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Revisiting the Appropriateness of Carotid Endarterectomy

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- *Background and Purpose*—In the 1980s, carotid endarterectomy was controversial because proof of efficacy was lacking, complication rates were high, and one third of cases were reported to be inappropriate. Since publication of several randomized controlled trials (RCTs), rates of carotid endarterectomy have doubled nationwide. This study assesses the appropriateness and use of carotid endarterectomy since publication of the RCTs.
- *Methods*—Using the literature, we developed a list of 1557 mutually exclusive indications for carotid endarterectomy and asked a panel of national experts to rate the appropriateness of each indication using the RAND methodology. We used these ratings to assess appropriateness in a sample of 2124 patients who underwent the procedure in 1997 to 1998 in 6 hospitals. We also analyzed the reasons for the procedure and rates of death, stroke, and myocardial infarction within 30 days of surgery.
- *Results*—Overall, 84.9% of operations were done for appropriate reasons, 4.5% for uncertain reasons, and 10.6% for inappropriate reasons. Among procedures considered inappropriate, the most common reasons were high comorbidity (46.6%) and minimal stenosis (27.1%). Overall, 72.5% were asymptomatic, 17.4% had a carotid transient ischemic attack, and 10.1% had a stroke. The 30-day rate of death or stroke was 5.47% for symptomatic patients and 2.26% for asymptomatic patients. Among patients having combined carotid and coronary artery bypass graft surgery, the rate was 10.32%. The complication rate in asymptomatic patients with high comorbidity was 5.56%.
- *Conclusions*—Since the RCTs, rates of overuse appear to have fallen considerably, although they are still significant. A major shift has occurred toward operating on asymptomatic patients. Although overall complication rates were low, rates among asymptomatic patients with high comorbidity exceeded recommended thresholds. (*Stroke*. 2003;34:1464-1472.)

Key Words: carotid endarterectomy ■ complications ■ health services misuse ■ outcome

A t the end of the 1980s, carotid endarterectomy was controversial. No rigorous data documented its efficacy; many studies reported high complication rates^{1–6}; and 1 large study of Medicare beneficiaries reported that 32% of the procedures were performed for inappropriate indications.⁷ Nationwide, the number of carotid endarterectomies fell from a peak of 107 000 in 1985 to a nadir of 67 000 in 1991, reflecting these concerns.^{8,9} In the 1990s, the procedure enjoyed a remarkable renaissance. Reports from a series of randomized controlled trials (RCTs) demonstrated that under certain circumstances the procedure could prevent stroke and improve survival.^{10–15}

The widespread dissemination of the results of these RCTs was accompanied by a dramatic increase in carotid endarterectomies nationally, reaching 131 000 in 1999.^{16–18} More recent research has shown that although complication rates have fallen overall, some hospitals and regions still have rates of perioperative stroke and death that are considerably higher than those achieved in clinical trials.^{19–23}

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Although there have been some attempts to examine subsequent rates of appropriateness since the original RAND Medicare study, most of these studies reflect practice before the publication of several key RCTs^{24–27} or considered only symptomatic patients as potentially appropriate operative candidates.^{27,28} The aim of this investigation was to determine whether and how the appropriateness and use of the procedure have changed since the publication of all the major RCTs. We used the RAND appropriateness method to assess the appropriateness and outcomes of the carotid endarterectomies performed by 67 surgeons in 1997 to 1998 in 6 hospitals.

Methods

Appropriateness Rating Process

We used the RAND appropriateness method to generate a detailed set of criteria to judge the appropriateness of carotid endarterectomy

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Received December 23, 2002; accepted January 8, 2003.

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as described previously.^{7,29–31} Briefly, a panel of 9 national experts in vascular surgery, neurosurgery, neurology, internal medicine, neuroradiology, and vascular medicine reviewed, rated, discussed, and rerated 1557 mutually exclusive indications for which this procedure might be considered. The results of all the RCTs were known at that time. Appropriateness for each indication was rated on a scale of 1 to 9 (1 to 3=inappropriate, 4 to 6=uncertain appropriateness, and 7 to 9=appropriate). Carotid endarterectomy was considered appropriate when the benefits exceeded the risks by a sufficient margin to make the procedure worth performing, uncertain when the benefits equaled the risks, and inappropriate when the risks outweighed the benefits.

Indication Structure

Indications were grouped into 13 broad clinical categories (outlined in Table 2) that include details regarding neurological symptoms (type, severity, recency, frequency, disability), degree of carotid stenosis, type of operation (ipsilateral or contralateral to symptoms, carotid endarterectomy alone or combined with coronary artery bypass graft [CABG] surgery), comorbidity risk, and the surgical team's complication rates. High comorbidity was defined as the presence of (1) end-stage disease, (2) severe disability,³² or (3) \geq 3 Revised Cardiac Risk Index risk factors.³³ Comorbidity was further stratified by the number of cardiac risk factors: 2 (moderate), 1 (low), and 0 (absent).³³

Study Population

We identified all patients who underwent carotid endarterectomy (*International Classification of Diseases*, revision 9, CM 38.12) between January 1, 1997, and December 31, 1998, using the administrative databases from each hospital. Five hospitals were located in the New York metropolitan area, and 1 was in upstate New York; 4 sites were university teaching hospitals, and 2 were community teaching hospitals. The study was approved by the Institutional Review Board at each site. Two surgeons had performed >250 carotid endarterectomies. We randomly sampled 50% of the cases of these 2 very-high-volume surgeons and 100% of all other physicians' cases.

We reviewed the medical records of 2365 of 2390 cases (98.9%). Among these, 2066 underwent carotid endarterectomy alone, 149 had carotid endarterectomy combined with CABG, and 175 were excluded. Reasons for exclusion included same-side reoperations (n=91), surgery combined with another major procedure (n=47), and no carotid endarterectomy performed (n=37). An additional 91 cases were excluded because we could not classify the degree of carotid stenosis as a result of missing data (n=75) or the case represented a scenario not rated by the consensus panel (n=16). Therefore, the analyses reported here are based on 2124 cases. Each hospital contributed between 130 and 583 cases.

Data Collection and Measurement

Detailed clinical information was abstracted from inpatient and outpatient medical records, including sociodemographic characteristics; neurological, medical, and surgical history; admission neurological examination; functional status; laboratory values; medications; and diagnostic test results. We abstracted data on the degree of stenosis of both internal carotid arteries, where carotid angiography was considered to be the most accurate test, followed by Doppler ultrasonography and then by MR angiography. If no diagnostic imaging test data were available, we used the degree of stenosis described in the preoperative notes (n=154).

Outcomes

We collected data on death, strokes, myocardial infarctions, and transient ischemic attacks (TIAs) within 30 days of surgery from the inpatient record and surgeon's postdischarge office records. We reviewed office records for 97% of surgeons (65 of 67) and 96% of patients (2048 of 2124). We also reviewed all readmissions to the index hospital within 30 days of surgery to identify complications. The vast majority of deaths and strokes within 30 days of carotid

endarterectomy occur early and during the index hospitalization.³⁴ Two investigators independently reviewed the medical records of all patients who sustained strokes and TIAs as complications of their surgery (including 1 neurologist). Initial agreement was 95%. Disagreements were resolved by consensus and the use of a third reviewer as needed.

Analysis Plan

Carotid endarterectomy was deemed appropriate for a specific indication if the median appropriateness rating was 7 to 9 and there was no disagreement. Disagreement was present when \geq 3 panel members scored an individual indication as inappropriate (1 to 3) and 3 others rated it as appropriate (7 to 9). It was classified as uncertain if the median score was 4 to 6 or there was disagreement regardless of median rating. The surgery was considered inappropriate if the median score was 1 to 3 and there was no disagreement.

We classified each case into 1 indication. If >1 indication could apply, we assigned the indication with the highest appropriateness rating. We judged appropriateness conservatively, using the ratings for surgical teams with the same low rates of death and stroke as required in the RCTs and advocated by national guidelines (<6% for symptomatic patients,^{11,15,35,36} <3% for asymptomatic patients¹²). Differences between sites in patient characteristics, indications for surgery, appropriateness, and outcomes were assessed with χ^2 tests, analysis of variance, and Cochrane-Mantel-Haenzel tests for trend. All statistical analyses also used 2-tailed significance levels of P<0.05 and were conducted with SAS statistical software 8.0 (SAS Institute).

Results

Patient and Surgeon Characteristics

Characteristics of the 2124 study patients are shown in Table 1. Most patients were elderly, white Medicare beneficiaries with hypertension, coronary artery disease, and 70% to 99% ipsilateral carotid artery stenosis. The median length of stay was 2 days for patients undergoing carotid endarterectomy alone and 11 days for those having a carotid endarterectomy combined with CABG surgery (P < 0.001).

The study cohort reflects the practices of 67 board-certified surgeons (vascular, n=38; neurosurgery, n=10; thoracic, n=10; and general, n=9). The vast majority of surgeries (89.4%) were performed by vascular surgeons (1898), followed by thoracic surgeons (112), neurosurgeons (84), and general surgeons (30).

Indications for Carotid Endarterectomy

The major reasons for surgery are given in Table 2. Two thirds of patients had asymptomatic carotid stenosis. The second-most-common indication was carotid TIA or amaurosis fugax (17.1%), followed by minor stroke (8.3%). Fewer than 1% of patients had crescendo TIA or stroke in evolution. Overall, 72.5% of all patients underwent carotid endarterectomy to repair asymptomatic arteries (asymptomatic patients and those with vertebrobasilar TIAs undergoing carotid endarterectomy alone or combined with CABG).

Although the overall rank order of reasons for surgery was largely similar at all sites, there were significant differences among hospitals in the proportion of various indications. The proportion of patients being operated on for asymptomatic carotid stenosis (carotid endarterectomy alone or with CABG or vertebrobasilar TIAs) ranged from 64.0% to 81.8% (P<0.001). We also observed hospital differences in the practice of combining carotid endarterectomy and CABG.

| | Hospital | | | | | | |
|--|----------|------|------|------|------|------|-------|
| Patient Characteristics | А | В | С | D | Е | F | Total |
| Sociodemographics, % | | | | | | | |
| Mean age‡ | 72.7 | 70.4 | 71.9 | 73.6 | 73.3 | 71.6 | 72.3 |
| <65 y | 12.0 | 24.6 | 17.8 | 12.9 | 15.1 | 20.8 | 17.5 |
| 65–79 y | 68.0 | 59.4 | 60.5 | 64.3 | 75.7 | 59.4 | 61.7 |
| ≥80 y | 20.0 | 16.0 | 21.7 | 22.8 | 23.2 | 19.8 | 20.8 |
| Male | 56.8 | 53.3 | 60.2 | 56.4 | 58.0 | 61.9 | 57.2 |
| White‡ | 89.6 | 95.4 | 85.9 | 80.1 | 90.2 | 78.7 | 87.3 |
| Medicare insurance† | 85.6 | 74.8 | 77.4 | 70.5 | 77.9 | 72.6 | 75.3 |
| Comorbid conditions | | | | | | | |
| Past stroke* | 22.4 | 17.1 | 23.0 | 19.1 | 21.5 | 29.4 | 20.9 |
| Past TIA† | 38.4 | 20.0 | 33.4 | 24.5 | 35.2 | 36.0 | 29.4 |
| Cerebrovascular disease‡ | 52.0 | 33.3 | 49.1 | 38.7 | 50.9 | 52.3 | 44.1 |
| Coronary artery disease† | 55.2 | 51.7 | 57.9 | 60.4 | 48.4 | 62.4 | 54.9 |
| Congestive heart failure‡ | 9.6 | 7.9 | 7.7 | 11.0 | 3.1 | 13.7 | 8.0 |
| Hypertension‡ | 81.6 | 73.3 | 73.4 | 76.7 | 64.8 | 79.7 | 73.1 |
| Diabetes mellitus* | 32.0 | 28.8 | 33.3 | 33.0 | 24.2 | 27.4 | 29.3 |
| Insulin-dependent diabetes† | 11.6 | 8.6 | 8.5 | 8.5 | 5.1 | 6.2 | 7.7 |
| Creatinine >2 preoperatively† | 4.1 | 2.7 | 3.8 | 6.8 | 4.1 | 4.6 | 4.4 |
| Chronic obstructive pulmonary disease† | 16.0 | 14.4 | 5.2 | 7.6 | 6.9 | 8.6 | 9.2 |
| Severe disability‡ | 3.2 | 1.0 | 3.0 | 4.3 | 1.3 | 1.5 | 2.4 |
| Stenosis of operated carotid artery, %‡ | | | | | | | |
| 100% | 0.8 | 1.9 | 0.9 | 1.0 | 1.8 | 2.5 | 1.5 |
| 70–99% | 92.8 | 85.0 | 92.7 | 89.8 | 93.6 | 88.3 | 90.1 |
| 50–69% | 4.0 | 7.7 | 4.9 | 5.6 | 1.4 | 7.6 | 5.0 |
| 0–49% | 2.4 | 5.5 | 1.5 | 3.6 | 3.3 | 1.5 | 3.3 |
| Stenosis of contralateral carotid artery, %‡ | | | | | | | |
| 100% | 6.4 | 6.2 | 6.4 | 5.0 | 7.0 | 7.6 | 6.3 |
| 70–99% | 28.0 | 19.6 | 30.9 | 22.2 | 34.8 | 24.9 | 26.6 |
| 50–69% | 10.4 | 16.2 | 13.2 | 16.7 | 4.4 | 11.1 | 11.2 |
| 0–49% | 55.2 | 57.9 | 49.5 | 60.1 | 53.8 | 56.3 | 54.9 |

TABLE 1. Characteristics of Patients Undergoing Carotid Endarterectomy

n=2124.

**P*<0.01; †*P*<0.001; ‡*P*<0.0001.

Appropriateness

Overall, 84.9% of cases were classified as appropriate, 10.6% as inappropriate, and 4.5% as of uncertain appropriateness. We found statistically significant differences in appropriateness across sites (range, 81.7% to 90.5%; P=0.002) and inappropriateness (range, 7.0% to 13.0%; P=0.03), but these differences were due entirely to 1 hospital that exhibited a greater proportion of appropriate cases and fewer inappropriate ones. After exclusion of this hospital, no significant differences in appropriateness were observed among the remaining 5 hospitals.

Table 3 presents the most commonly observed appropriate indications. These 5 indications accounted for 88.4% of the total number of appropriate cases. Most cases rated as appropriate (69.6%) were operations for asymptomatic patients with carotid stenoses of \geq 60% and low or moderate comorbidity.

Table 4 presents the 5 most frequent groups of inappropriate indications that together accounted for 83.6% of all inappropriate cases. Patients who were asymptomatic or had vertebrobasilar TIAs and who had high surgical risk because of major comorbid illness burden made up half of the inappropriate cases. Operating on an artery with minimal stenosis (<50% in symptomatic and <60% in asymptomatic patients) was almost always considered inappropriate by the panel and accounted for 28.0% of inappropriate surgeries. Less common reasons for rating cases as inappropriate included major or disabling strokes (9.8%), and operating on arteries contralateral to symptoms (despite significant ipsilateral stenosis) (6.2%), or arteries that were completely occluded (1.8%). Cases exhibiting combinations of factors accounted for the remaining 5.3% of inappropriate cases.

Complication Rates

The rates of major perioperative complications are displayed in Table 5. For patients with symptomatic carotid disease, the combined rate of death and nonfatal stroke within 30 days of

| | Hospital | | | | | | |
|---|----------|------|------|------|------|------|-------|
| Major Clinical Group* | А | В | С | D | Е | F | Total |
| Carotid TIAs or amaurosis fugax | | | | | | | |
| Within 3 mo before surgery | 24.0 | 7.3 | 15.9 | 9.8 | 22.6 | 16.2 | 14.7 |
| 3 to 12 mo before surgery | 0.8 | 3.3 | 2.4 | 1.9 | 2.1 | 3.0 | 2.4 |
| Crescendo carotid TIAs | 0.0 | 0.4 | 0.0 | 0.4 | 0.2 | 1.0 | 0.3 |
| Stroke in evolution | 0.0 | 0.4 | 0.3 | 0.2 | 0.2 | 1.0 | 0.3 |
| Minor stroke | | | | | | | |
| Within 6 wk before surgery | 4.8 | 2.5 | 4.6 | 1.5 | 4.8 | 6.6 | 3.7 |
| 6 wk to 12 mo before surgery | 4.0 | 3.1 | 7.0 | 4.8 | 4.3 | 5.1 | 4.6 |
| Major stroke | | | | | | | |
| Within 6 wk before surgery | 0.8 | 0.8 | 0.3 | 0.8 | 1.0 | 1.0 | 0.8 |
| 6 wk to 12 mo before surgery | | | | | | | |
| Moderately severe disabling stroke | 0.8 | 0.2 | 0.3 | 0.0 | 0.0 | 0.5 | 0.2 |
| Severe disabling stroke | 0.0 | 0.0 | 0.6 | 0.6 | 0.8 | 0.5 | 0.5 |
| Vertebrobasilar TIAs | 2.4 | 1.0 | 0.3 | 0.6 | 2.5 | 2.0 | 1.4 |
| Asymptomatic | 62.4 | 68.3 | 60.2 | 72.0 | 60.5 | 62.9 | 65.2 |
| Asymptomatic undergoing simultaneous CABG | 0.0 | 12.5 | 8.0 | 7.3 | 1.0 | 0.0 | 5.9 |

TABLE 2. Major Clinical Groups of Patients Who Underwent Carotid Endarterectomy

Rows are rounded to the nearest tenth, so they may not exactly add up to 100%.

*P<0.0001 for differences among hospitals in distribution of patients among 3 groups (any carotid TIA or amaurosis fugax, any stroke, all others).

surgery was 5.47%. For asymptomatic patients undergoing carotid endarterectomy alone, the rate of death or nonfatal stroke was 2.26%; for asymptomatic patients who underwent the procedure combined with CABG, the rate was 10.32%. There were no significant differences among hospitals in complication rates among these 3 clinical groups.

When all patients are considered together, the risk of death, stroke, and myocardial infarction was directly related to the degree of comorbidity (P < 0.001, data not shown), and patients with high comorbidity had more than twice the odds of death or stroke (odds ratio [OR], 2.62; 95% CI, 1.48 to 4.64; P < 0.001). Within major clinical groups, the effect of

TABLE 3. Most Frequent Appropriate Indications for Carotid Endarterectomy

| Description of Indication | Cases, n | % of All Appropriate Cases |
|--|-------------|----------------------------------|
| Asymptomatic patients with 60–99% stenosis of the operated carotid artery and low comorbidity | 1027 | 56.9 |
| Patients with carotid TIAs or amaurosis fugax within 3 mo before surgery, 70–99% stenosis of operated artery ipsilateral to symptoms, and low or moderate comorbidity | 235 | 13.0 |
| Asymptomatic patients with 60–99% stenosis of the operated carotid artery and moderate comorbidity | 230 | 12.7 |
| Patients with minor strokes between 6 wk and 12 mo before surgery, 70–99% stenosis of operated artery ipsilateral to stroke, and low or moderate comorbidity | 60 | 3.3 |
| Patients with minor strokes within 6 wk before surgery, 70–99% stenosis of operated artery ipsilateral to stroke, and low or moderate comorbidity | 45 | 2.5 |

All of these indications assumed that the surgical team had a combined rate of stroke and mortality of \leq 3% for asymptomatic patients and \leq 6% for symptomatic patients.

TABLE 4. Most Frequent Inappropriate Indications for Carotid Endarterectomy

| | Casos | % of All |
|---|-------|----------|
| Description of Indication | n | Cases |
| Asymptomatic patients with 60–99% stenosis of the operated carotid artery and <u>high comorbidity</u> | 82 | 36.4 |
| Asymptomatic patients with $\underline{<60\%}$ stenosis of the operated carotid artery and low or moderate comorbidity* | 41 | 18.2 |
| Asymptomatic patients whose operations were combined with CABG with 60–99% stenosis of the operated carotid artery and <u>high comorbidity</u> * | 23 | 10.2 |
| Patients with <u>major strokes</u> within 6 wk before surgery or <u>severe disabling strokes</u> between 6 wk and 12 mo before surgery and 70–99% stenosis of the operated artery ipsilateral to stroke (all comorbidity levels)* | 22 | 9.8 |
| Patients with carotid TIAs or minor strokes within 12 mo before surgery, \leq 50% stenosis of the operated artery, ipsilateral to symptoms, and low or moderate comorbidity* | 20 | 8.9 |

Principal determinant of inappropriateness is underlined. All of these indications assumed that the surgical team had a combined stroke/mortality rate of \leq 3% for asymptomatic patients and \leq 6% for symptomatic patients. *These descriptions represent \geq 2 indications that have been grouped under the principal determinant of inappropriateness.

| | | Comorbidity Category, % | | | | | | |
|--|--------------|-------------------------|--------------|-------|-------|-------|--|--|
| Outcome | None | Low | Moderate | High | Total | Value | | |
| Asymptomatic patients undergoing carotid endarterectomy | | | | | | | | |
| n | 390 | 680 | 253 | 90 | 1413 | | | |
| Death | 0.26 | 0.59 | 0.79 | 1.11 | 0.57 | 0.25 | | |
| Nonfatal stroke | 1.03 | 1.62 | 1.98 | 4.44 | 1.69 | 0.04 | | |
| Death/stroke* | 1.28 | 2.21 | 2.77 | 5.56 | 2.26 | 0.02 | | |
| Nonfatal MI† | 0.0 | 0.74 | 1.58 | 3.33 | 0.85 | 0.008 | | |
| Symptomatic patients | s undergoing | carotid end | darterectomy | | | | | |
| n | | 237 | 259 | 89 | 585 | | | |
| Death | | 0.42 | 0.39 | 3.37 | 0.85 | 0.02 | | |
| Nonfatal stroke | | 4.22 | 4.63 | 5.62 | 4.62 | 0.56 | | |
| Death/stroke* | | 4.64 | 5.02 | 8.99 | 5.47 | 0.19 | | |
| Nonfatal MI† | | 0.42 | 1.54 | 1.12 | 1.02 | 0.35 | | |
| Patients undergoing combined CABG and carotid endarterectomy | | | | | | | | |
| n | | 68 | 35 | 23 | 126 | | | |
| Death | | 2.94 | 0.0 | 13.04 | 3.97 | 0.10 | | |
| Nonfatal stroke | | 5.88 | 11.43 | 0.0 | 6.35 | 0.59 | | |
| Death/stroke* | | 8.82 | 11.43 | 13.04 | 10.32 | 0.53 | | |
| Nonfatal MI† | | 0.0 | 2.86 | 0.0 | 0.79 | 0.64 | | |

 TABLE 5.
 Rates of Major Perioperative Complications By Degree of Comorbidity

*Combined outcome of death or nonfatal stroke.

†Nonfatal myocardial infarction (MI) in a patient who did not suffer stroke.

comorbidity on the risk of adverse outcomes was most consistent among asymptomatic patients (Table 5). High comorbidity conferred a significantly higher risk of death or stroke among asymptomatic patients (OR, 2.8; 95% CI, 1.1 to 7.5; P=0.03) but was of borderline significance among symptomatic patients (OR, 1.9; 95% CI, 0.8 to 4.5; P=0.11).

Discussion

We studied the clinical indications, appropriateness, and outcomes of carotid endarterectomy in a cohort of 2124 patients who underwent the procedure in 6 hospitals by 67 different surgeons during 1997 and 1998. Our data document major improvements in appropriateness compared with a large 1981 study that found that 35% of Medicare cases were judged as appropriate, 32% as uncertain, and 32% as inappropriate.⁷ We found a large increase in appropriate cases (to 84.9%) and large decreases in uncertain (to 4.5%) and inappropriate (to 10.6%) cases. These findings represent major changes either in practice or in the criteria used to judge appropriateness.

The data strongly suggest that changes in practice explain the decrease in inappropriate cases. Virtually all cases judged inappropriate in 1981 would have received the same categorization in the present study and vice versa. The same 4 reasons (high comorbidity, minimal stenosis, contralateral operations, and occluded arteries) accounted for three quarters or more of inappropriate cases in both studies. The only significant difference between the 2 groups of criteria is that our criteria use the Asymptomatic Carotid Atherosclerosis Study (ACAS) stenosis threshold of 60% for asymptomatic patients (compared with 50% for the 1981 study). The stenosis criteria for symptomatic cases were similar. The impact of this small discrepancy is negligible because only 1% of patients had between 50% to 59% stenosis. Favorable decreases in the reasons for inappropriateness from 1981 to 1997 to 1998 include a decrease in minimal stenosis (48% versus 28%) and operations on arteries contralateral to symptoms (9% versus 6%) or occluded (6% versus 2%). High comorbidity accounted for a larger proportion of inappropriate cases in the present study (49% versus 11%).

The explanation of the changes in proportions of appropriate and uncertain cases has 2 components. All cases represented in the 2 most frequent appropriate indications in the present study (Table 3) would also have been judged appropriate in 1981.²⁹ These 2 groups of patients alone constituted some 70% of the appropriate cases. Thus, the increase in the proportion of appropriate cases is due in large part to more operations in 1997 to 1998 being performed on patients with indications that would have been considered appropriate in both time periods. In addition, some indications judged uncertain in 1981 were rated as appropriate in 1997 to 1998. For example, asymptomatic patients with significant stenosis but moderate comorbidity were rated uncertain in 1981 and appropriate in 1997 to 1998. Thus, some of the increase in appropriate cases (and the concomitant decrease in uncertain cases) occurred because of these shifts in the criteria.

We also observed a dramatic shift in the patient population undergoing carotid endarterectomy. In 1981, only 34% of procedures were performed for asymptomatic carotid stenoses.⁷ During the 1980s and mid 1990s, between 41% and 47% of operations were performed on asymptomatic patients.^{27,28,37} A large multistate study of Medicare beneficiaries undergoing carotid endarterectomy in 1995 to 1996 reported that 39% of patients were asymptomatic and 37% had nonspecific symptoms.²³ In our 1997 to 1998 sample, nearly three quarters of carotid endarterectomies were for asymptomatic patients.

The improvements in appropriateness probably reflect a growing consensus about which patients benefit from carotid endarterectomy caused in large part by the wide dissemination of results of the large RCTs. For both symptomatic and asymptomatic patients, the RCTs clearly established thresholds of carotid stenosis below which surgery conveys no benefit. In the 1981 study, 15% of all operations were performed on carotid arteries that showed minimal stenosis compared with 3% in our study. All of us can take some satisfaction in the positive effect of this large, international investment in RCTs that pointed the way to reducing the use of the procedure for indications of no clinical benefit. However, several important challenges remain.

Although the proportion of inappropriate cases fell considerably, it remains an issue of concern. If our results are typical of practice in the United States, then $\approx 14\,000$ operations are performed annually without clear evidence of appropriateness.

The emergence of asymptomatic patients as the overwhelming majority of those undergoing carotid endarterectomy raises other concerns because these patients on average have less to gain from surgery compared with those with symptomatic carotid disease. The ACAS trial found that for surgical teams with rates of stroke and death <3%, asymptomatic patients averaged an absolute reduction in the risk of ipsilateral stroke or death of 5.9% in 5 years.¹² This benefit contrasts sharply with the absolute reduction in risk of stroke or death of 16.5% in 2 years that is conveyed to symptomatic patients with 70% to 99% carotid stenosis when surgical teams with perioperative stroke or death rates <6% perform the procedure.^{11,15} The narrow margin between risk and benefit for asymptomatic patients places even greater importance on minimizing the risk of major perioperative complications.

Our national expert panel identified high comorbidity and its associated greater risk of perioperative complications as a critical mitigating factor that would cause the risks of carotid endarterectomy to outweigh its benefits for asymptomatic patients. Our data confirm the importance of these countervailing risks. Asymptomatic patients with high comorbidity (an indication judged inappropriate by our criteria) experienced a rate of perioperative stroke or death of 5.56%nearly twice the level considered acceptable in this patient group by national guideline criteria³⁶ and more than double the 2.3% rate experienced in ACAS.12 Moreover, this complication rate occurred in the hands of surgical teams whose overall performance matched that of the most demanding clinical trial. Indeed, extrapolating the risks and benefits measured in ACAS to the patients with high comorbidity in our study is fraught with uncertainty because many of them would have been excluded from that trial because of their advanced age or poor prognosis.38

Therefore, we believe that physicians should focus more attention on objective assessment of perioperative risk when balancing benefits and harms of carotid endarterectomy among asymptomatic patients. Several validated, generic cardiac risk assessment tools and guidelines are currently available to clinicians.^{33,39,40} In addition, further work should be directed to developing and operationalizing risk assessment tools specific to patients undergoing carotid endarterectomy.^{6,19,20,41-43}

The sequencing of carotid endarterectomy and CABG in patients with coexisting coronary and carotid atherosclerosis is controversial. No controlled trials have addressed this question, and none are likely to be undertaken. The high rates of death and stroke we observed among patients undergoing combined carotid endarterectomy and CABG with skilled surgical teams who demonstrated low complication rates for carotid endarterectomy alone suggest that such a strategy, even in the best hands, is risky.

Our study had certain strengths and limitations. We abstracted detailed clinical information from hospital and outpatient records, which enabled us to classify cases into 1 of 1557 mutually exclusive indications. Most previous studies classified cases into general categories (symptomatic versus asymptomatic). Prior research has also focused largely on the elderly or Medicare beneficiaries with fee-for-service insurance. Our cohort study had no age or insurance exclusions.

Our findings from 6 hospitals in 1 region may not be generalizable to other settings within and outside of the United States. However, the 5 New York hospitals accounted for 20% of all carotid endarterectomies done in that state in 1998, and New York accounted for 8.2% of all carotid endarterectomies performed in the United States in 1998.44,45 This was an observational cohort study of usual care. There was no standard preoperative or postoperative assessment by neurologists during the index admission. The study team did have a neurologist and another physician independently review major neurological complications to confirm their occurrence and classification. Although the ratio of vascular surgeons to neurosurgeons performing carotid endarterectomy in our sample (3.8:1) was similar to the that of the overall statewide ratio (3.5:1), vascular surgeons performed a larger proportion of the procedures in this study than the state average.46 The complication rates we present were not formally risk adjusted. However, we did stratify our analyses by clinical severity groups that national guidelines have identified as being associated with different levels of complications, as well as comorbid illness burden. Caution is also warranted because the complication rates reported in these hospitals were lower than those reported in other observational studies, particularly among asymptomatic patients.^{20-23,42} Finally, although the expert judgments that helped generate the appropriateness ratings are inherently subjective, the internal consistency, reliability, and validity of this methodology are quite good for procedures about which there is a strong evidence base of RCTs.31,47-50 The RCTs rarely provide the level of subgroup analyses needed to inform every indication, so the appropriateness ratings should be seen as a blend of best evidence, informed extrapolation, and expert opinion.

In conclusion, since the large public investment in RCTs of carotid endarterectomy, rates of overuse appear to have fallen dramatically, although they are still significant. There has been a major shift toward operating on asymptomatic patients who have much less to gain from carotid endarterectomy compared with those who are symptomatic. Although overall complication rates among these 6 hospitals were comparable to the benchmark performance of the highly selected RCT sites, the adverse event rates among asymptomatic patients with high comorbid illness burden exceeded recommended thresholds.

Acknowledgments

This study was supported by a research grant from the Agency for Healthcare Research and Quality (RO1 HS09754-01). Dr Halm was supported in part by The Robert Wood Johnson Generalist Physician Faculty Scholars Program. Special thanks go to Patricia Formisano, MPH, for her incomparable management of the project and R. Edward Park, PhD, for his expert assistance. We would like to thank the following individuals for their contribution to this project. National expert panelists: Philip Gorelick, MD; Joseph E. Heiserman, MD; Norman R. Hertzer, MD; Richard L. Hughes, MD; Francis J. Kazmier, MD; Christopher M. Loftus, MD; David Matchar, MD; Malcolm O. Perry, MD; and Thomas S. Riles, MD. Study participants: Albany Medical College: Linda Graca, LPN; Englewood Hospital and Medical Center: Karen Hessler, RN; Long Island Jewish Hospital: Jacqueline Burdis, RN, Robin Gitman, and Maria Verderber, RN; Maimonides Medical Center: Sameh Samy and Rosemary Soldiervo; New York University Medical Center: Ronnie Landis, RN, and Caron Rockman, MD; Mount Sinai School of Medicine: Anna Arreglado, Bernadette Rynne, RN, Virginia Chan, Camille Cohen, RN, Hugh Dai, Wilfredo Gaerlan, Edwin Gravereaux, MD, Chiaki Nakzono, Ying Qiu, Mary Rojas, PhD, Diane Thomas, MD, and George Wang.

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Editorial Comment

How Appropriate Is Carotid Endarterectomy?

Because evidence for the efficacy of many treatments was lacking, methodology to measure appropriateness was developed in the 1980s at RAND to provide a contemporary means of determining if health care interventions were done appropriately; that is, if they were worth doing in specific situations.1 One of the first such studies examined Medicare patients from that era undergoing carotid endarterectomy and found the startling result that two thirds had surgery for uncertain or inappropriate reasons.² Subsequently, the publication of major randomized controlled trials3-5 has provided evidence for the efficacy of endarterectomy in many scenarios to guide practitioners, so now one might expect an improved rate of appropriateness. Indeed, this was demonstrated by Halm et al⁶ in this issue of *Stroke*, where they showed in a population of patients from 6 New York hospitals in 1997-1998 that only 15% of patients were operated on for less than appropriate reasons. Appropriateness can also be used even more directly to improve quality. Recently, Findlay and colleagues7 showed that appropriateness, used in repeated audit cycles involving feedback to the operating surgeons, resulted in marked improvement in both appropriateness and outcomes.

The role of comorbid disease in determining both appropriateness and outcome of endarterectomy is another important result of the current study.⁶ Some indications, especially for asymptomatic cases, were deemed inappropriate because of high comorbidities. This view was borne out by the excess stroke and/or death rate (OR 2.8; CI 1.1 to 7.5, P=0.03) found in asymptomatic cases with high comorbidities. This should caution physicians to consider such issues in case selection and to remember that the patients studied in the clinical trials that demonstrated efficacy were screened to ensure low comorbidity.

The high stroke and/or death rate (10.3%) in those undergoing combined endarterectomy and coronary bypass grafting is a sober reminder that this is a hazardous combination.⁶ There is no randomized controlled trial evidence supporting its use. Furthermore, a recent large review of endarterectomy cases in mid-American states showed an even higher negative outcome rate (17.4%).⁸

One of the most striking results of the current study is that 72.5% of the patients had asymptomatic carotid stenosis.⁶ This reflects the remarkable surge of American enthusiasm for surgery in this setting sparked by publication of the ACAS trial on endarterectomy for asymptomatic stenosis in 1995 and especially the prepublication alert released by the NIH.9 This enthusiasm was apparently not blunted by the fact that the potential gain per patient in terms of the absolute risk reduction in asymptomatic cases is so much lower than in those with symptomatic stenosis \geq 70% (5.9%⁵ versus 15.9%¹⁰ over 5 years) because of their lower baseline risk. The number needed to treat to prevent 1 stroke over 5 years for high-grade symptomatic patients is only 6.3, whereas for asymptomatic cases it is 17. This means that a surgeon must operate on almost 3 asymptomatic patients for every 1 symptomatic case to have an equivalent effect on stroke prevention. In contrast to the American experience, however, recent endarterectomy audits in Canada and Australia have found that only 36% and 31% of cases, respectively, were asymptomatic.7,11

Because of the narrow margin of benefit for asymptomatic patients, the American Heart Association recommended in its guidelines that the 30-day stroke and/or death rate should be below 3% to make this procedure worth doing.¹² That the complication rate in the current study for such cases was only 2.26% is encouraging and shows what might be achieved.⁶ However, it raises the important issue of generalizability. What is the performance in the broader community? The results of the large multistate study showing a complication rate of 4.5% in 7604 patients without carotid symptoms

suggest that there is cause for concern. In fact, the appropriateness of endarterectomy for asymptomatic cases has been controversial,^{13,14} and Canadian guidelines¹⁵ and appropriateness processes⁷ have judged it to be in the uncertain category. It is hoped that the soon-to-be-completed Asymptomatic Carotid Surgery Trial will provide useful guidance.

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