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The Practice of Carotid Revascularization within a Large Metropolitan Population

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Abstract

Background—Carotid endarterectomy (CEA) and carotid artery stenting (CAS) reduce stroke risk when performed with acceptable perioperative morbidity and mortality. Studies from the 1980s in the Greater Cincinnati/Northern Kentucky population showed that perioperative risk following CEA exceeded the recommended boundaries of 3.0% for asymptomatic stenosis and 6.0% for symptomatic stenosis. We investigated the indications and outcomes for CEA and CAS in the same population during 2005.

Methods—We ascertained all residents of the Greater Cincinnati/Northern Kentucky region who underwent CEA or CAS at any local hospital during 2005. Identified TIAs or strokes that occurred before or after CEA or CAS were abstracted by study nurses and reviewed by a study physician. The main outcome of interest was 30-day risk of stroke or death following CEA or CAS. Events were analyzed using Kaplan-Meier statistics.

Results—Among approximately 1.3 million Greater Cincinnati/Northern Kentucky residents, 525 CEAs were performed, 343 (65%) for asymptomatic stenosis and 182 (35%) for symptomatic stenosis. There were 43 CAS procedures, 23 (53%) for asymptomatic stenosis and 20 (47%) for symptomatic stenosis. The 30-day perioperative risks of stroke or death following CEA were 3.3% (95% CI: 1.8–5.9%) for asymptomatic stenosis and 6.3% (3.5–11.1%) for symptomatic stenosis. The 30-day perioperative risks of stroke or death following CAS were 4.6% (0.7–28.1%) for asymptomatic stenosis and 21.1% (8.5–46.8%) for symptomatic stenosis.

Conclusions—Point estimates for perioperative risk following CEA were improved from prior studies but remained above the recommended benchmarks. The number of CAS procedures was small but perioperative risk was significant.

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Introduction

Large vessel atherosclerotic disease accounts for approximately 15% of ischemic strokes in the United States.^{1–3} In the 1990s, several large, randomized trials reported that carotid endarterectomy (CEA) following cerebral or ocular ischemia attributable to high grade (70%) carotid stenosis dramatically reduced recurrent stroke risk.⁴ For patients with symptomatic carotid stenosis of 50–70%, CEA confers a modest benefit, with an absolute annual risk reduction of 1–2% for stroke.⁴ Trials of CEA for asymptomatic carotid stenosis of 60% have shown an absolute annual risk reduction of approximately 1% per year over five years.^{5, 6}

Extracranial carotid artery stenting (CAS) is a potentially attractive alternative to CEA because it is less invasive and is less likely to produce cranial nerve palsy. CAS has not been compared to best medical management in randomized trials. Trials comparing CAS with CEA have produced mixed results. Two European trials enrolling patients with symptomatic carotid stenosis reported higher perioperative stroke risk with CAS.^{7, 8} The North American Carotid Revascularization Endarterectomy versus Stent Trial (CREST), which included patients with both symptomatic and asymptomatic carotid stenosis, showed equivalence between CAS and CEA for an endpoint of stroke, death, or myocardial infarction after a median follow-up of 2.5 years. Patients in the CAS arm had higher stroke risk while those in the CEA arm had greater risk of myocardial infarction.⁹

Carotid endarterectomy has been widely performed in the United States for decades, with 66,698 procedures among Medicare beneficiaries in 2005.¹⁰ There were 7,357 carotid artery stents placed among Medicare beneficiaries in 2005 and 12,087 carotid artery stents placed in 2006.¹⁰ Accrual of benefit following either CEA or CAS depends upon a skilled operator who can minimize the risk of perioperative stroke or death. Based upon surgical risk in randomized trials, it is recommended that 30-day perioperative risk not exceed 3.0% for asymptomatic carotid stenosis and 6.0% for symptomatic carotid stenosis.^{11–13} Greater risk, especially following revascularization for asymptomatic stenosis, may negate benefit from the procedure or confer harm. Community-wide studies in our population in the 1980s showed that perioperative risk following CEA exceeded recommended boundaries for asymptomatic and symptomatic stenoses.^{14, 15} Such findings led to more rigorous trials of CEA as well as an emphasis upon proper patient selection, risk mitigation, and outcome tracking. We provide a perspective on CEA in the same population 25 years later, while adding surveillance of CAS.

Methods

The Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS) is a population-based epidemiologic study of all stroke types in our region. The GCNKSS is approved by the Institutional Review Boards of all participating hospitals. During study periods (1993–4, 1999, 2005) we attempt to ascertain all strokes and TIAs among patients who present to a local emergency room or hospital as well as hospital-based outpatient clinics, health department clinics, and a sampling of outpatient physician offices and nursing homes.^{16–18} In 2005 study nurses screened the medical records of all inpatients with primary or secondary stroke-related ICD-9 discharge diagnoses (430–436) from all acute-care hospitals in the study region. Patients with stroke not found by inpatient screening were ascertained by monitoring all stroke-related visits to hospital emergency departments and screening of coroner's cases. Residents of the five county GCNK region who have a stroke seek acute care almost exclusively at one of the participating metropolitan hospitals included in each study period.¹⁹ Patients whose residence was outside of the five counties of interest were excluded. In all periods, nurses performed chart abstraction for all potential cases.

Physicians determined whether or not abstracted events met criteria for an acute stroke or transient ischemic attack and assigned a stroke category and mechanism to each event based upon all available information.

For this report we also ascertained all CEAs and CASs performed at the 17 acute care hospitals within the GCNK region during 2005. Study nurses used an ICD-9 code of 433.1x with a DRG of 533 or 534 to identify cases. Procedures were also included if they were identified as part of routine study surveillance for stroke and TIA. The indication for carotid revascularization was categorized as symptomatic or asymptomatic stenosis. Stenosis was considered symptomatic if it was associated with ipsilateral stroke or TIA in the preceding six months. Stroke after CEA was ascertained if it occurred during the index hospitalization or if the patient returned to an emergency room or hospital after discharge with stroke symptoms. Complete chart abstraction was not performed for patients who underwent CEA or CAS for asymptomatic stenosis and did not have a subsequent stroke or TIA during the study period. Thus, for these patients complete past medical history was not available. Death following CEA or CAS was tracked using study records, the Ohio and Kentucky death registers, and the Social Security Death Index. Outcomes of stroke, death, and stroke or death were analyzed using Kaplan-Meier statistics with censoring at the end of the study period. Patients who had more than one carotid revascularization procedure were censored at the time of the second procedure. Perioperative complications other than stroke or death (such as myocardial infarction) were not routinely tracked.

Results

As part of GCNKSS surveillance we identified 2234 ischemic strokes and 940 TIAs in our region during 2005. There were 525 CEAs performed at 15 different hospitals and 43 CASs performed at five hospitals. Eighteen patients had two revascularization procedures during the study period. After censoring of second revascularization procedures, there were 509 CEAs (334 asymptomatic, 175 symptomatic) and 41 CASs (22 asymptomatic, 19 symptomatic) remaining for analysis. Characteristics of patients having revascularization for symptomatic stenosis are presented in Table 1. Compared to patients undergoing CEA, patients undergoing CAS for symptomatic stenosis had higher rates of coronary artery disease and trends toward higher rates of diabetes, atrial fibrillation, and heart failure. Among patients who had CEA for asymptomatic stenosis, 95% were white, 54% were male, and the mean age was 71 years (SD= 9.0). Patients undergoing CAS for asymptomatic stenosis were mostly white (86%) and male (68%) with a mean age of 72 years (SD=11.4). There were 130 (26%) CEA patients and 12 (29%) CAS patients under 65 years of age.

During 2005, carotid artery stenting was FDA approved but procedures were reimbursed by the US Centers for Medicare and Medicaid Services (CMS) only for patients with symptomatic, high grade (≥ 70%) stenosis and medical comorbidities that made them high risk for CEA. For patients undergoing CAS, we found chart evidence documenting that 11/19 (58%) of symptomatic patients were high risk for CEA based upon CMS criteria. There was chart documentation that 14/22 (64%) of asymptomatic patients were high risk for CEA. The Acculink/Accunet stenting system (which includes a distal protection device) was used in 31/41 CAS cases. In three cases other stent systems were used and in seven cases the type of system used could not be determined from available records.

Event rates following revascularization, stratified by procedure and symptom status, are presented in Table 2. Perioperative risks of stroke or death following CEA were 3.3% (95% CI: 1.8–5.9%) for asymptomatic stenosis and 6.3% (3.5–11.1%) for symptomatic stenosis. Perioperative risks following CAS were 4.6% (0.7–28.1%) for asymptomatic stenosis and 21.1% (8.5–46.8%) for symptomatic stenosis. The risk of stroke or death following CEA did

not differ between men and women operated on for symptomatic (men = 9.5% vs. women = 1.4%, $p = 0.88$) or asymptomatic (men = 4.4% vs. women = 2.0%, $p=0.25$) stenosis, but sample size limited power. Analysis of event rates stratified by hospital CEA volumes, comparing hospital groups in tertiles, did not show a significant difference by group for procedures done for symptomatic or asymptomatic stenosis, but the relatively low number of events again limited power. Likewise, a comparison of event rates between the three hospitals with surgical residency programs and the remaining hospitals without residency programs showed no significant differences in outcomes.

Table 3 shows the time from index event to revascularization by CEA and CAS in the GCNK region. The median time from symptom onset to CEA in our population was 22 days. Among patients with TIA or nondisabling stroke (NIHSS score ≤ 5), 72 (45%) had a CEA within two weeks.

Discussion

Carotid endarterectomy remains a common procedure in our population. Similar studies were conducted in the same region for the years 1980 and 7/1983-6/1984. During 1980, 431 CEAs were performed. By 1984, 750 CEAs were performed.^{14, 15} During both periods CEAs were evenly divided between procedures for symptomatic and asymptomatic stenosis. In 2005 we found a majority of CEAs were performed for asymptomatic stenosis. The indication for carotid revascularization is directly relevant to benefit and determines acceptable rates of perioperative complications. Early CEA for high grade (70–99%) symptomatic carotid stenosis produces a robust benefit. In contrast, CEA for asymptomatic stenosis produces a marginal benefit. Because of improvements in medical therapy in the years following the sentinel studies which included medical management arms, some have argued that CEA may no longer benefit most patients with asymptomatic stenosis.²⁰

The previous studies of CEA in our region reported unacceptably high perioperative risk. In 1980 perioperative stroke or death occurred in 6.9% (95% CI 3.6–10.3) of asymptomatic patients and 12.1% (7.7–16.5) of symptomatic patients. In 1983–4 risk was 5.3% (3.0–7.5) for asymptomatic patients and 7.8% (5.1–10.6) for symptomatic patients. Data from 2005 show improvement in both measures. While the 6.3% perioperative risk for symptomatic stenosis remains above the recommended boundary, the substantial risk reduction with surgery compared to medical management means that the balance of risk and benefit will still favor revascularization. In contrast, because of the marginal benefit of CEA for asymptomatic stenosis, the 3.3% perioperative risk for revascularization in 2005 remains a cause for concern. For asymptomatic patients, further restriction of revascularization procedures to patients at lower surgical risk would appear prudent. Medical systems and individual surgeons should also track outcomes as quality assurance measures.

The risk of recurrent stroke is high early after an index event caused by carotid stenosis, and the benefit for CEA is greatest in patients undergoing revascularization within two weeks of TIA or stroke, waning rapidly thereafter.²¹ It is therefore recommended that for patients with TIA or nondisabling stroke, CEA be performed within two weeks.¹³ In a survey-based audit of CEA in the United Kingdom from 2008–2009, the median time from symptoms to CEA was 28 days (IQR 12–64), with 33% of CEAs performed within two weeks of the index event.²² An evaluation of 12 stroke centers in Ontario, Canada from 2003–2006 documented a median time from index event to CEA of 30 days (IQR 10–81) with 36% undergoing CEA within two weeks.²³ In the GCNK population the median time to CEA was better at 22 days, but CEA was still performed after two weeks for a majority of patients. While timing of revascularization must be individualized for each patient, educational

efforts directed at primary care physicians, neurologists, and surgeons should emphasize the importance of early revascularization for patients with symptomatic carotid stenosis.

There were many fewer CASs than CEAs in our population in 2005 but CAS is being performed with increasing frequency. Among Medicare beneficiaries the number of CASs increased by 64% between 2005 and 2006. Our data raises concerns about the translation of results from registries and randomized trials to general clinical practice. However, CAS numbers were small and proceduralists have gained experience in CAS since 2005. As expected based upon CMS indications for CAS, patients with symptomatic carotid stenosis undergoing CAS had higher rates of diabetes, coronary artery disease, atrial fibrillation and heart failure than those undergoing CEA. Given the high risk of stroke from severe, symptomatic carotid stenosis, CAS is a valuable tool for symptomatic patients considered high risk for CEA based upon medical comorbidities or anatomic considerations. In contrast, the practice of stenting asymptomatic patients deemed at high risk for CEA is dubious as these patients have relatively low stroke risk and may have limited life expectancies, resulting in front-loaded risk without assurance of subsequent benefit.

A considerable strength of our study is its population-based case ascertainment, which includes all local residents who underwent carotid revascularization in the Greater Cincinnati/Northern Kentucky region. Unlike single-center studies, our data is therefore not subject to referral bias. Likewise, we tracked revascularization procedures performed at academic and community hospitals, regardless of physician specialty or experience. In contrast to analyses of administrative databases in the United States (such as provided by Medicare), our study included patients of all ages with all types of (or no) insurance coverage. A sizable minority (26%) of patients undergoing carotid revascularization in our region were under 65 years of age and would not have been included in Medicare-based analyses. Perioperative strokes in our study were adjudicated on an individual basis by physicians, which is more accurate than reliance upon administrative coding. We also provide a unique, longitudinal view of carotid revascularization performed in the same large population over three decades, a rare opportunity.

Our study has several limitations. While patients within our region seek acute care for stroke almost exclusively at regional hospitals, patients undergoing non-urgent carotid revascularization may have traveled to distant referral centers for procedures, which would not have been captured. Mild perioperative strokes that occurred after hospital dismissal and did not prompt readmission may have been missed, resulting in slightly underestimated event rates. We also did not track some perioperative complications of clinical relevance, such as myocardial infarction and cranial nerve palsy. Although our sample size for CEA was large, the relatively small number of perioperative events means confidence intervals surrounding point estimates include values both below and above recommended boundaries.

In summary, CEA is now performed more frequently for asymptomatic than symptomatic stenosis. Perioperative risk following CEA in the GCNK region has improved considerably since the 1980s, but remains above the recommended benchmarks. Carotid artery stenting was performed much less commonly than CEA but carried higher perioperative risk. Continued surveillance of population-based outcomes following both CEA and CAS is warranted. We intend to continue this study by tracking carotid revascularization in our region during 2010.

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Table 1

Characteristics of patients who underwent endarterectomy or stenting for symptomatic internal carotid artery stenosis.

	CEA n=163 [*]	CAS n=16 [†]	p-value
Age, mean (SD)	69.8 (11.3)	72.3 (9.1)	0.40
White, n (%)	155 (95.1)	15 (93.8)	0.58
Male	98 (60.1)	10 (62.5)	0.99
Hypertension	135 (82.8)	14 (87.5)	0.99
Diabetes	41 (25.2)	7 (43.8)	0.14
Coronary disease	69 (42.3)	12 (75.0)	0.02
Atrial fibrillation	14 (8.6)	4 (25.0)	0.06
Heart failure	16 (9.8)	4 (25.0)	0.09

^{*} 12 symptomatic CEA patients missing demographic data

[†] Three symptomatic CAS patients missing demographic data

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Table 2

Outcome event rates with 95% confidence intervals.

Outcome	Symptomatic stenosis		Asymptomatic stenosis	
	CEA n=175	CAS n=19	CEA n=334	CAS n=22
Stroke (95% CI)	4.6% (2.3–9.0)	16.1% (5.5–42.1)	3.0% (1.6–5.5)	4.6% (0.7–28.1)
Death	1.8% (0.6–5.5)	5.9% (0.9–35.0)	0.3% (0–2.2)	0%
Stroke or death	6.3% (3.5–11.1)	21.1% (8.5–46.8)	3.3% (1.8–5.9)	4.6% (0.7–28.1)

CEA = carotid endarterectomy; CAS = carotid artery stenting; CI = confidence interval

Table 3

Time from stroke or TIA to carotid revascularization.

Event triggering revascularization	Carotid endarterectomy		Carotid artery stenting	
	Median time [interquartile range]	< 2 weeks (%)	Median time [interquartile range]	< 2 weeks (%)
Any stroke or TIA	n=170 * 22 days [6–42]	76 (45)	n=18 24 days [13–51]	5 (28)
Mild stroke [†] or TIA	n=160 21 days [6–42]	72 (45)	n=16 24 days [15–46]	4 (25)
Moderate to severe stroke [‡]	n=10 66 days [6–111]	4 (40)	n=2 34 days [10–58]	1 (50)

* Five CEAs and one CAS were excluded for uncertain date of index event. For 45 CEAs and 6 CASs the month but not the day of the index event prompting revascularization was known. For these cases the index event was assigned to the first day of the month.

[†] Estimated National Institutes of Health Stroke Scale score ≤ 5.

[‡] Estimated National Institutes of Health Stroke Scale score > 5.