Review Article

Using Risk Models to Improve Patient Selection for High-Risk Vascular Surgery

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Received 27 August 2012; Accepted 16 October 2012

Academic Editors: A. Kalangos and M. Morasch

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Vascular surgeons frequently perform procedures aimed at limiting death, stroke, or amputation on patients who present with diseases such as aortic aneurysms, carotid atherosclerosis, and peripheral arterial occlusive disease [1]. These operations, whether they involve repair of an aneurysmal segment of aorta [2], bypass of an occluded artery in the leg [3], or removal of atherosclerotic plaque in a carotid artery [4], all serve a palliative purpose. The operations themselves, of course, do not cure atherosclerosis. Rather, they serve to mitigate its effects and limit its manifestations during the remainder of the patient’s life. In other words, they must prevent death from ruptured aneurysms, limit limb loss from lower extremity vascular disease, and provide prophylaxis from stroke from carotid atherosclerosis.

However, given the current cost constraints in health care, surgeons must, now more than ever, balance the potential benefits associated with these surgical interventions with alternative strategies [5, 6]. They must consider, against the background of medical alternatives, the physiologic insult that surgery entails in these elderly patients, who often carry with them significant comorbidity burdens [7–10]. One of the most important elements in effectively utilizing expensive, morbid procedures, such as thoracic aneurysm repair, lower extremity bypass, and carotid endarterectomy, is to perform these procedures on patients who will benefit from the procedure and not suffer complications from it.

While “good patient selection” may sound like a simple objective, achieving good patient selection remains a constantly evolving and sometimes elusive goal. New, less invasive endovascular alternatives can change the risk profile of an operation, such as thoracic endovascular grafting for thoracic aortic aneurysms [11]. New medications, such as high-dose statins and antiplatelet agents, can enhance the durability and effectiveness of lower extremity bypass procedures [12]. And both of these changes—less invasive alternatives and new medical adjuncts—have influenced which patients undergo, and garner benefit from carotid revascularization [13, 14].

To best select patients for these high-risk operations, surgeons need data that incorporates these complex covariates in their decision-making algorithms. In this paper, we highlight how regional and national datasets can help surgeons identify which patients are most likely to benefit

1. Introduction

Vascular surgeons frequently perform procedures aimed at limiting death, stroke, or amputation on patients who present with diseases such as aortic aneurysms, carotid atherosclerosis, and peripheral arterial occlusive disease [1]. These operations, whether they involve repair of an aneurysmal segment of aorta [2], bypass of an occluded artery in the leg [3], or removal of atherosclerotic plaque in a carotid artery [4], all serve a palliative purpose. The operations themselves, of course, do not cure atherosclerosis. Rather, they serve to mitigate its effects and limit its manifestations during the remainder of the patient’s life. In other words, they must prevent death from ruptured aneurysms, limit limb loss from lower extremity vascular disease, and provide prophylaxis from stroke from carotid atherosclerosis.

However, given the current cost constraints in health care, surgeons must, now more than ever, balance the potential benefits associated with these surgical interventions with alternative strategies [5, 6]. They must consider, against the background of medical alternatives, the physiologic insult that surgery entails in these elderly patients, who often carry
from these operations and which patients are most likely to suffer complications in the postoperative period. By using these guidelines to improve patient selection, our risk models can help patients, physicians, and policymakers improve the clinical effectiveness of surgical and endovascular treatments for vascular disease [15–18].

Herein, we will use three illustrative examples—(1) survival following thoracic aneurysm repair [19], (2) amputation following lower extremity bypass [20], and (3) stroke following carotid revascularization [21]—to demonstrate how we can use past experience to inform which patients should be selected for vascular surgery in the future.

2. Predicting Survival following Thoracic Aneurysm Repair

2.1. An Overview: What Is at Stake in Thoracic Aneurysm Repair? Given the significant potential for morbidity and mortality involved with descending thoracic aortic aneurysm (TAA) repair, surgeons have sought to balance the chance of dying from aneurysm rupture with the risk of surgical intervention [22–25]. Thoracic endovascular repair (TEVAR) has further complicated this relationship [26, 27], as this less-invasive intervention has expanded the pool of patients who are physiologically able to undergo surgery. Subsequently, single-center, regional, and national studies have described a significant increase of utilization of TEVAR, with a significant short-term benefit in perioperative mortality.

Several reports have described similar mid-term survival following open repair and TEVAR. However, these studies have been limited to single institution series from centers of excellence, or results from industry-sponsored trials and registries [23, 28], and only one clinical trial has reported five-year outcomes [26, 27]. Little population-based data describing TEVAR and open TAA repair is available that allows examination of survival differences for distinct TAA, especially across rupture status at presentation, or by repair type [28]. In this summary of our prior work, we describe our efforts in comparing perioperative and long-term mortality in the contemporary, real-world practice of open TAA repair and TEVAR.

2.2. Establishing a Cohort of Patients Who Underwent Repair of TAA. First, using Medicare claims, we created a cohort of patients who underwent a broad range of thoracic aortic procedures, as defined by the ICD-9 codes [29]. Next, we selected from this cohort those patients who underwent TEVAR and open repair of TAA. As outlined in Figure 1, we eliminated all claims that were not contained in the Medicare Denominator File as well as patients not at least aged 66. We required patients to have at least one year of Medicare eligibility prior to surgery and used this time period to establish comorbidities and construct patient-specific Charlson scores [30, 31]. In addition to the procedural codes for TAA, we required that each patient has a diagnosis code for TAA. We excluded any patient with diagnosis codes for ascending thoracic aortic aneurysm, or with procedural codes for cardiopulmonary bypass occurring with circulatory arrest, and patients with thoracoabdominal aneurysms, thoracic aortic dissections, and “other” aortic pathology from our analysis, as these entities are clinically distinct from TAA. Finally, we examined the effect of changes in practice pattern over time. First, in prior work [32], we demonstrated that between 1998 and 2003, a significant increase in the use of TEVAR occurred. Before 2003, fewer than 10% of all intact TAA were repaired using TEVAR. After 2003, more than 10% of all intact TAA were repaired with TEVAR, and this rate grew to 27% by 2007. We studied the effect of time across this pattern using time-dependent analyses. We followed this cohort over time to establish our two main outcome measures: perioperative and long-term survival, using one- and five-year survival rates. First, to define perioperative mortality, we sought to capture all deaths occurring in the period following surgery. We defined perioperative mortality as death occurring within the index hospitalization (regardless of postoperative day), as well as any death within thirty days (irrespective of inpatient or outpatient status). Second, survival at one and five years was established using the Medicare Denominator file to establish the date of death. We censored those patients who survived until the end of our analysis (at December 31, 2007).

Finally, we used a survivor function wherein age, gender, race, era of procedure, and Charlson score [30] were adjusted using a Cox proportional hazards model to estimate survival. This allowed comparison of survival estimates, adjusted to reflect survival within the strata of minimal patient-level risk within each group [33]. For ruptured patients, we stratified our Cox models by repair type and calculated hazard ratios for the remaining covariates. Additionally, we used propensity matching methods to create similar cohorts for survival analysis [34]. First, we generated a propensity score for the likelihood of undergoing TEVAR, based on a multivariable logistic model that described the association between preoperative patient characteristics and the choice to perform TEVAR. Within a sample of patients between age 65 and 75 who underwent surgery during the latter 4 years of our study period, we matched patients by age and comorbidity. This allowed us to generate two cohorts that were matched in terms of age, gender, race, era of procedure, comorbidities that constitute the Charlson score, as well as the Charlson score itself.

2.3. Comparison of Outcomes by Procedure Type. In this analysis, we studied 12,573 Medicare patients who underwent open procedures and 2,732 patients who underwent TEVAR (Figure 1). By presentation status, 13,998 patients presented for surgery with intact TAA (11,565 open repair, 2,433 TEVAR), while 1,307 patients underwent surgery for ruptured TAA (1,008 open repair, 299 TEVAR). Several demographic differences existed between open repair and TEVAR patients with intact TAA. First, patients undergoing TEVAR were significantly older than patients undergoing open repair (75.9 years versus 73.8 years, P < 0.0001). Second, the proportion of male patients was slightly higher among patients undergoing TEVAR than open repair (58.7 versus 55.4%, P < 0.0001).
In terms of outcomes the lowest perioperative mortality rate occurred in patients undergoing repair of intact TAA using TEVAR (6.1% (95% CI 5.1–7.0%)). While the perioperative mortality rate for open repair was slightly higher (7.1% (95% CI 6.7–7.6%)), the clinical magnitude of this difference was small and borderline in terms of statistical significance ($P = 0.07$). Among patients presenting with ruptured thoracic aneurysms, perioperative mortality was 28.4% (95% CI 23.2–33.5%) for TEVAR and 45.6% (95% CI 42.5–48.7%) for open repair ($P = 0.0001$). Crude long-term survival varied by presentation (intact versus ruptured) as well as repair type (open repair versus TEVAR) as shown in Figure 2(a). Even though patients with intact TAA selected for TEVAR had lower perioperative mortality, patients selected for open repair reclaimed the survival advantage within the first year after surgery (1-year survival by life table analysis: 87% open repair (95% CI 86–88%), 82% TEVAR (95% CI 80–83%), log rank $P = 0.001$). This survival advantage continued to accumulate over time, as seen in our five-year survival data (5-year survival by life table analysis: 72% (95% CI 71–73%) open repair, 62% TEVAR (95% CI 60–65%), log rank $P = 0.001$). This survival advantage was also seen in patients who underwent repair of ruptured TAA (Figure 2(b)). After five years, by life table analysis, fewer than 30% of patients were alive after repair of their ruptured TAA, irrespective of the type of repair (26% (95% CI 23–30%) open repair, 23% (95% CI 16–32%) TEVAR, log rank $P = 0.37$).
Figure 2: (a) Unadjusted five-year survival in thoracic aneurysms, by procedure type and diagnosis. (b) Adjusted five-year survival in thoracic aneurysms, by procedure type and diagnosis. Results represent male, nonblack patients under age of 75 with Charlson score < 2, performed after 2003. (c) Propensity-matched five-year survival in thoracic aneurysms, by procedure type. These patients represent a randomly selected, propensity-matched sample of low-risk patients who are at equal likelihood of undergoing either open repair or TEVAR.

while perioperative mortality is lower in TEVAR, patients selected for TEVAR have worse long-term survival than patients selected for open repair. These results suggest that higher risk patients are being offered TEVAR and that some do not benefit based on long-term survival. This study demonstrates that the treatment of TAA follows a similar course to infrarenal AAA, with one important exception. As with infrarenal AAA, we found a survival advantage in short-term mortality for patients who undergo TEVAR as compared to open repair. Further, as with infrarenal AAA, any survival advantage gained in the perioperative period following endovascular repair was lost within two years after
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surgery. But unlike infrarenal AAA, adjusted survival at five years was significantly worse for patients selected for TEVAR as compared to open repair. Therefore, the widespread application of TEVAR has resulted in a cohort of patients who may have previously not undergone surgery, but now undergo TEVAR. Patients selected for TEVAR achieve worse survival than patients undergoing open repair, and many of these deaths occur within the first two years after TEVAR. These deaths could be due to the selection of “sicker” patients for TEVAR, although our finding of poorer survival following TEVAR persists, even in propensity-matched analyses that account for differences in patient risk measurable using administrative claims. Alternatively, these differences in survival could be explained by device-related complications occurring within the first five years following surgery.

Survival following aortic aneurysm surgery has been a topic of extensive study, but primarily in patients with infrarenal abdominal aortic aneurysm (AAA) [35, 36]. Several randomized trials [37–39] have demonstrated lower perioperative mortality with endovascular techniques. It is well known that patients who experience late death following infrarenal AAA repair most commonly die from cardiopulmonary comorbidities unrelated to their aneurysm, and relatively few experience aneurysm-related death, in either open or endovascular repair [40]. As with patients with infrarenal AAA, we suspect that the loss of survival advantage is secondary to patient-level comorbidities. For example, in the EVAR-2 trial [41], survival was similar among patients treated with endovascular repair and patients who did not undergo repair. The data available from our study supports this presumption, as TEVAR patients tend to be older and have higher comorbidity scores than the patients selected for open repair. However, it is important to acknowledge that our findings are based solely on administrative claims, and our analysis is therefore limited in terms of clinical detail.

This study provides an important focus on the data used to demonstrate the efficacy of endovascular repair of TAA [42, 43]. First, when compared to data from TEVAR clinical trials (Table 1), it is evident that perioperative mortality is higher in “real-world” practice than in the centers of excellence where the clinical trials were performed. Second, in real-world practice, patients selected for open repair had better survival that the surgical controls used in clinical trials (72% five-year survival in Medicare, 67% five-year survival in the single trial that reported this measure). Collectively, these two differences resulted in the disparity in conclusions between our study, wherein TEVAR patients fared significantly worse at five years and the clinical trial, wherein outcomes were similar at five years. Given the findings in our study and others, there is little evidence to suggest that long-term survival is better in patients selected for TEVAR as compared to open surgical repair, and it may in fact be worse [44].

In conclusion, the consistent short-term survival advantage offered by TEVAR disappears within the first two years after surgery. These results suggest that higher risk patients are being offered TEVAR and that some do not benefit based on long-term survival. Patient selection in TEVAR requires better risk stratification to better select patients for this new procedure.

3. Lower Extremity Bypass: How Do We Select Patients Who Will Avoid Amputation?

3.1. Introduction. Now, we turn our attention to a different type of vascular disease. Lower extremity peripheral arterial disease (PAD) affects over 8 million Americans, with significant associated morbidity and mortality [45–49]. Significant morbidity and mortality are encountered when elderly, medically complex patients undergo prolonged, invasive arterial reconstruction [47, 49]. One of the key elements in minimizing morbidity and mortality is optimal patient selection, especially in the current era wherein endovascular alternatives may exist [50]. To this end, we examined the risk factors associated with amputation or graft occlusion one year after surgery.

3.2. Studying a Cohort of Lower Extremity Bypass Patients Using a Regional Dataset. In this analysis, we utilized data collected prospectively by the Vascular Study Group of Northern New England (VSGNNE), a regional cooperative quality improvement initiative developed in 2002 to study regional outcomes in vascular surgery. Further details on this registry have been published previously [51] and described in detail at vsgnne.org. Our unit of analysis was the bypass graft. Our main outcome measure was a combined measure of either permanent graft occlusion (loss of secondary patency) or major amputation (above or below knee) following surgery. Between January 1, 2003, and December 31, 2006, we identified 2,036 patients in our database that underwent 2,301 bypass procedures. Graft patency and major amputation rates were determined at several stages: first preoperatively, then at discharge following surgery, and again at 1 year postoperatively. Major amputation was defined as above-knee amputation or below-knee amputation. This outcome was assessed both at discharge and again at one-year followup.

We used life table analysis given that not all follow-up data was obtained at exactly one year. Patients who died within one year of surgery were censored after their date of death. Risk factors found by univariate analysis to be associated with a P value of <0.1 were then used in a multivariate Cox proportional hazards model. This model was then used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for ability to ambulate one year after surgery. To examine the validity of our risk prediction model, we constructed our risk model from the data obtained between 2003 and 2006. We then applied the risk model to the data acquired from the VSG sites in 2007. Lastly, using our model, we predicted a one-year amputation/occlusion rate for each patient, based on that patient’s individual risk factor profile. We also compared results across centers, based on the characteristics of the patients treated at each center. The predictive ability of each model was then evaluated by generating an observed-to-expected outcome ratio across the range of risk identified.

3.3. Outcomes and Their Association with Amputation. In our study, 2,036 patients underwent lower extremity bypass in
Table 1: Outcomes at 30 days, 1 year, and 5 years, by repair type and study.

| Repair type | Outcome measure               | Medicare 1998–2007 | TAG [43] | VALOR [42] | TX2 [11] |
|-------------|-------------------------------|---------------------|----------|------------|----------|
|             | In hospital/30-day mortality |                     |          |            |          |
| Open repair | 1-year survival               | 7.1%                | 6.4%     | 8.0%       | 6.0%     |
|             | 5-year survival               | 72%                 | 67%      | -          | -        |
| TEVAR       | In hospital/30-day mortality  | 6.1%                | 1.2%     | 2.0%       | 1.9%     |
|             | 1-year survival               | 82%                 | 82%      | 84%        | 84–94%   |
|             | 5-year survival               | 62%                 | 68%      | -          | -        |

Northern New England at one of the 11 centers participating in our registry. Patients were most commonly male (67%), aged 70–80 (30%), and nearly all were Caucasian. Nearly all patients had a history of either prior or current smoking (82%). About half of patients had a history of diabetes, 40% had coronary disease, and nearly a third had a history of COPD. Indication for surgery was claudication in 25% of patients, while the remaining patients had critical ischemia. In claudicants, one-year primary patency was 79% and secondary patency 87%. However, one-year primary and secondary patency was significantly lower (73% and 81%, respectfully) in patients with critical limb ischemia. As expected, limb salvage rates in our cohort were lower in patients with critical limb ischemia compared to claudication (86% versus 98%, P < 0.0001). Of 143 major amputations (8% of all bypasses) that occurred in our cohort, 17% were performed in patients who had a patent bypass graft. Similarly, 277 graft occlusions were noted in our cohort, of which 42% resulted in amputation. Our combined amputation or permanent graft occlusion rate was 3% at discharge and 16% at 1 year, by life table analysis.

In univariate analyses, several physiologic parameters such as advanced age, diabetes, and hypertension were associated with amputation or graft occlusion at 1 year. Additionally, functional parameters such as baseline ambulatory status prior to surgery, living status prior to surgery, and presence of tissue loss were also highly closely correlated with loss of graft patency or amputation at 1 year. The factors associated with amputation or graft occlusion at one year are shown in Table 2. These were of age less than 50, nonambulatory status preoperatively, dialysis dependence, diabetes, critical limb ischemia, conduit requiring venovenostomy, tarsal target, and nursing home residence preoperatively. The likelihood of amputation or graft occlusion at one year varied from less than 0.5% in patients with no risk factors to nearly 30% in patients with three or more risk factors (Figure 3).

Lastly, to examine the validity of our risk prediction model, we constructed our risk model from the data obtained between 2003 and 2006 and applied the risk model to the data acquired from the VSG sites in 2007 (Figure 4). We found that our model performed well in discriminating risk. For example, patients with no risk factors had no episodes of graft occlusion or amputation, while those patients with three or more risk factors had a 30% incidence of amputation or graft occlusion. Differences between groups were statistically significant (<0.002). This risk prediction models allow benchmarking and facilitate comparison of risk-adjusted outcomes across centers as part of quality improvement efforts. To this end, we used our risk prediction model to calculate expected amputation/occlusion rates across centers and compared observed results with the expected results using O/E ratios. Predicted risks of amputation or graft occlusion varied from 3% at our lowest risk centers to 19% at the highest risk center.

Table 2: Multivariable predictors of amputation or graft occlusion 1 year following lower extremity bypass.

| Variable                                      | Hazard ratio | 95% CI | P value |
|-----------------------------------------------|--------------|--------|---------|
| Age                                           |              |        |         |
| <40                                           | 1.4          | 0.4–4.7| 0.645   |
| 40–49                                         | 1.9          | 1.2–3.1| 0.007   |
| 50–59                                         | 1.2          | 0.8–1.7| 0.424   |
| 60–69                                         | 1.2          | 0.8–1.7| 0.334   |
| 70+                                           | 1            | 0.7–1.5| 0.757   |
| Nonambulatory preoperatively                   | 1.6          | 1–2.5  | 0.044   |
| Dialysis                                      | 1.6          | 1.1–2.2| 0.008   |
| Diabetes                                      | 1.6          | 1.1–2.5| 0.029   |
| Critical limb ischemia                        | 1.7          | 1.3–2.3| 0.0001  |
| Two vein segments                             | 2            | 1.4–2.8| 0.0001  |
| Tarsal target for bypass                      | 2.5          | 1.2–5.3| 0.021   |
| Nursing home residence                        | 2.8          | 1.3–6  | 0.011   |

Figure 3: Predicted risk of amputation or graft occlusion, by the number of risk factors.

3.4. Implications of Our Findings for Patient Selection in Lower Extremity Bypass. This review of factors associated
Patients and surgeons can use this risk model not only to guide their expectations for success with bypass surgery but to also weigh the risks and benefits when considering surgery or endovascular intervention. Patients with only 1 or 2 risk factors have excellent outcomes in terms of graft patency and limb salvage, and in these patients bypass surgery represents a durable and effective treatment for both claudication and critical limb ischemia. However, in patients with 3 or more risk factors, nearly 1 in 3 will not have a patent graft or an intact limb within a year of their surgery. As to whether open bypass surgery or endovascular interventions should be used first, while many believe an “endovascular first” strategy should be employed [50, 60, 61], practice patterns vary significantly, and best practices have yet to be established with high quality evidence. We believe future comparative effectiveness research and clinical trials are necessary to address this question directly.

But in addition to helping surgeons predict amputation risk, one of the main goals of the VSGNE is to study and improve the care of vascular surgery patients. By comparing risk adjusted outcomes, surgeons can set benchmarks and compare results across centers. By studying those centers that do things well, surgeons can identify processes of care that contribute towards the best outcomes. Then, by widely implementing these processes of care, we hope to improve our results across the region. This model has been used effectively in cardiac surgery [62, 63], myocardial infarction care [64, 65], and in the treatment of pulmonary disease [66] and cancer [67]. In addition to our ongoing efforts in quality improvement in lower extremity bypass surgery, we are applying similar strategies in improving results after carotid endarterectomy in our region [21].

In conclusion, this study identified several risk factors that allow surgeons to predict which patients are at risk for amputation or graft occlusion following lower extremity bypass. Moreover, this model permits benchmarking and comparison of results across hospitals, key activities within our quality improvement initiative, which aims to use these data to broadly improve vascular care for patients at risk for amputation.

4. Carotid Atherosclerosis: Who Will Benefit from Carotid Revascularization?

4.1. Introduction: Who Is at Risk for Stroke during and after CEA? Finally, we turn our attention to one last, and hotly debated, vascular territory—the carotid artery. While many believe that carotid endarterectomy, or surgical removal of plaque from the carotid arteries, can prevent stroke, debate has persisted for more than three decades as to which patients are best served by undergoing this procedure. Many investigators have studied risk factors associated with stroke or death following carotid endarterectomy (CEA), with the intent of improving preoperative assessment and patient selection [68–73]. Across these studies, the most consistent risk factor found to predict stroke or death following CEA has been preoperative neurologic symptoms (Table 3). Other variables associated with increased operative risk have...
and logistic regression, which was used to generate odds ratios. A multivariate model, using backwards stepwise multivariate anova, was based on previous publications [87,89–92]. We generated an appropriate patient preoperative variables for comparison 

comemeasures and many patient level variables. We selected performed univariate comparisons between our main out-

put of approximately equal size from our dataset. In order to predict 30-day postoperative stroke or death, we initially included emergent operation [74], renal failure [75], and diabetes [72]. Interestingly, preoperative antiplatelet medications were found to be protective in only one of these models [76], despite evidence that such therapy reduces stroke risk associated with CEA [77, 78]. And, as with our efforts in lower extremity revascularization, another role for risk prediction models is to allow comparison of risk-adjusted outcomes among different centers. An important element in surgical quality improvement is to establish benchmarks for performance [79–82]. Most outcome benchmarks require risk adjustment, to account for potential differences in patient populations that could influence outcomes [83], and multivariate risk prediction models are developed to account for differences in patient characteristics when comparing outcomes [84, 85].

4.2. Selecting a Cohort of Carotid Endarterectomy Patients Using a Regional Dataset. As with the project described earlier, we included only patients in the Vascular Study Group of New England but in this analysis included those who underwent primary CEA (excluding redo operations or those combined with coronary bypass grafting). We selected 30-day postoperative stroke or death as our main outcome measure. The determination of major or minor stroke was made according to these definitions by the nurse clinician or trained research assistant responsible for entering the data into the database at each participating institution. Operative volume categories were defined using cutpoints guided by prior studies [86–88], modified to create terciles of approximately equal size from our dataset. In order to predict 30-day postoperative stroke or death, we initially performed univariate comparisons between our main outcome measures and many patient level variables. We selected appropriate patient preoperative variables for comparison based on previous publications [87, 89–92]. We generated a multivariate model, using backwards stepwise multivariate logistic regression, which was used to generate odds ratios and 95% confidence intervals for 30-day postoperative stroke or death. We used the resulting model to calculate an expected stroke/death rate for each patient, based on that particular patient's characteristics.

4.3. Outcomes and Their Association with Stroke or Death. Overall, we studied 2,714 patients undergoing 3,092 primary CEAs. Most patients were males, with a history of smoking and hypertension, and nearly half were symptomatic. We observed, across 3,092 CEAs, 38 minor strokes, 14 major strokes, and 8 deaths, 5 of which were stroke related, within 30 days of the index procedure (30-day stroke or death rate = 1.8%); 5 of the 52 strokes (10%) and 2 of the 8 deaths (25%) were reported after discharge but before 30 days.

We found that, on univariate analysis, emergent operation, contralateral internal carotid artery (ICA) occlusion, ipsilateral cortical symptoms (both TIA and stroke), congestive heart failure, performance of a completion study, and ICA stenosis <60% all were associated with increased risk of 30-day stroke or death. By multivariate analysis, emergent procedure, contralateral ICA occlusion, pre-operative ipsilateral cortical stroke, congestive heart failure, and age over 70 were associated with a significantly higher risk of stroke or death, while preoperative ASA or clopidogrel use was protective (Table 4). We examined the impact and additive effects of the number of risk factors present (Figure 5). In patients with 0-1 of these risk factors, the risk of stroke or death was less than 1%. However, when patients had 3 or more risk factors, the risk of stroke or death increased to nearly 5%. When expected stroke or death rates were compared to the observed stroke or death rates, excellent correlation was observed ($r = 0.96$). The model was found to have reasonable discriminative ability (area under ROC curve 0.71). Finally, in benchmarking analyses across the 8 hospitals in our region, the expected stroke/death rate ranged from 1.5% to 2.0%, while observed results varied from 0% to over 4%. Two hospitals had O/E ratios greater than 1, indicating a higher observed 30-day stroke and death rate than expected.

| Author          | Year | n, study type                                      | Risk factors                                                                 |
|-----------------|------|---------------------------------------------------|------------------------------------------------------------------------------|
| Musser et al.   | 1994 | 562 patients, single center, retrospective series | AF, emergent operation, PVCs, intraop hypotension, ESRD                      |
| Goldstein et al.| 1998 | 1,160 patients, multicenter, retrospective        | Female, age over 75, CHF                                                     |
| Rothwell et al. | 1999 | 2,060 patients, multicenter, prospective trial    | Symptomatic status, DM, recent MI Plaque characteristics                     |
| Frawley et al.  | 2000 | 1,000 patients, single center retrospective series | Female gender                                                                |
| Kresowik et al. | 2001 | 10,561 patients, retrospective chart review of    | Aspirin/ticlopidine use, heparin use, patch angioplasty                      |
| Tu et al.       | 2003 | 6,038 patients, regional retrospective database   | Symptomatic status, AF, contralateral occlusion, CHF, DM                     |
| Nicolaides et al.| 2005| 1,115 patients, prospective clinical trial        | Symptomatic status, degree of stenosis, creatinine                           |

AF: atrial fibrillation; MI: myocardial infarction; PVC: premature ventricular contractions; ESRD: end stage renal disease; CHF: congestive heart failure; DM: diabetes mellitus.
Table 4: Multivariate analysis of factors associated with thirty-day stroke/death after CEA.

| Variable                                  | Odds ratio | 95% CI    | P value |
|-------------------------------------------|------------|-----------|---------|
| Age over 70 years                         | 1.3        | 0.8–2.3   | 0.315   |
| Contralateral ICA occlusion               | 2.8        | 1.3–6.2   | 0.009   |
| Antiplatelet agent use                    | 0.4        | 0.2–0.9   | 0.02    |
| Congestive heart failure                  | 1.6        | 1.1–2.4   | 0.03    |
| Emergent procedure (within 6 hours of admission) | 7.0 | 1.8–26.9 | 0.004   |
| Preoperative ipsilateral cortical symptoms (stroke) | 2.4 | 1.1–5.1 | 0.02    |

Area under ROC: 0.71; TIA: transient ischemia attack.

**Figure 5:** Comparison of observed and expected 30-day stroke/death rate. Risk factors include emergent procedure, preoperative ipsilateral stroke, age over 70, lack of antiplatelet agent, contralateral ICA occlusion, and congestive heart failure.

### 4.4. Implications of Our Findings for Patient Selection in Carotid Endarterectomy

In our study of contemporary carotid surgical revascularization, we identified emergent procedure, contralateral ICA occlusion, preoperative cortical stroke, congestive heart failure, increased age, and (lack of) antiplatelet agent use as predictive of postoperative 30-day stroke or death following CEA. Our model describes several risk factors reported in previous studies, with similar effect sizes. Two prior models reported odds ratios of 30-day stroke or death of 1.8 for contralateral ICA occlusion, which is similar in magnitude to our odds ratio of 2.8 [18, 87]. These same studies [70, 72] also reported that ipsilateral cerebral symptoms increased the risk of stroke and death nearly twofold, similar to our finding of an odds ratio of 2.4 for preoperative ipsilateral stroke. Patients with pre-operative stroke before CEA have been shown to be at higher risk for postoperative stroke, independent of whether or not they have TIs at the time of CEA [93]. And finally, emergent CEA, usually indicated for free-floating thrombus or crescendo symptoms, has been well described as having worse surgical outcomes compared to routine or urgent carotid endarterectomy [94], in keeping with our findings.

Our study found a protective effect with antiplatelet therapy. The benefit of ASA to reduce postoperative stroke or death was shown in the North American Symptomatic Carotid Endarterectomy Trial [91], as well as a small randomized trial that showed stroke rates were reduced with lower dose perioperative ASA (81 mg/day) versus placebo [95]. Moreover, the ASA and Carotid Endarterectomy (ACE) trial [96] further emphasized the benefit of low-dose ASA. Finally, Kresowik et al. noted a significant reduction in stroke or death with the use of preoperative antiplatelet therapy in review of over 10,000 Medicare beneficiaries undergoing CEA between 1995 and 1996 [76]. Other antiplatelet agents have not been as extensively studied in terms of their benefit for stroke reduction after CEA, but recent studies of clopidogrel provide evidence that perioperative embolization is reduced [97, 98]. Given this evidence, one might assume that nearly all patients undergoing carotid revascularization are on antiplatelet medication. However, a recent study from The Netherlands indicated that only 66% of patients undergoing CEA were on preoperative antiplatelet agents, showing the opportunity for improvement using this simple process [77]. Even within our region, prior to starting our quality improvement efforts, only 73% of patients undergoing CEA were on antiplatelet agents. However, this percentage has increased to over 93% after dedicated efforts to improve this process measure across our participating centers [51].

We feel that our regional efforts in quality improvement have helped in this process, a technique that has been successfully used to improve processes of care by cardiac surgeons in our region [99].

We found it interesting that our study found no influence of surgeon or hospital volume on outcome; this is likely a type II error, given prior publications in this area [86–88]. Most studies that found a surgeon volume effect for CEA outcome required hundreds of surgeons and tens of thousands of patients to find a relatively small effect [86, 87], while we studied a relatively small number of surgeons performing approximately 3,000 CEAAs. And finally, we found our stroke rates to be relatively low in our analysis, and we found little measurable benefit in statin therapy [100–102]. These findings may reflect a type II error, and future work will investigate these endpoints as our sample size increases.

In conclusion, we identified factors associated with 30-day stroke or death following CEA using our regional prospective database. Surgeons can easily preoperatively “risk-stratify” patients by considering these easily available variables (emergent nature of procedure, contralateral ICA occlusion, preoperative ipsilateral cortical stroke, congestive heart failure, and age). From a quality improvement perspective, risk adjustment models like this allow valuable benchmarking among different centers and help regional collaboratives improve practice.

### 5. Summary

As we have demonstrated in these three examples, improving patient selection for high-risk vascular surgery involves a complex interaction between patient-level variables,
procedure-related covariates, and insight the patient’s underlying short- and long-term risk of adverse outcomes, all within the context of their life expectancy. As technology improves, analytic techniques evolve and our understanding of detailed regional and national datasets expands, we hope to eventually arrive at a time and place in vascular surgery where surgeons will know, before an intervention is performed, if their choice to perform surgery is the right one. And while a “crystal ball” that is able to predict surgical outcomes may seem like a far-fetched idea, it may not be as far off as you think.

Acknowledgment

This paper incorporates, with permission, excerpts, tables, and figures from three previously published manuscripts.

References

[1] A. T. Hirsch, Z. J. Haskal, N. R. Hertzer 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*, vol. 113, no. 11, pp. e463–e654, 2006.

[2] S. D. Killeen, E. J. Andrews, H. P. Redmond, and G. J. Fulton, “Provider volume and outcomes for abdominal aortic aneurysm repair, carotid endarterectomy, and lower extremity revascularization procedures,” *Journal of Vascular Surgery*, vol. 45, no. 3, pp. 615–626, 2007.

[3] J. H. Ix and M. H. Criqui, “Epidemiology and diagnosis of peripheral arterial disease in patients with chronic kidney disease,” *Advances in Chronic Kidney Disease*, vol. 15, no. 4, pp. 378–383, 2008.

[4] R. A. Hanel, A. R. Xavier, J. F. Kirmani, A. M. Yahia, and A. I. Qureshi, “Management of carotid artery stenosis: comparing endarterectomy and stenting,” *Current Cardiology Reports*, vol. 5, no. 2, pp. 153–159, 2003.

[5] C. Mihalopoulos, D. A. Cadilhac, M. L. Moodie et al., “Development and application of Model of Resource Utilization, Costs, and Outcomes for Stroke (MORUCOS): an Australian economic model for stroke,” *International Journal of Technology Assessment in Health Care*, vol. 21, no. 4, pp. 499–505, 2005.

[6] E. H. Morreim, “Managed care, ethics, and academic health centers: maximizing potential, minimizing drawbacks,” *Academic Medicine*, vol. 72, no. 5, pp. 332–340, 1997.

[7] A. Berni, A. Giuliani, F. Tartaglia et al., “Effect of vascular risk factors on increase in carotid and femoral intima-media thickness: Identification of a risk scale,” *Atherosclerosis*, vol. 216, no. 1, pp. 109–114, 2011.

[8] M. S. Conte, “Understanding objective performance goals for critical limb ischemia trials,” *Seminars in Vascular Surgery*, vol. 23, no. 3, pp. 129–137, 2010.

[9] J. B. Dimick, S. L. Chen, P. A. Taheri, W. G. Henderson, S. F. Khuri, and D. A. Campbell Jr., “Hospital costs associated with surgical complications: a report from the private-sector National Surgical Quality Improvement Program,” *Journal of the American College of Surgeons*, vol. 199, no. 4, pp. 531–537, 2004.

[10] J. B. Dimick, W. B. Weeks, R. J. Karia, S. Das, and D. A. Campbell Jr., “Who pays for poor surgical quality? Building a business case for quality improvement,” *Journal of the American College of Surgeons*, vol. 202, no. 6, pp. 933–937, 2006.

[11] J. S. Matsumura, R. P. Cambria, M. D. Bake, R. D. Moore, L. G. Svensson, and S. Snyder, “International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results,” *Journal of Vascular Surgery*, vol. 47, no. 2, pp. 247–257, 2008.

[12] A. Schanzer, N. Hevelone, C. D. Owens, J. A. Beckman, M. Belkin, and M. S. Conte, “Statins are independently associated with reduced mortality in patients undergoing infrainguinal bypass graft surgery for critical limb ischemia,” *Journal of Vascular Surgery*, vol. 47, no. 4, pp. 774–781, 2008.

[13] P. P. Goodney and R. J. Powell, “Carotid artery stenting: What have we learned from the clinical trials and registries and where do we go from here?” *Annals of Vascular Surgery*, vol. 22, no. 1, pp. 148–158, 2008.

[14] P. P. Goodney, M. L. Schermerhorn, and R. J. Powell, “Current status of carotid artery stenting,” *Journal of Vascular Surgery*, vol. 43, no. 2, pp. 406–411, 2006.

[15] S. R. G. Finlayson, J. D. Birkmeyer, M. F. Fillingar, and J. L. Cronenwett, “Should endovascular surgery lower the threshold for repair of abdominal aortic aneurysms?” *Journal of Vascular Surgery*, vol. 29, no. 6, pp. 973–985, 1999.

[16] M. R. Harrigan, J. U. Howington, R. A. Hanel, L. R. Guterman, and L. N. Hopkins, “Patient selection for revascularization in cervical carotid artery disease: angioplasty and stenting versus endarterectomy,” *The American Heart Hospital Journal*, vol. 2, no. 1, pp. 8–15, 2004.

[17] Z. Luo, J. C. Gardiner, and C. J. Bradley, “Applying propensity score methods in medical research: pitfalls and prospects,” *Medical Care Research and Review*, vol. 67, no. 5, pp. 528–554, 2010.

[18] P. M. Rothwell and C. P. Warlow, “Prediction of benefit from carotid endarterectomy in individual patients: a risk-modelling study,” *The Lancet*, vol. 353, no. 9170, pp. 2105–2110, 1999.

[19] P. P. Goodney, L. Travis, F. L. Lucas et al., “Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the medicare population,” *Circulation*, vol. 124, no. 24, pp. 2661–2669, 2011.

[20] P. P. Goodney, B. W. Nolan, A. Schanzer et al., “Factors associated with amputation or graft occlusion one year after lower extremity bypass in northern New England,” *Annals of Vascular Surgery*, vol. 24, no. 1, pp. 57–68, 2010.

[21] P. P. Goodney, D. S. Likosky, and J. L. Cronenwett, “Factors associated with stroke or death after carotid endarterectomy in Northern New England,” *Journal of Vascular Surgery*, vol. 48, no. 5, pp. 1139–1145, 2008.

[22] J. S. Coselli, “Thoracoabdominal aortic aneurysms: experience with 372 patients,” *Journal of Cardiac Surgery*, vol. 9, no. 6, pp. 638–647, 1994.
[23] M. F. Conrad, R. S. Crawford, J. K. Davison, and R. P. Cambria, "Thoracoabdominal aneurysm repair: a 20-year perspective," *Annals of Thoracic Surgery*, vol. 83, no. 2, pp. S856–S861, 2007.

[24] E. S. Crawford, K. R. Hess, E. S. Cohen, J. S. Coselli, and H. J. Safi, "Ruptured aneurysm of the descending thoracic and thoracoabdominal aorta: analysis according to size and treatment," *Annals of Surgery*, vol. 213, no. 5, pp. 417–426, 1991.

[25] E. S. Crawford, L. G. Svensson, J. S. Coselli, H. J. Safi, and H. R. Hess, "Surgical treatment of aneurysm and/or dissection of the ascending aorta, transverse aortic arch, and ascending aorta and transverse aortic arch. Factors influencing survival in 717 patients," *Journal of Thoracic and Cardiovascular Surgery*, vol. 98, no. 5, pp. 659–674, 1989.

[26] J. A. Cowan Jr., J. B. Dimick, P. K. Henke, T. S. Huber, J. C. Stanley, and G. R. Upchurch Jr., "Surgical treatment of intact thoracoabdominal aortic aneurysms in the United States: hospital and surgeon volume-related outcomes," *Journal of Vascular Surgery*, vol. 37, no. 6, pp. 1169–1174, 2003.

[27] J. A. Cowan Jr., J. B. Dimick, R. M. Wainess, P. K. Henke, J. C. Stanley, and G. R. Upchurch Jr., "Ruptured thoracoabdominal aortic aneurysm treatment in the United States: 1988 to 1998;* Journal of Vascular Surgery*, vol. 38, no. 2, pp. 319–322, 2003.

[28] M. F. Conrad, E. A. Ergul, V. I. Patel, V. Paruchuri, C. J. Kwolek, and R. P. Cambria, "Management of diseases of the descending thoracic aorta in the endovascular era: a medicare population study," *Annals of Surgery*, vol. 252, no. 4, pp. 603–609, 2010.

[29] Current procedural technology manual, 2010.

[30] L. I. Iezzoni, *Risk Adjustment for Measuring Health Care Outcomes*, Health Administration Press, Ann Arbor, Mich, USA, 1994.

[31] S. M. Kieszak, W. D. Flanders, A. S. Kosinski, C. C. Shipp, and H. Karp, "A comparison of the Charlson Comorbidity Index derived from medical record data and administrative billing data," *Journal of Clinical Epidemiology*, vol. 52, no. 2, pp. 137–142, 1999.

[32] S. T. Scali, R. J. Feezor, C. K. Chang, and D. H. Stone, "Safety of elective management of synchronous aortic disease with simultaneous thoracic and aortic stent graft placement," *Journal of Vascular Surgery*, vol. 56, no. 4, pp. 957.e1–964.e1, 2012.

[33] S. J. Pocock, T. C. Clayton, and D. G. Altman, "Survival plots of time-to-event outcomes in clinical trials: good practice and pitfalls," *The Lancet*, vol. 359, no. 9318, pp. 1686–1689, 2002.

[34] P. R. Rosenbaum and D. B. Rubin, "The central role of the propensity score in observational studies for causal effects," *Biometrika*, vol. 70, no. 1, pp. 41–55, 1983.

[35] M. L. Schermerhorn, S. R. G. Finlayson, M. F. Fillinger et al., "Life expectancy after endovascular versus open abdominal aortic aneurysm repair: results of a decision analysis model on the basis of data from EUROSTAR," *Journal of Vascular Surgery*, vol. 36, no. 6, pp. 1112–1120, 2002.

[36] M. L. Schermerhorn, A. J. O'Malley, A. Jhaveri, P. Cotterill, F. Pomposelli, and B. E. Landon, "Endovascular versus open repair of abdominal aortic aneurysms in the medicare population," *New England Journal of Medicine*, vol. 358, no. 5, pp. 464–474, 2008.

[37] R. M. Greenhalgh, L. C. Brown, G. P. Kwong, J. T. Powell, and S. G. Thompson, "Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial," *The Lancet*, vol. 364, no. 9437, pp. 843–848, 2004.

[38] R. M. Greenhalgh, D. J. Allison, P. R. F. Bell et al., "Endovascular repair of aortic aneurysm in patients physically ineligible for open repair," *New England Journal of Medicine*, vol. 362, no. 20, pp. 1872–1880, 2010.

[39] J. D. Blankensteijn, S. E. C. A. de Jong, M. Prinsen et al., "Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms," *New England Journal of Medicine*, vol. 352, no. 23, pp. 2398–2405, 2005.

[40] P. P. Goodney, D. Tavis, F. L. Lucas, T. Gross, E. S. Fisher, and S. R. G. Finlayson, "Causes of late mortality after endovascular and open surgical repair of infrarenal abdominal aortic aneurysms," *Journal of Vascular Surgery*, vol. 51, no. 6, pp. 1340–1347, 2010.

[41] "Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial," *The Lancet*, vol. 365, no. 9478, pp. 2187–2192, 2005.

[42] R. M. Fairman, F. Criado, M. Farber et al., "Pivotal results of the medtronic vascular talent thoracic stent graft system: the VALOR trial," *Journal of Vascular Surgery*, vol. 48, no. 3, pp. 546–554, 2008.

[43] M. S. Makaroun, E. D. Dillavou, G. H. Wheatley, and R. P. Cambria, "Five-year results of endovascular treatment with the Gore TAG device compared with open repair of thoracic aortic aneurysms," *Journal of Vascular Surgery*, vol. 47, no. 5, pp. 912–918, 2008.

[44] J. S. Cho, S. E. A. Haider, and M. S. Makaroun, "Endovascular therapy of thoracic aneurysms: gore TAG trial results," *Seminars in Vascular Surgery*, vol. 19, no. 1, pp. 18–24, 2006.

[45] M. M. McDermott, "The magnitude of the problem of peripheral arterial disease: epidemiology and clinical significance," *Cleveland Clinic Journal of Medicine*, vol. 73, supplement 4, pp. S2–S7, 2006.

[46] A. B. Newman, L. Shemanski, T. A. Manolio et al., "Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study," *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 19, no. 3, pp. 538–545, 1999.

[47] R. Nowygrod, N. Egorova, G. Greco et al., "Trends, complications, and mortality in peripheral vascular surgery," *Journal of Vascular Surgery*, vol. 43, no. 2, pp. 205–216, 2006.

[48] B. Sigvant, K. Wiberg-Hedman, D. Bergqvist et al., "A population-based study of peripheral arterial disease prevalence with special focus on critical limb ischemia and sex differences," *Journal of Vascular Surgery*, vol. 45, no. 6, pp. 1185–1191, 2007.

[49] L. Norgren, W. R. Hiatt, J. A. Dormandy et al., "Inter-society consensus for the management of peripheral arterial disease (TASC II)," *Journal of Vascular Surgery*, vol. 45, no. 1, pp. S5–S67, 2007.

[50] D. J. Adam, J. D. Beard, T. Cleveland et al., "Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial," *The Lancet*, vol. 366, no. 9501, pp. 1925–1934, 2005.

[51] J. L. Cronenwett, D. S. Likosky, M. T. Russell, J. Eldrup-Jorgensen, A. C. Stanley, and B. W. Nolan, "A regional registry for quality assurance and improvement: the Vascular Study Group of Northern New England (VSGNNE)," *Journal of Vascular Surgery*, vol. 46, no. 6, pp. 1093–1102, 2007.

[52] F. Biancari, A. Albäck, L. Ihlberg, I. Kantonen, M. Luther, and M. Lepantalo, "Angiographic runoff score as a predictor of outcome following femorocaval bypass surgery," *European Journal of Vascular and Endovascular Surgery*, vol. 17, no. 6, pp. 480–485, 1999.
[85] E. D. Peterson, E. R. DeLong, L. H. Muhlbaier et al., "Challenges in comparing risk-adjusted bypass surgery mortality results: results from the Cooperative Cardiovascular Project," *Journal of the American College of Cardiology*, vol. 36, no. 7, pp. 2174–2184, 2000.

[86] J. D. Birkmeyer, T. A. Stukel, A. E. Siewers, P. P. Goodney, D. E. Wennberg, and F. L. Lucas, "Surgeon volume and operative mortality in the United States," *New England Journal of Medicine*, vol. 349, no. 22, pp. 2117–2127, 2003.

[87] J. A. Cowan Jr., J. B. Dimick, B. G. Thompson, J. C. Stanley, and G. R. Upchurch, "Surgeon volume as an indicator of outcomes after carotid endarterectomy: an effect independent of specialty practice and hospital volume," *Journal of the American College of Surgeons*, vol. 195, no. 6, pp. 814–821, 2002.

[88] P. J. E. Holt, J. D. Poloniecki, I. M. Loous, and M. M. Thompson, "Meta-analysis and systematic review of the relationship between hospital volume and outcome following carotid endarterectomy," *European Journal of Vascular and Endovascular Surgery*, vol. 33, no. 6, pp. 645–651, 2007.

[89] J. F. Toole, "Endarterectomy for asymptomatic carotid artery stenosis," *Journal of the American Medical Association*, vol. 273, no. 18, pp. 1421–1428, 1995.

[90] E. Ballotta, L. Renon, G. da Giau, B. Barbon, O. Terranova, and C. Baracchini, "Octogenarians with contralateral carotid artery occlusion: a cohort at higher risk for carotid endarterectomy?" *Journal of Vascular Surgery*, vol. 39, no. 5, pp. 1003–1008, 2004.

[91] K. D. Calligaro, "Impact of clinical pathways on hospital costs and early outcome after major vascular surgery," *Journal of Vascular Surgery*, vol. 22, no. 6, pp. 649–660, 1995.

[92] A. F. Bhatti, L. R. Leon, N. Labropoulos et al., "Free-floating thrombus of the carotid artery: literature review and case reports," *Journal of Vascular Surgery*, vol. 45, no. 1, pp. 199–205, 2007.

[93] M. Eliasziw, J. Y. Streifler, J. D. Spence, A. J. Fox, V. C. Hachinski, and H. J. M. Barnett, "Prognosis for patients following a transient ischemic attack with and without a cerebral infarction on brain CT," *Neurology*, vol. 45, no. 31, pp. 428–431, 1995.

[94] A. F. Bhatti, L. R. Leon, N. Labropoulos et al., "Free-floating thrombus of the carotid artery: literature review and case reports," *Journal of Vascular Surgery*, vol. 45, no. 1, pp. 199–205, 2007.

[95] B. Lindblad, N. H. Persson, R. Takolander, and D. Bergqvist, "Does low-dose acetylsalicylic acid prevent stroke after carotid surgery? A double-blind, placebo-controlled randomized trial," *Stroke*, vol. 24, no. 8, pp. 1125–1128, 1993.

[96] D. W. Taylor, H. J. M. Barnett, R. B. Haynes et al., "Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomised controlled trial," *The Lancet*, vol. 353, no. 9113, pp. 1379–1387, 1999.

[97] D. A. Payne, C. I. Jones, P. D. Hayes, A. R. Naylor, and A. H. Goodall, "Therapeutic benefit of low-dose clopidogrel in patients undergoing carotid surgery is linked to variability in the platelet adenosine diphosphate response and patients’ weight," *Stroke*, vol. 38, no. 9, pp. 2464–2469, 2007.

[98] D. A. Payne, C. I. Jones, P. D. Hayes et al., "Beneficial effects of clopidogrel combined with aspirin in reducing cerebral emboli in patients undergoing carotid endarterectomy," *Circulation*, vol. 109, no. 12, pp. 1476–1481, 2004.

[99] D. J. Malenka and G. T. O’Connor, "The northern new England cardiovascular disease study group: a regional collaborative effort for continuous quality improvement in cardiovascular disease," *The Joint Commission Journal on Quality Improvement*, vol. 24, no. 10, pp. 594–600, 1998.

[100] B. A. Perler, "The effect of statin medications on perioperative and long-term outcomes following carotid endarterectomy or stenting," *Seminars in Vascular Surgery*, vol. 20, no. 4, pp. 252–258, 2007.

[101] M. J. McGirt, B. A. Perler, B. S. Brooke et al., "3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors reduce the risk of perioperative stroke and mortality after carotid endarterectomy," *Journal of Vascular Surgery*, vol. 42, no. 5, pp. 829–836, 2005.

[102] J. Kennedy, H. Quan, A. M. Buchan, W. A. Ghali, and T. E. Feasby, "Statins are associated with better outcomes after carotid endarterectomy in symptomatic patients," *Stroke*, vol. 36, no. 10, pp. 2072–2076, 2005.