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## Risk index for predicting perioperative stroke, myocardial infarction, or death risk in asymptomatic patients undergoing carotid endarterectomy

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### Abstract

**Objective**—The latest guidelines recommend performance of carotid endarterectomy (CEA) on asymptomatic patients with high-grade carotid stenosis, only if the combined perioperative stroke, myocardial infarction (MI), or death risk is < 3%. Our objective was to develop and validate a risk index to estimate the combined risk of perioperative stroke, MI, or death in asymptomatic patients undergoing elective CEA.

**Methods**—Asymptomatic patients who underwent an elective CEA (n = 17,692) were identified from the 2005-2010 National Surgical Quality Improvement Program, a multicenter, prospective database. Multivariable logistic regression analysis was performed with primary outcome of interest being the composite of any stroke, MI, or death during the 30-day perioperative period. Bootstrapping was used for internal validation. A risk index was created by assigning weighted points to each predictor using the  $\beta$ -coefficients from the regression analysis.

**Results**—Fifty-eight percent of the patients were men with a median age of 72 years. Thirty-day incidences of stroke, MI, and death were 0.9% (n = 167), 0.6% (n = 108), and 0.4% (n = 72), respectively. The combined 30-day stroke, MI, or death incidence was 1.8% (n = 324). On

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multivariable analysis, six independent predictors were identified and a risk index created by assigning weighted points to each predictor using the  $\beta$ -coefficients from the regression analysis. The predictors included age in years (<60: 0 point; 60-69: -1 point; 70-79: -1 point; 80: 2 points), dyspnea (2 points), chronic obstructive pulmonary disease (3 points), previous peripheral revascularization or amputation (3 points), recent angina within 1 month (4 points), and dependent functional status (5 points). Patients were classified as low (<3%), intermediate (3%-6%), or high (>6%) risk for combined 30-day stroke, MI, or death, based on a total point score of <4, 4-7, and >7, respectively. There were 15,249 patients (86.2%) in the low-risk category, 2233 (12.6%) in the intermediate-risk category, and 210 (1.2%) in the high-risk category.

**Conclusions**—The validated risk index can help identify asymptomatic patients who are at greatest risk for 30-day stroke, MI, and death after CEA, thereby aiding patient selection.

The Asymptomatic Carotid Atherosclerosis Study (ACAS) recommended addition of carotid endarterectomy (CEA) to best medical therapy (BMT) for asymptomatic carotid stenosis if CEA could be performed with a <3% perioperative major morbidity and mortality rate.<sup>1</sup> This finding has been corroborated over the years, and the selection of surgeons for the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) required that their rates of complications and death be <3% among asymptomatic patients.<sup>2</sup> Current American Heart Association/American College of Cardiology/American Stroke Association/Society for Vascular Surgery guidelines recommend (class IIa, level A evidence) CEA in asymptomatic patients who have >70% stenosis of the internal carotid artery, if the risk of perioperative stroke, myocardial infarction (MI), and death is low.<sup>3</sup>

These guidelines further recommend (class I, level C evidence) that selection of asymptomatic patients for carotid revascularization be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences.<sup>3</sup> The objective of our study was to develop and validate a risk index to predict combined 30-day stroke, MI, or death risk in asymptomatic patients undergoing elective CEA. This risk index would enable an estimation of a patient's perioperative risk after CEA and thus aid in careful patient selection, which is essential in ensuring low perioperative morbidity and mortality after CEA.

## METHODS

### Dataset

Data were extracted from the 2005-2010 National Surgical Quality Improvement Program (NSQIP) Participant Use Data Files.<sup>4</sup> These are multicenter, prospective databases with more than 250 participant academic and community U.S. hospitals. In NSQIP, a participating hospital's surgical clinical reviewer (SCR) captures data using a variety of methods, one of which is medical chart abstraction. Events occurring after hospital discharge are identified using comprehensive strategies.<sup>5</sup> In addition to examining inpatient medical records and outpatient patient charts, a minimum of three attempts to contact the patient by telephone or mail are made to ensure accurate documentation of postdischarge events. If no response is obtained, the Social Security Death Index and the National Obituary Archives are queried to investigate the potential of a death. Hospitals are required to provide complete 30-day follow-up on at least 95% of patients.<sup>5</sup> In NSQIP, morbidity is identified by independent chart review or patient encounter after patient discharge vs the SVS Vascular Quality Initiative (Society of Vascular Surgery, Chicago, Ill), where outcomes are tracked but depend on self-reporting.

In NSQIP, the data are collected based on strict criteria formulated by a committee. To ensure the data collected are of high quality, the NSQIP has developed different training mechanisms for the SCR and conducts an inter-rater reliability audit of participating sites.<sup>4</sup> Inter-rater reliability audits show that overall disagreement rates on variables was 1.56% (>140,000 audited fields) in 2008.<sup>6</sup> The processes of SCR training, inter-rater reliability auditing, data collection, and sampling methodology have been previously described in detail.<sup>4,7,8</sup>

## Patients

Patients undergoing elective CEA in the NSQIP datasets were identified using the American Medical Associations' current procedural terminology code for the procedure (35301) in combination with an *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code of occlusion and stenosis of the carotid artery without mention of cerebral infarction (433.10). To eliminate any potentially symptomatic patients, those with cerebrovascular accident with or without residual neurologic deficit, a history of transient ischemic attack, impaired sensorium, coma, tumor involving the central nervous system, hemiplegia/hemiparesis, paraplegia/paraparesis, or quadriplegia/quadruparesis were excluded. Subsequently, to improve generalizability, the following exclusion criteria were also applied: preoperative do-not-resuscitate status, on ventilator prior to procedure, ascites, esophageal varices, disseminated cancer, open wound with or without infection, preoperative transfusion of more than four units packed red blood cells, emergency case classification, chemotherapy within 30 days, radiotherapy within 90 days, systemic sepsis within 48 hours, contaminated/dirty wound class, cases with a simultaneous procedure, and previous operation within 30 days. Preoperative data obtained included demographics, lifestyle, comorbidity, functional status, and other variables.

## Outcome

The primary outcome of interest was the composite of any stroke, MI, or death during the 30-day perioperative period. This composite end point was chosen based on recent guidelines of the American Heart Association/American College of Cardiology/American Stroke Association/Society for Vascular Surgery stating "It is reasonable to perform CEA in asymptomatic patients who have more than 70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low."

Stroke has been defined in the NSQIP database as "Patient develops an embolic, thrombotic, or hemorrhagic vascular accident or stroke with motor, sensory, or cognitive dysfunction (for example, hemiplegia, hemiparesis, aphasia, sensory deficit, impaired memory) that persists for 24 or more hours."

Myocardial infarction has been defined in the NSQIP database as "Presence of one of the following: (1) documentation of electrocardiogram (ECG) changes indicative of acute MI (one or more of the following): (a) ST elevation > 1 mm in two or more contiguous leads (b) new left bundle branch (c) new Q-wave in two of more contiguous leads or (2) new elevation in troponin greater than three times upper level of the reference range in the setting of suspected myocardial ischemia."<sup>9</sup>

## Definitions of relevant preoperative variables

Chronic obstructive pulmonary disease (COPD) is defined by NSQIP as follows: "COPD (such as emphysema and/or chronic bronchitis) resulting in any one or more of the following: (1) Functional disability from COPD (eg, dyspnea, inability to perform activities of daily living); (2) hospitalization in the past for treatment of COPD; (3) requires chronic bronchodilator therapy with oral or inhaled agents; (4) a forced expiratory volume in 1

second of <75% of predicted on pulmonary function testing. Patients are not included whose only pulmonary disease is asthma, an acute and chronic inflammatory disease of the airways resulting in bronchospasm. Patients with diffuse interstitial fibrosis or sarcoidosis are not included.”

Dyspnea is defined by NSQIP as follows: “difficult, painful, or labored breathing” upon moderate exertion (for example, is unable to climb one flight of stairs without shortness of breath) or at rest. The dyspneic patient is subjectively aware of difficulty with breathing. The time frame is within 30 days prior to surgery.

Previous peripheral revascularization or amputation (PAD) is defined by NSQIP as follows: “Any type of angioplasty (including stent placement) or revascularization procedure for atherosclerotic peripheral vascular disease (for example, aorta-femoral, femoral-femoral, femoral-popliteal) or a patient who has had any type of amputation procedure for peripheral vascular disease (for example, toe amputations, transmetatarsal amputations, below-the-knee or above-the-knee amputations). Patients who have had amputation for trauma should not be included.”

Functional status “focuses on the patient’s abilities to perform activities of daily living (ADLs) in the 30 days prior to surgery. Activities of daily living are defined as ‘ the activities usually performed in the course of a normal day in a person’s life. ADLs include bathing, feeding, dressing, toileting, and mobility.” The patient is considered independent if “the patient does not require assistance from another person for any activities of daily living. This includes a person who is able to function independently with prosthetics, equipment, or devices.” If some assistance is required, the patient is considered dependent.

### Statistical analysis

Stepwise multivariable logistic regression analysis was used to identify preoperative variables associated with increased risk of combined stroke, MI, or death within 30 days of an elective CEA. The *P* value entry and stay criteria for the logistic regression model were .1 and .05, respectively. Interactions between the significant predictors were assessed.

Categorical predictors such as race were incorporated into the model using reference coding. This means that one level of the categorical predictor is chosen as a reference category, and the remaining levels of the predictor are compared with the reference. Statistical analysis was performed using SAS (version 9.2; SAS Institute, Cary, NC). *P* < .05 was considered significant.

### Risk model performance

The accuracy of the logistic regression model was assessed by its discrimination and calibration.<sup>10</sup> Discrimination measures how well a model can distinguish between cases (stroke/MI/death) vs non-cases (favorable outcome). Discrimination was assessed by *c*-statistic, also known as the area under the receiver-operating characteristic curve. The *c*-statistic ranges from 0.50 (no better than flipping a coin) to 1.00 (model is 100% correct).

Calibration measures a model’s ability to generate predictions that are close to the observed outcomes in the data. The most widely used method for doing this for hospital-based mortality models is the Hosmer-Lemeshow test, which examines how well the percentage of observed stroke/MI/death matches the percentage of predicted stroke/MI/death over deciles of predicted risk.<sup>10</sup>

## Risk model validation

Because predictive models perform better on the data from which they were derived than on new data, we performed bootstrap resampling to obtain a bias-corrected *c*-statistic, thereby providing a more accurate estimate of model performance in other populations.<sup>11</sup> This method of internal validation was chosen over others, such as split-sample modeling, because bootstrap resampling techniques have been shown to produce stable and nearly unbiased estimates of predictive accuracy, with better efficiency than other methods.<sup>11</sup> For this purpose, 1000 random bootstrap samples with replacement and of the same size as the original sample were drawn from the original dataset consisting of all patients.

## Development of risk index

Once the model was developed using the regression equation, it was used to develop a risk index. We used the methods described by Sullivan et al<sup>12</sup> to modify the parameter estimates of the regression model into an index. The number of points assigned to each variable equaled its regression coefficient divided by 0.2, followed by rounding to the nearest whole number. Thus, the association of a variable assigned 2 points as twice as “strong” as that of a variable with 1 point but half as “strong” as that with 4 points. The points for each risk factor were then summed to obtain the total number of points for a patient.

To estimate the risk associated with each total point score, the intercept in the regression equation (−4.3392) was added to 0.2 times the total point score to obtain  $\hat{L}$ . The risk estimate for each total point score was then calculated using the formula for back-transforming from a logistic regression estimated score to a probability, as:

$$\text{Estimated probability percentage} = 100\% * \frac{e^{\hat{L}}}{1 + e^{\hat{L}}}$$

## RESULTS

Median age of the 17,692 asymptomatic patients (57.9% men) who underwent a CEA was 72 years. The demographic characteristics, comorbidities, and laboratory values are listed in Table I. Thirty-day incidences of stroke, MI, and death were 0.9% (n = 167), 0.6% (n = 108), and 0.4% (n = 72), respectively. The combined 30-day stroke, MI, or death incidence was 1.8% (n = 324). The 30-day perioperative complications are listed in Table II.

On multivariable analysis (Table III), six independent predictors for combined 30-day stroke, MI, or death were identified and points assigned to them based on their regression coefficients: age in years (<60: 0 point; 60-69: 1 point; 70-79: −1 point; 80: 2 points), dyspnea at rest or moderate exertion (2 points), COPD (3 points), PAD (3 points), recent angina within 1 month (4 points), and dependent functional status (5 points). Gender was not a significant predictor. The multivariable regression model demonstrated moderate discrimination (*c*-statistic, 0.64; bias-corrected *c*-statistic, 0.64) and calibration (Hosmer-Lemeshow test  $\chi^2 = 7.37$ ; *P* = .19). There was not a significant interaction (*P* > .05) between the significant predictors in the model.

The estimated risk for each patient was calculated by adding the points assigned to each risk factor present in the patient, thereby obtaining the point total for the patient, and then using Table IV to calculate the risk. Patients were classified as low (<3%), intermediate (3%-6%), or and high (>6%) risk for 30-day stroke, MI, or death based on a total point score of <4, 4-7, and >7, respectively. There were 15,249 patients (86.2%) in the low-risk category, 2233 (12.6%) in the intermediate-risk category, and 210 (1.2%) in the high-risk category.

### Subgroup analysis for age

The higher risk for combined 30-day stroke, MI, or death seen in patients age “<60 years” compared with “60-69 years” and “70-79 years” was further investigated using separate individual multivariable analyses for each of stroke, MI, and death. Age “<60 years” was independently associated with a higher risk for postoperative stroke than age “60-69 years” (odds ratio [OR], 1.97; 95% confidence interval [CI], 1.22-3.19) and “70-79 years” (OR, 2.01; 95% CI, 1.26-3.19) but not 80 years (OR, 1.34; 95% CI, 0.82-2.19).

Although no difference was seen in the association with postoperative MI between age “<60 years” and ages “60-69 years” and “70-79 years,” age “<60 years” was associated with lower risk for MI than age 80 years (OR, 0.25; 95% CI, 0.10-0.63). Similarly, no difference was seen in the association with postoperative death between age “<60 years” and ages “60-69 years” and “70-79 years.” Age “<60 years” was associated with lower risk for postoperative death than age “80 years” (OR, 0.30; 95% CI, 0.10-0.88).

### Subgroup analysis for type of anesthesia

Subset analysis was performed for regional and general anesthesia with regard to dyspnea and COPD. For patients who received regional anesthesia, COPD remained a significant predictor ( $P = .005$ ); however, dyspnea dropped out ( $P = .24$ ). For patients who received a general anesthetic, both remained strong independent predictors ( $P < .0001$  for both).

## DISCUSSION

Three-fourths of the 117,000 CEAs done annually in the United States are for asymptomatic disease.<sup>13</sup> Given the low rates of stroke for asymptomatic disease with BMT alone, carotid revascularization is recommended only if accompanied by low rates of perioperative complications.<sup>3</sup> This necessitates careful patient selection based on patient comorbidities and life expectancy. Since ACAS, there has been a lack of objective tools for physicians, neurologists, interventionalists, and surgeons to guide them on patient selection.

Only one risk score estimating perioperative stroke and death risk after CEA in asymptomatic patients based on patient demographics and comorbidities exists.<sup>14</sup> However, it is based on 15-year-old population data, with perioperative stroke and death rates >3%. Since then, there has been a tremendous improvement in perioperative complication rates. As seen in our study, 30-day stroke and death incidence after CEA in asymptomatic patients has decreased to 1.3% in the United States, whereas 30-day stroke, MI, or death incidence is low at 1.8%. Although overall perioperative complication rates currently are low, there are select subsets of patients with periprocedural risk >3%. Careful patient selection necessitates identification of patients at low operative risk who may benefit from CEA, in contrast to patients at high risk, whose asymptomatic carotid disease may be best suited to BMT alone.

In the present study with the largest published cohort of asymptomatic patients, we identified risk factors associated with 30-day stroke, MI, or death after CEA. The risk factors included age, dyspnea, COPD, PAD, recent angina, and dependent functional status, and, using these, a risk index was developed. Patients in the low-risk tier have a perioperative risk <3%, in contrast to intermediate- and high-risk tier, with risk of 3%-6% and >6%, respectively.

Octogenarians have long been known to have higher risk for perioperative stroke, MI, or death after CEA.<sup>15-17</sup> These patients have been excluded from most trials due to their higher perioperative risk and relatively shorter life expectancy.<sup>18</sup> ACAS and the Asymptomatic Carotid Surgery Trial showed an absolute stroke risk reduction of approximately 5% over 5 years,<sup>1,19</sup> which necessitates a long enough life expectancy for the benefits to be realized.

Given the growing number of older adults and a current life-table analysis that predicts that patients who survive to the age of 80 to 85 years will live another 8 years on average, the number of octogenarians who will require CEA likely will increase exponentially in the near future.<sup>20,21</sup> The findings from our study show that otherwise healthy octogenarians should not be denied CEA solely based on their age. Although these patients are at higher risk compared with younger patients, based on our risk index, otherwise healthy octogenarians would still be in the low-risk category with a perioperative risk <3%.

It was surprising to find age “<60 years” to be associated with a higher risk than “60-69 years” and “70-79 years” (but lower risk than “80 years”). A more detailed analysis of the data for the age component of our series indicates that the increased risk for patients “<60 years” was secondary to an increased risk for perioperative stroke in these patients. Although this finding has not been previously demonstrated in major trials, several studies have demonstrated that younger patients have a higher incidence of stroke after CEA<sup>22</sup> and a particularly “virulent” course after lower extremity surgical revascularization, requiring frequent multiple interventions and leading to a relatively poor limb salvage rate compared with older patients who underwent similar surgical procedures.<sup>23,24</sup> We speculate that this probably is due to more aggressive atherosclerotic and prothrombotic processes in these patients.<sup>22,25,26</sup>

Previous studies on coronary revascularization have shown PAD to be independently associated with adverse postoperative outcomes.<sup>27</sup> Previous peripheral revascularization or amputation encompasses such disease contributors as tobacco use, diabetes, previous MI, heart failure, hypertension, and obesity, and, as such, it is not surprising that such patients were found to be at an increased perioperative risk.<sup>28</sup> Furthermore, the recently described and still incompletely understood association of PAD with a systemic inflammatory state may further worsen the outcomes of any carotid revascularization operation.<sup>29</sup>

Chronic obstructive pulmonary disease and severe dyspnea are known to be associated with higher risk after vascular surgery, in general, and CEA, in particular.<sup>15,30,31</sup> Adverse surgical outcomes are more common in patients with COPD as it leads to impairment of mucociliary clearance, increased propensity for arrhythmias, and left ventricular dysfunction.<sup>32</sup> Patients with recent angina are predisposed to adverse cardiac events and were at higher risk for adverse perioperative events. Dependent functional status was associated with the highest risk for adverse perioperative outcomes after CEA, a finding that has been previously shown after other vascular operations.<sup>14,15,31,33</sup> Even with a favorable age profile, these patients have a point score 4, classifying them into intermediate or high risk, with risk of adverse events >3%. A thorough risk-benefit analysis needs to be performed before considering these patients for carotid revascularization.

This study based on the NSQIP database has many strengths not seen in other studies. These include a large sample size from a broad nationwide population that enables smaller confidence intervals in the assessment of risk factors. It is based on data obtained from both academic and community hospitals, includes data that have been independently validated and audited, and takes into account multiple preoperative variables. This is in contrast to the many registry-based and Medicare analyses, which are primarily administrative discharge datasets lacking the accuracy of NSQIP because their data are not validated.

The present study has certain limitations. This study is a retrospective analysis of prospectively recorded data. The NSQIP was built for all surgeries and is not CEA specific; thus, it does not take into account many factors that are relevant to CEA. There is no information on the degree of stenosis; the side of disease; presence of contralateral occlusion; diagnostic imaging methods; preoperative stress test and other cardiac workup;

technical details of the procedure, such as type of closure and use of shunts; surgeon characteristics, including specialty and volume; and lack of objective observer analysis for determination of stroke after the procedure. Use of medications such as antiplatelets, statins, and  $\beta$ -blockers is also not available in the NSQIP dataset. Patients with certain comorbidities may already have been pre-excluded from undergoing a CEA due to presumed high risk, thus creating a sampling bias. However, this bias exists for all risk estimation tools,<sup>34,35</sup> as these tools are based on a sample of patients who have already undergone surgery and might have had exclusions for presumed high risk. Lastly, discrimination of the risk model (*c*-statistic) was only moderate, with  $>0.8$  considered excellent and  $<0.6$  poor. It must be remembered, however, that this is similar to all the previously existing risk assessment tools for vascular surgery patients, such as Lee's revised cardiac risk index and Gupta's cardiac risk calculator, which also show only moderate discrimination.<sup>18,34</sup> This could be due to the fact that as the study case mix is restricted and patients become more homogeneous (only one type of surgery), the *c*-statistic tends to drop and thus is less informative.<sup>36</sup>

Current guidelines define MI as elevation of troponin above the reference range. In this study, new elevation in troponin  $>3$  times the upper level of the reference range in the setting of suspected myocardial ischemia was used as the definition. Although this would lead to exclusion of some MI, one can also argue that this makes MI a harder end point as minor myocardial damage is excluded. This approach of using a harder troponin end point to diagnose MI has been previously validated and published.<sup>18</sup>

Current guidelines recommend CEA for asymptomatic patients with high-grade internal carotid artery stenosis, with the caveat that the expected postoperative major adverse event rate be  $<3\%$ , as beyond this, the advantage of carotid revascularization over BMT diminishes. The risk index proposed in this study would aid in identifying high-risk patients. Patients in the low-risk category probably would benefit from CEA, in contrast with patients in the high-risk category, who probably would benefit from BMT. Thus, we foresee this index as an objective adjunct to the clinician's subjective judgment in the patient selection process.

Apart from identifying high-risk patients, the risk index can serve as an important tool in the informed consent process. Accurate individualized assessment of perioperative risk after CEA certainly would assist in the presentation of adequate information regarding risks and benefits. Physicians have long quoted the most current literature to explain risks of adverse outcomes associated with a procedure. This has not always been an easy task, as each patient is different with a unique set of risk factors. Thus, this risk index will simplify the informed consent process by providing an estimate of postoperative stroke, MI, and mortality risk after CEA.

## CONCLUSIONS

The 30-day stroke and death incidence after CEA in asymptomatic patients is 1.3% in the United States. A risk index was developed classifying patients into low ( $<3\%$ ), intermediate (3%-6%), and high ( $>6\%$ ) risk for 30-day stroke, MI, or death. The proposed validated risk index can help identify the subgroup of asymptomatic patients who are at greatest risk for 30-day stroke, MI, and death after CEA, thereby aiding patient selection and informed consent.

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## References

1. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA*. 1995; 273:1421–8. [PubMed: 7723155]
2. Brott TG, Hobson RW, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med*. 2010; 363:11–23. [PubMed: 20505173]
3. Brott TG, Halperin JL, Abbara S, Bacharach JM, Barr JD, Bush RL, et al. ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Neuro-Interventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery. *Circulation*. 2011; 124:489–532. [PubMed: 21282505]
4. [March 1, 2009] ACS NSQIP PUF. Available at: [http://www.acsnsqip.org/puf/docs/ACS\\_NSQIP\\_Participant\\_User\\_Data\\_File\\_User\\_Guide.pdf](http://www.acsnsqip.org/puf/docs/ACS_NSQIP_Participant_User_Data_File_User_Guide.pdf)
5. Bilimoria KY, Cohen ME, Ingraham AM, Bentrem DJ, Richards K, Hall BL, et al. Effect of postdischarge morbidity and mortality on comparisons of hospital surgical quality. *Ann Surg*. 2010; 252:183–90. [PubMed: 20531000]
6. Shiloach M, Frencher SK Jr, Steeger JE, Rowell KS, Bartzokis K, Tomeh MG, et al. Toward robust information: data quality and inter-rater reliability in the American College of Surgeons National Surgical Quality Improvement Program. *J Am Coll Surg*. 2010; 210:6–16. [PubMed: 20123325]
7. Khuri SF, Daley J, Henderson W, Barbour G, Lowry P, Irvin G, et al. The National Veterans Administration Surgical Risk Study: risk adjustment for the comparative assessment of the quality of surgical care. *J Am Coll Surg*. 1995; 180:519–31. [PubMed: 7749526]
8. Khuri SF, Daley J, Henderson W, Hur K, Gibbs JO, Barbour G, et al. Risk adjustment of the postoperative mortality rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *J Am Coll Surg*. 1997; 185:315–27. [PubMed: 9328380]
9. [March 21, 2010] ACS NSQIP. Available at: [https://acsnsqip.org/documents\\_section/documents\\_chapter4.pdf](https://acsnsqip.org/documents_section/documents_chapter4.pdf)
10. Kramer AA, Zimmerman JE. Assessing the calibration of mortality benchmarks in critical care: the Hosmer-Lemeshow test revisited. *Crit Care Med*. 2007; 35:2052–6. [PubMed: 17568333]
11. Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol*. 2001; 54:774–81. [PubMed: 11470385]
12. Sullivan LM, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: the Framingham Study risk score functions. *Stat Med*. 2004; 23:1631–60. [PubMed: 15122742]
13. Halm EA, Tuhim S, Wang JJ, Rojas M, Hannan EL, Chassin MR. Has evidence changed practice?: appropriateness of carotid endarterectomy after the clinical trials. *Neurology*. 2007; 68:187–94. [PubMed: 17224571]
14. Calvillo-King L, Xuan L, Zhang S, Tuhim S, Halm EA. Predicting risk of perioperative death and stroke after carotid endarterectomy in asymptomatic patients: derivation and validation of a clinical risk score. *Stroke*. 2010; 41:2786–94. [PubMed: 21051669]
15. Gupta PK, Pipinos II, Miller WJ, Gupta H, Shetty S, Johannig JM, et al. A population-based study of risk factors for stroke after carotid endarterectomy using the ACS NSQIP database. *J Surg Res*. 2011; 167:182–91. [PubMed: 21109261]

16. Rothwell PM, Slattery J, Warlow CP. Clinical and angiographic predictors of stroke and death from carotid endarterectomy: systematic review. *BMJ*. 1997; 315:1571–7. [PubMed: 9437274]
17. Saleh SS, Hannan EL. Carotid endarterectomy utilization and mortality in 10 states. *Am J Surg*. 2004; 187:14–9. [PubMed: 14706579]
18. Gupta PK, Gupta H, Sundaram A, Kaushik M, Fang X, Miller WJ, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation*. 2011; 124:381–7. [PubMed: 21730309]
19. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet*. 2004; 363:1491–502. [PubMed: 15135594]
20. US Census Bureau. [April 17, 2012] An Aging World: 2001. Available at: <http://www.census.gov/prod/2001pubs/p95-01-1.pdf>
21. McKenna RJ Sr. Clinical aspects of cancer in the elderly. Treatment decisions, treatment choices, and follow-up. *Cancer*. 1994; 74:2107–17. [PubMed: 8087778]
22. Pedrini L, Pisano E, Sacca A, Magnoni F, D'Addato M. Carotid endarterectomy in young adults. *Int Angiol*. 1991; 10:220–3. [PubMed: 1797931]
23. Levy PJ, Hornung CA, Haynes JL, Rush DS. Lower extremity ischemia in adults younger than forty years of age: a community-wide survey of premature atherosclerotic arterial disease. *J Surg*. 1994; 19:873–81. [PubMed: 8170042]
24. Olsen PS, Gustafsen J, Rasmussen L, Lorentzen JE. Long-term results after arterial surgery for arteriosclerosis of the lower limbs in young adults. *Eur J Vasc Surg*. 1988; 2:15–8. [PubMed: 3224712]
25. McCready RA, Vincent AE, Schwartz RW, Hyde GL, Mattingly SS, Griffen WO Jr. Atherosclerosis in the young: a virulent disease. *Surgery*. 1984; 96:863–9. [PubMed: 6333732]
26. Nagayama M, Shinohara Y, Nagayama T. Lipoprotein(a) and ischemic cerebrovascular disease in young adults. *Stroke*. 1994; 25:74–8. [PubMed: 8266386]
27. O'Rourke DJ, Quinton HB, Piper W, Hernandez F, Morton J, Hettleman B, et al. Survival in patients with peripheral vascular disease after percutaneous coronary intervention and coronary artery bypass graft surgery. *Ann Thorac Surg*. 2004; 78:466–70. [PubMed: 15276497]
28. Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation*. 2006; 113:e463–654. [PubMed: 16549646]
29. Brevetti G, Giugliano G, Brevetti L, Hiatt WR. Inflammation in peripheral artery disease. *Circulation*. 2010; 122:1862–75. [PubMed: 21041698]
30. Bertges DJ, Goodney PP, Zhao Y, Schanzer A, Nolan BW, Likosky DS, et al. The Vascular Study Group of New England Cardiac Risk Index (VSG-CRI) predicts cardiac complications more accurately than the Revised Cardiac Risk Index in vascular surgery patients. *J Vasc Surg*. 2010; 52:674–83. [PubMed: 20570467]
31. Gupta PK, Mactaggart JN, Natarajan B, Lynch TG, Arya S, Gupta H, et al. Predictive factors for mortality after open repair of paravisceral abdominal aortic aneurysm. *J Vasc Surg*. 2012; 55:666–73. [PubMed: 22209613]
32. Leavitt BJ, Ross CS, Spence B, Surgenor SD, Olmstead EM, Clough RA, et al. Long-term survival of patients with chronic obstructive pulmonary disease undergoing coronary artery bypass surgery. *Circulation*. 2006; 114:1430–4. [PubMed: 16820614]

33. Crawford RS, Cambria RP, Abularrage CJ, Conrad MF, Lancaster RT, Watkins MT, et al. Preoperative functional status predicts perioperative outcomes after infrainguinal bypass surgery. *J Vasc Surg.* 2010; 51:351–8. [PubMed: 20141958]
34. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation.* 1999; 100:1043–9. [PubMed: 10477528]
35. Goldman L, Caldera DL, Nussbaum SR, Southwick FS, Krogstad D, Murray B, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. *N Engl J Med.* 1977; 297:845–50. [PubMed: 904659]
36. Merkow RP, Hall BL, Cohen ME, Dimick JB, Wang E, Chow WB, et al. Relevance of the c-statistic when evaluating risk-adjustment models in surgery. *J Am Coll Surg.* 2012; 214:822–30. [PubMed: 22440055]

**Table I**

Preoperative characteristics for the 2005-2010 National Surgical Quality Improvement Program (NSQIP) dataset

Category	Preoperative variable		N (%)
Cardiac	Angina within 1 month	Yes	381 (2.2)
	Cardiac surgery prior	Yes	4279 (24.2)
	Congestive heart failure	Yes	120 (0.7)
	Myocardial infarction (within 6 months)	Yes	218 (1.2)
	Percutaneous coronary intervention prior	Yes	3481 (19.7)
Circulatory	Bleeding disorder	Yes	2497 (14.1)
	Previous peripheral arterial revascularization or amputation	Yes	1720 (9.7)
	Rest pain in lower extremity	Yes	121 (0.7)
General	Age, years	<60	1896 (10.7)
		60-69	5465 (30.9)
		70-79	6808 (38.5)
		80	3523 (19.9)
		American Society of Anesthesiologists class	1
		2	4641 (26.3)
		3	11,238 (63.6)
		4	1362 (7.7)
		5	3 (0.02)
	Body mass index, median (interquartile range), kg/m <sup>2</sup>		28.5 (25.4-32.3)
	Corticosteroid use (chronic)	Yes	319 (1.8)
	Diabetes mellitus	On insulin	2844 (16.1)
		On medication	1934 (10.9)
	Functional status	Dependent	290 (1.6)
	Hypertension	Yes	15,144 (85.6)
	Race	American Indian	44 (0.3)
		Asian/Pacific Islander	176 (1.0)
		Black	580 (3.3)
		Hispanic	506 (2.9)
		Unknown	1037 (5.9)
White		15,162 (86.6)	
Sex		Male	10,217 (57.9)
	Female	7437 (42.1)	
Systemic inflammatory response syndrome	Yes	78 (0.5)	
Transition (admitted from:)	Home	17,520 (99.0)	
	Acute care	89 (0.5)	
	VA acute care	1 (0.01)	
	Chronic care	55 (0.3)	
	VA chronic care	0	
	Others	27 (0.2)	

Category	Preoperative variable		N (%)
	Weight loss >10% within 6 months	Yes	71 (0.4)
Laboratory	Albumin	Abnormal	914 (5.2)
	Alkaline phosphatase	Abnormal	544 (3.1)
	Blood urea nitrogen	Abnormal	7310 (41.3)
	Creatinine	Abnormal	2197 (12.4)
	Hematocrit	Abnormal	3379 (19.1)
	Platelets	Abnormal	2360 (13.3)
	Prothrombin time	Abnormal	3311 (18.7)
	Partial thromboplastin time	Abnormal	1081 (6.1)
	Serum glutamic oxaloacetic transaminase	Abnormal	922 (5.2)
	Sodium	Abnormal	1950 (11.0)
	White blood cell count	Abnormal	1700 (9.6)
Renal	Dialysis (preoperative)	Yes	143 (0.8)
Respiratory	COPD	Yes	1755 (9.9)
	Dyspnea	At rest or moderate exertion	3310 (18.7)
	Pneumonia (preoperative)	Yes	14 (0.1)
Social	Alcohol intake within last 2 weeks	Yes	746 (4.2)
	Smoking within past year	Yes	4588 (25.9)
Therapy	Anesthesia	General	14,649 (82.8)
		Regional	3040 (17.2)

*COPD*, Chronic obstructive pulmonary disease; *VA*, Veterans Affairs.

**Table II**

Intraoperative/postoperative characteristics for the 2005-2010 National Surgical Quality Improvement Program (NSQIP) dataset

Intraoperative/postoperative variables	N (%)
Intraoperative	
Anesthesia time, median (lower quartile-upper quartile), minutes	168 (137-204)
Operative time, median (lower quartile-upper quartile), minutes	107 (83-136)
Postoperative	
Major complications	
Cardiac	
Cardiac arrest	30 (0.2)
Myocardial infarction	108 (0.6)
Circulatory	
Postoperative packed red blood cells transfusion >4 units	74 (0.4)
Graft	
Graft/prosthesis failure	13 (0.1)
Infection	
Sepsis	52 (0.3)
Septic shock	26 (0.2)
Neurologic	
Coma	12 (0.1)
Peripheral nerve deficit	40 (0.2)
Stroke	167 (0.9)
Renal	
Acute renal failure	23 (0.1)
Renal insufficiency	21 (0.1)
Respiratory	
Pneumonia	119 (0.7)
Reintubation	134 (0.8)
Ventilator >48 hours	74 (0.4)
Return to operating room	768 (4.3)
Venous thromboembolism	
Deep venous thrombosis	26 (0.2)
Pulmonary embolism	23 (0.1)
Wound	
Deep wound infection	14 (0.1)
Wound dehiscence	23 (0.1)
Minor complications	
Superficial wound infection	73 (0.4)
Urinary tract infection	103 (0.6)
Other postoperative parameters	
Length of stay for survivors, median (lower quartile-upper quartile), days	1 (1-2)
Mortality	72 (0.4)
Combined postoperative parameters	
Stroke or death	225 (1.3)
Stroke, MI, or death	324 (1.8)

*MI*, Myocardial infarction.

**Table III**

Risk factors associated with combined 30-day stroke, myocardial infarction (MI), and death after carotid endarterectomy (CEA) in asymptomatic patients on multivariate analysis

Risk factor	Adjusted OR	95% CI	Regression coefficients	Points assigned
Age, years				
<60	Reference	Reference	Reference	0
60-69 (vs <60)	0.75	0.50-1.12	-0.29	-1
70-79 (vs <60)	0.84	0.57-1.24	-0.17	-1
80 (vs <60)	1.52	1.03-2.26	0.42	2
Dyspnea at moderate exertion or rest				
No	Reference	Reference	Reference	0
Yes	1.43	1.10-1.86	0.36	2
Previous peripheral revascularization or amputation				
No	Reference	Reference	Reference	0
Yes	1.80	1.33-2.45	0.59	3
COPD				
No	Reference	Reference	Reference	0
Yes	1.73	1.27-2.36	0.55	3
Recent angina within 1 month				
No	Reference	Reference	Reference	0
Yes	2.05	1.21-3.47	0.72	4
Dependent functional status				
No	Reference	Reference	Reference	0
Yes	2.77	1.68-4.58	1.02	5

CI, Confidence interval; COPD, chronic obstructive pulmonary disease; NSQIP, National Surgical Quality Improvement Program; OR, odds ratio. Preoperative functional status has been defined in the National Surgical Quality Improvement Program (NSQIP) as the ability to perform activities of daily living in the 30 days before surgery. Activities of daily living are defined as the activities usually performed in the course of a normal day in a person's life; they include bathing, feeding, dressing, toileting, and mobility.

COPD is defined by the NSQIP as follows: "COPD (such as emphysema and/or chronic bronchitis) resulting in any one or more of the following: (1) functional disability from COPD (eg, dyspnea, inability to perform activities of daily living); (2) hospitalization in the past for treatment of COPD; (3) requires chronic bronchodilator therapy with oral or inhaled agents; (4) an forced expiratory volume in 1 second of <75% of predicted on pulmonary function testing."

**Table IV**

Estimated risk of combined 30-day stroke, myocardial infarction (MI), or death after carotid endarterectomy (CEA) in asymptomatic patients

Total points for the patient	Estimated risk percentage for the patient	Risk tier categorization	N (%)
-1	1.18	Low	15,249 (86.2%)
0	1.44		
1	1.75		
2	2.13		
3	2.6		
4	3.15	Intermediate	2233 (12.6%)
5	3.82		
6	4.63		
7	5.6		
8	6.75	High	210 (1.2%)
9	8.13		
10	9.75		
11	11.66		
12	13.88		
13	16.45		
14	19.38		
15	22.7		
16	26.4		
17	30.47		
18	34.86		
19	39.53		