sum of these integer values for each patient, a scale that varies from –5 to 55. We used this scale to assign a comorbidity score to each patient in the 2002–2010 NIS data, and we then used this score and patient age as the only predictors of poor outcome, mortality, length of stay (LOS), and hospital charges in 4 GEE models. We used the *c* statistic to assess the predictive ability of the comorbidity score, and we bootstrapped each model 50 times to estimate the performance of the comorbidity index as a predictor in a new data set.

For additional external validation, we then used the Pennsylvania Health Care Cost Containment Council (PHC4) database, a collection of all inpatient hospitalizations in Pennsylvania, for the fiscal years 2013–2014 (<http://www.phc4.org/>). We queried the database for all patients matching the previously noted inclusion and exclusion criteria. We then compared the predictive abilities of our neurovascular comorbidities index for the NIS and PHC4 database to predict mortality, poor outcome, and LOS; cost could not be compared because the PHC4 database does not include cost data elements.

Results

There were 18,423 total patients within the NIS database who met inclusion criteria for this study. Of these, 8268 underwent clipping, 9834 underwent coiling, and

321 underwent both treatments for their unruptured cerebral aneurysms. Of the 18,423 patients included, 405 died after treatment (2.2% overall mortality rate), findings in line with those of Raaymakers, et al.¹⁹ On querying the PHC4 database, we found there were 1090 patients who met inclusion criteria, with a similar distribution of clipping and coiling.

Significant Comorbidities

Multivariate analysis of 37 of the 43 patient comorbidities listed in Table 2 found the following variables to be significant predictors of poor outcome: age, neurological disorder, renal insufficiency, gastrointestinal (GI) bleeding, paralysis, acute myocardial infarction (MI), electrolyte disorder, weight loss, metastatic cancer, drug abuse, arrhythmia, coagulopathy, cerebrovascular accident (CVA), psychosis, alcoholism, perivascular disease, tobacco use, hypothyroidism, depression, and hypercholesterolemia (*p* < 0.05 for all).

Predictive Model

The statistically significant comorbidities were weighted based on their relative impact on patient outcomes to create a comorbidity index (see Table 3 for results). Individual scores ranged from –2 to 7, with positive scores denoting increased odds of poor outcome and negative scores denoting an inverse relationship with poor outcome.

To calculate a patient's comorbidity score, all individual comorbidity scores must be added. For example, a patient with renal insufficiency (+6) and CVA (+2) would

TABLE 3. Comorbidity scoring index

Comorbidity	Point Score	p Value
Neurological disorder	7	<0.001
Renal insufficiency	6	<0.001
GI bleeding	6	<0.05
Paralysis	5	<0.001
Acute MI	5	<0.001
Electrolyte disorder	4	<0.001
Weight loss	4	<0.001
Metastatic cancer	4	<0.01
Drug abuse	3	<0.001
Arrhythmia	2	<0.001
Coagulopathy	2	<0.01
CVA	2	<0.001
Psychosis	2	<0.01
Alcoholism	1	<0.05
Perivascular disease	1	<0.01
Valvular disease	1	<0.05
No comorbidities	0	NA
Tobacco use	–1	<0.001
Hypothyroidism	–1	<0.01
Depression	–1	<0.01
Hypercholesterolemia	–2	<0.001

NA = not applicable.

have a total score of +8. A patient with history of tobacco use (−1) and valvular disease (+1) would have a score of 0. A patient with hypercholesterolemia (−2) and tobacco use (−1) would have a score of −3. The sum score can then be used to stratify patients based on their preoperative comorbidities, the same as with the CCI and ECI. See Fig. 1 for the distribution of index scores.

Of note, to make this model comparable to the CCI and ECI, we did not assign a point value to age. It should be noted that increasing age was associated with an increasing mortality rate and poor outcome. Age should be used in conjunction with our scoring index to best stratify risk in patients.

Accuracy of the Model

We compared the performance of our model against the CCI in predicting mortality, poor outcome, LOS, and hospital costs because these are results for which the ECI and CCI are commonly used.^{1,3,12,18} To compare our index to the CCI and ECI as a predictor of mortality and poor outcome, we used the *c* statistic, a measure of how well a model can discriminate between subjects experiencing an event and not experiencing an event. The *c* statistic is equal to the AUC, with *c* = 1 indicating perfect prediction and *c* = 0.5 indicating no predictive ability.

A GEE model with our neurovascular comorbidities index and age as the only covariates was a highly significant predictor of mortality (*p* < 0.001) for patients with unruptured cerebral aneurysms in the 2002–2010 NIS data. The model had a *c* statistic of 0.775. In 50 bootstrap iterations, the mean *c* statistic was 0.773 (95% CI 0.754–0.792), suggesting that our index's predictive ability would remain consistent for other groups of patients with unruptured aneurysms. Similar models using CCI and ECI in place of our index had *c* statistics of 0.635 and 0.657, respectively, when used to predict outcomes for 2002–2010 NIS data. This demonstrates the significantly superior ability of our index to predict mortality compared with that of the CCI and ECI.

For predicting poor outcome, a model with our index and age as the only covariates was highly significant (*p* < 0.001) and had a *c* statistic of 0.814. In 50 bootstrap runs, the mean *c* statistic was also 0.814 (95% CI 0.798–0.830). Similar models using CCI and ECI in place of our index had *c* statistics of 0.694 and 0.712, respectively.

To assess the indices' abilities to predict LOS and total hospital charges, we categorized the outcomes and compared the proportion of patients who were correctly classified by each index. For LOS, we compared the ability of each index to predict a short stay (< 6 days), medium stay (6–14 days), or long stay (> 14 days). A model with our index and age as the only predictors correctly classified 69.5% of patients in 2002–2010 NIS data, compared with 63% for the CCI and 61.4% for the ECI (61.4%). None of the indices performed well in classifying patients who experienced long stays, but although the accuracy of the CCI and ECI for predicting this category was near 0, our index captured 18% of these patients (see Table 4 for details).

For comparing the indices' abilities to predict costs, we categorized charges as low, low to medium, medium to high, and high according to the quartiles of the distribu-

FIG. 1. Bar graph depicting distribution of patient comorbidity scores for the neurovascular comorbidity index. The values on the x axis represent the total patient comorbidity index score.

tion of hospital charges in the 2002–2010 NIS data, and we evaluated each index's ability to correctly classify patients (see Table 4 for details). All indices were poor predictors of costs. A model with our index and age as the only covariates demonstrated an overall accuracy of only 31%, compared with 25.8% for the CCI and 27% for the ECI (see Table 4 for details).

For external validation, we analyzed the ability of our neurovascular index to predict mortality, poor outcome, and LOS using the PHC4 database. We found that our neurovascular index performed similarly well with the PHC4 database compared with its performance in the NIS database. Concerning mortality, our neurovascular index demonstrated a *c* statistic of 0.775, slightly better than its performance in the NIS database. Regarding poor outcome, our neurovascular index had a *c* statistic of 0.814, not significantly different than its value of 0.814 in the NIS database. For LOS, our index demonstrated an accuracy of 89.8% for predicting short, 33.5% for medium, and 17.9% for long hospitalizations.

Discussion

The identification of preoperative risk factors and the ability to stratify patients based on their risk is the cornerstone of large database reviews. Until recently, much of the literature has used the CCI or the ECI for patient stratification.^{1,3,5,6,11,12,15,16,18,21} However, groups such as Liu et al. have demonstrated the inferiority of general indexes, specifically the CCI, to more disease-specific indexes in their paper on outcomes in dialysis patients.¹⁷ Similarly, neurovascular diseases are in need of a more disease-specific model for patient stratification.

Our neurovascular index for unruptured cerebral aneurysms receiving clipping or coiling was compared with

TABLE 4. Comparison of CCI, ECI, and our neurovascular comorbidities index from 2002 to 2010

Variable	Our Index + Age	CCI + Age	ECI + Age
Mortality	$c = 0.775$	$c = 0.635$	$c = 0.657$
Poor outcome	$c = 0.814$	$c = 0.694$	$c = 0.712$
LOS (correct categorizations)*	Overall: 69.5% Short stays: 89.8% Medium stays: 33.5% Long stays: 17.9%	Overall: 63.0% Short stays: 86.5% Medium stays: 22.9% Long stays: 0.25%	Overall: 61.4% Short stays: 79.8% Medium stays: 35.7% Long stays: 0.35%
Costs (correct categorizations)†	Overall: 31.0% Low costs: 0.1% Low/medium: 66.2% Medium/high: 35.0% High: 19.3%	Overall: 25.8% Low costs: 0% Low/medium: 25.5% Medium/high: 76.4% High: 0.9%	Overall: 27.0% Low costs: 0% Low/medium: 54.5% Medium/high: 50.4% High: 1.0%

* Short stays, < 6 days; medium stays, 6–14 days; long stays, > 14 days.

† Low costs, < \$45,000; low/medium costs, \$45,001–\$69,000; medium/high costs, \$69,001–\$113,000; high costs, > \$113,000.

the CCI and ECI with respect to mortality, poor outcome, LOS, and costs. Our model demonstrated a marked improvement in prediction for all 4 outcomes, particularly poor outcome and mortality, without a significant increase in the number of variables incorporated into the model.

Similar results were seen when we applied our neurovascular index to the PHC4 database: prediction of mortality and poor outcome maintained levels of accuracy as high as those seen in the NIS database. Although the ability to predict LOS was worse with the PHC4 database, the average LOS in the NIS database was significantly shorter than in the PHC4 database (6.4 days vs 3.9 days, respectively). However, neither our neurovascular index nor the CCI or ECI demonstrated good predictive abilities for LOS.

The most significant factors affecting patient outcomes were neurological disorder, renal insufficiency, GI bleeding, paralysis, and acute MI. Neurological disorder may carry such a significant weight because it may be a surrogate marker for cerebral aneurysm size, with larger aneurysms producing neurological deficits due to mass effect. In their meta-analysis, Raaymakers et al. found aneurysm size to be strongly predictive of patient outcomes.¹⁹ Similarly, aneurysms of sufficient size could produce paralysis as a manifestation of their neurological deficit.

Renal insufficiency, acute MI, arrhythmias, valvular disease, perivascular disease, and CVA also conferred significant risk of poor outcome. This is not unexpected; the recent American Heart Association guidelines for perioperative cardiovascular risk for noncardiac surgery listed these preoperative comorbidities as significant predictors of perioperative cardiac events.⁹

Other disorders such as GI bleeding, coagulopathy, metastatic cancer, and significant weight loss do not have firm support in the literature for their effects on postoperative mortality in unruptured cerebral aneurysms. It is possible that these disorders are surrogate markers for overall patient health status and that their presence implies less ability to tolerate procedural interventions. Further investigation into the role of these comorbidities is warranted.

Interestingly, hypercholesterolemia and tobacco use were negative predictive factors for mortality. The seemingly protective effect of hypercholesterolemia could be

due to the potential benefits of statin therapy in unruptured cerebral aneurysms.²⁰

Concerning tobacco use, Eftekhar and Morgan demonstrated no significant impact of tobacco use on outcomes after surgical treatment of unruptured aneurysms.⁷ Moreover, Juvela demonstrated that although smoking may carry an increased risk of subarachnoid hemorrhage ($p < 0.01$), there is not an associated increase in mortality rate after subarachnoid hemorrhage.¹³ Tobacco use has, however, been linked to increased aneurysm formation.¹⁴ Taken together, the seemingly protective nature of tobacco use may reflect its ability to bring this population of people to earlier screening, detection, and intervention based on their known risk factor.

The absence of diabetes and hypertension as significant predictors of patient outcomes is also an interesting aspect of our index. This may be the result of the confounding effects of the end organ complications of these diseases. For example, hypertension and diabetes are linked to renal insufficiency, acute MI, perivascular disease, and CVA, all of which are significant predictors of poor outcome in our study. Although hypertension and diabetes are known to be associated with poor outcomes in general, their predictive power may be overshadowed in our analysis by their end effects, which were included in our models and which we found to have even stronger associations with poor outcome.

Many groups are using the NIS database to study cerebral aneurysms. Our neurovascular index demonstrates superior performance compared with the CCI or ECI. Therefore, future studies should make use of our index for stratifying patients with unruptured cerebral aneurysms.

Study Limitations

There are several important limitations to this study. In using the NIS database, coding inaccuracies are inevitable, which can lead to a skewing of results. During our period of study from 2002 to 2010 there was a uniform set of codes for the procedures analyzed, and our methodology has been consistent with the published literature,^{1,3,12,18} but this does not eliminate data entry inaccuracies. Another limitation is the lack of data regarding aneurysm charac-

teristics in the NIS database. The NIS does not contain data about location, size, or geometry, which impact surgical decision making as well as patient outcomes. Additionally, the retrospective nature of our study introduces a degree of selection bias inherent to all retrospective reviews.

Another limitation of this study is our inability to use the modified Rankin Scale, a commonly used scale for disability. Information regarding pre- and postoperative disability is not available within the NIS database, and we therefore used discharge status as a surrogate marker for postoperative functional status. However, this limitation is seen throughout retrospective administrative database analyses.

Conclusions

Large database reviews need accurate methods for patient stratification to produce the most accurate results. We created a novel neurovascular comorbidity index for unruptured cerebral aneurysms, which significantly outperforms both the CCI and the ECI in predicting mortality, poor outcome, LOS, and costs. The index's improved predictive abilities suggest that perhaps it should be used in preference to the CCI or ECI for risk stratification in patients with unruptured cerebral aneurysms. Reevaluation of other patient cohorts is warranted to determine the impact of more accurate patient stratification on studies.

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Disclosures

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Author Contributions

Conception and design: Hoh, Newman. Acquisition of data: Newman, Neal. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Neal. Study supervision: Hoh.

Supplemental Information

Previous Presentations

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