Surgical *Versus* Nonoperative Treatment of Asymptomatic Carotid Stenosis

290 Patients Documented by Intravenous Angiography

NORMAN R. HERTZER, M.D. RICHARD A. FLANAGAN, JR., M.D. PATRICK J. O'HARA, M.D.
EDWIN G. BEVEN, M.D.

From 1980 through 1982, intravenous extracranial digital subtraction angiography (DSA) was performed in 6684 patients at the Cleveland Clinic. Of these, 290 previously unoperated patients had asymptomatic carotid stenosis exceeding 50% of lumen diameter on unequivocal DSA studies. Either the presence or the absence of carotid bruits substantially misrepresented the severity of angiographic stenosis on approximately 30% of sides. Nonoperative management was employed in 195 patients, including 104 (53%) who received antiplatelet therapy, while another group of 95 patients underwent prophylactic carotid endarterectomy. During mean follow-up intervals of 33–38 months, surgical treatment significantly reduced the cumulative incidence of subsequent neurologic events in men ($p = 0.05$). Statistically unconfirmed trends also suggested that carotid endarterectomy tended to prevent late strokes in subsets of patients with >70% stenosis or bilateral carotid lesions. The overall stroke rate for women was higher in the surgical group ($p = 0.03$), in part because of their unusual risk for perioperative complications (9%) in this particular series.

From the Department of Vascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio

FEW TOPICS concerning vascular disease are as controversial as the management of asymptomatic carotid stenosis. The merit of prophylactic carotid endarterectomy is debatable even among surgeons, and scores of references may be cited to support the conflicting opinions that elective surgical treatment either does or does not prevent strokes among patients who never have experienced transient ischemic attacks (TIA).[1] Since the introduction and wide deployment of reliable noninvasive methods to detect asymptomatic extracranial lesions, however, the number of carotid endarterectomies performed throughout the United States has escalated dramatically during the past decade.[2–4] In response to this trend, some prominent neurologists contend that sudden stroke without premonitory TIA is an unusual complication of carotid stenosis and have proposed a prospectively randomized trial of antiplatelet agents as well as surgical treatment in asymptomatic patients.[5–7] Chambers and Norris[7] calculated that such a study must identify a subset of patients with an annual stroke rate in excess of 5% despite medical therapy in order to justify carotid reconstruction.

A number of independent attempts already have been made to clarify the natural history of untreated asymptomatic stenosis. In addition to population surveys in Evans County, Georgia, and the Framingham Study, clinical reports of patients with asymptomatic carotid bruits have suggested that this nonspecific physical finding is associated with higher risk for neurologic complications, myocardial infarction and cardiac mortality than is anticipated within the general population.[8–11] Nevertheless, these and similar bruit studies are open to speculation because of the inconsistent relationship of bruits, carotid stenosis, and subsequent neurologic events.[12,13] Other investigations employing noninvasive blood flow assessment or ultrasound carotid imaging have demonstrated that late TIA and strokes are significantly more common in patients who have objective evidence of high-grade asymptomatic stenosis at the time they entered the follow-up period.[14–20] Despite their convincing data and the presumed accuracy of their noninvasive methods, however, none of these important studies was monitored by cerebral angiography. Unfortunately, angiographic confirmation of the severity of stenosis under observation usually has been restricted to the contralateral bifurcation in series of patients who previously have undergone unilateral carotid endarterectomy, a situation that may not accurately reflect the natural history of untreated asymptomatic stenosis.[21,22]

In selected patients, the quality of intravenous digital subtraction angiography (DSA) is comparable to that of conventional intra-arterial techniques.[23] Since the Cleve-

Reprint requests: Norman R. Hertzer, M.D., The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44106.

Submitted for publication: March 18, 1986.

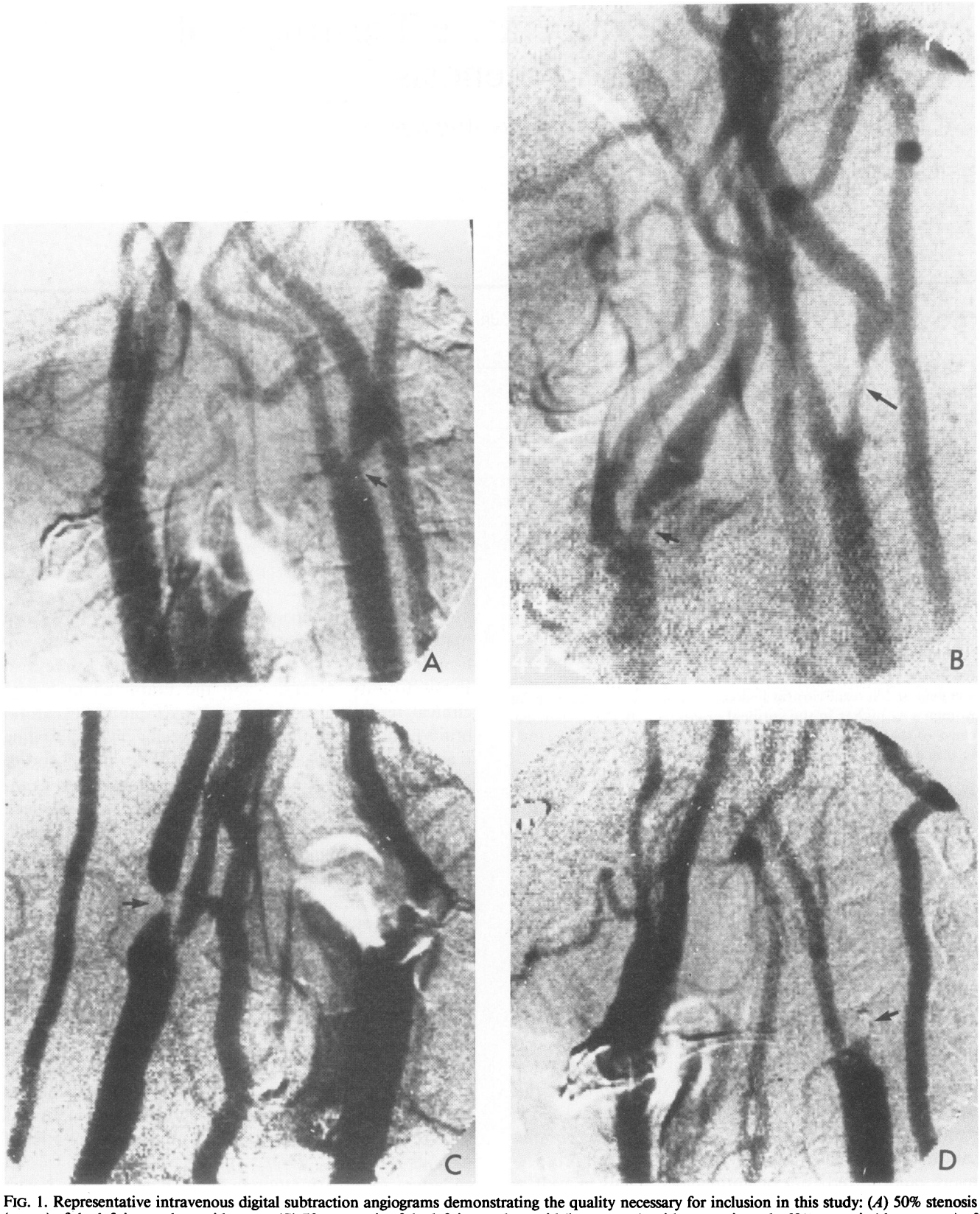

FIG. 1. Representative intravenous digital subtraction angiograms demonstrating the quality necessary for inclusion in this study: (*A*) 50% stenosis (arrow) of the left internal carotid artery; (*B*) 70% stenosis of the left internal carotid (long arrow), with approximately 60% stenosis (short arrow) of the right internal carotid; (*C*) 90% stenosis (arrow) of the right internal carotid in conjunction with (*D*) left internal carotid occlusion (arrow).

land Clinic has provided the facilities to test prototype DSA equipment for several years, considerable experience with intravenous contrast imaging of the carotid arteries has been accumulated at this center. To compare the late results of nonoperative and surgical treatment of carotid stenosis documented by some form of angiography, we have critically reviewed all carotid DSA examinations performed during the study period of 1980–1982. Data concerning 211 symptomatic patients who were evaluated because of previous TIA or strokes have been presented elsewhere.[24] The present report is a review of 290 patients with asymptomatic carotid stenosis confirmed by unequivocal DSA studies.

Material and Methods

From 1980 to 1982, the Cleveland Clinic maintained the first, if not the only, DSA unit in northeastern Ohio. During this interval, 6684 patients underwent intravenous extracranial DSA examinations, and many then returned to their referring physicians for subsequent management. For the purpose of this report, each of these DSA studies was personally reviewed, and complete follow-up data were obtained from patients, their surviving family members, or physicians for all candidates who met the following requirements:

(1) The extracranial DSA was unquestionably diagnostic and demonstrated at least 50% stenosis of one or both common carotid or internal carotid arteries.

(2) There was no history of prior cerebrovascular operations.

(3) Any carotid endarterectomy following the DSA examination was performed by one of the authors. Patients who required simultaneous carotid reconstruction and coronary bypass were excluded.

(4) Complete late information was available (none lost to follow-up).

No DSA was accepted unless it demonstrated both extracranial carotid systems clearly enough to be comparable to standard angiography (Fig. 1). Under these strict criteria, a total of 290 patients qualified for the study, including 195 who received nonoperative management following their DSA examinations and 95 others who underwent carotid endarterectomy. While this investigation is neither prospective nor randomized in the traditional sense, late information was obtained for all patients who satisfied the entrance requirements, and their treatment was as random as the advice of the many family physicians, internists, neurologists, and surgeons who were responsible for it.

Clinical Features

A summary of several clinical features is presented in Table 1. The 187 men (64%) and the 103 women (36%) comprising the two treatment cohorts ranged from 39 to 90 years of age (mean: 66 years). None had experienced hemispheric or vertebrobasilar TIA or strokes preceding DSA evaluation. Hypertension requiring medical management was present in 188 patients (65%), and 56 patients (19%) were insulin-dependent diabetics. The follow-up interval for all 290 patients presently extends to 54 months (mean: 34 months).

TABLE 1. *Comparison of Clinical Features between the Nonoperated and Surgical Groups*

Clinical Features	No Operation No.	No Operation %	Carotid Endarterectomy No.	Carotid Endarterectomy %
Patients	195	100	95	100
Men	124	64	63	66
Women	71	36	32	34
Age				
Range	39–90		43–85	
Mean	67		64	
Risk Factors				
Hypertension	121	62	67	71
Diabetes mellitus	37	19	19	20
Follow-up interval (mos.)				
Range	1–53		0–54	
Mean	33		38	

Angiographic Carotid Disease

The severity of extracranial carotid disease demonstrated by DSA is described in Table 2. The maximum degree of angiographic stenosis was 50–69% of lumen di-

TABLE 2. *Maximum Severity of Carotid Disease Documented by Intravenous Digital Subtraction Angiography in the Nonoperated and Surgical Groups*

Angiographic Findings	No Operation (N = 195) No.	No Operation (N = 195) %	Carotid Endarterectomy (N = 95) No.	Carotid Endarterectomy (N = 95) %
Carotid stenosis				
50–69%	90	46	4	4
70–89%	51	26	36	38
>90%	19	10	48	51
Occlusion	35	18	7	7
Atheromatous ulceration				
None	114	58	68	72
Unilateral	68	35	21	22
Bilateral	13	7	6	6

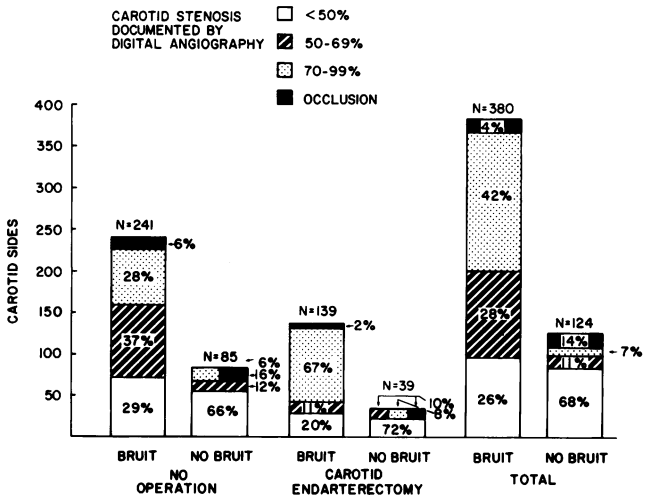

FIG. 2. Graphic correlation of asymptomatic carotid bruits and digital angiographic findings in the 252 patients who had bruits.

ameter in 94 patients (32%), 70–89% of the diameter in 87 (30%), and >90% of the diameter in 67 (23%). Complete occlusion of the common carotid or internal carotid artery was demonstrated in another 42 patients (14%). Conceding the fact that intimal erosion often may escape detection by intravenous DSA, unilateral atheromatous ulceration was identified in 89 patients (31%), and bilateral changes were interpreted in another 19 (7%).

Although each angiographic subset was represented in both treatment cohorts, several differences in the composition of the nonoperated and surgical groups could be confirmed by statistical analysis. Intermediate degrees (50–69%) of stenosis ($p = 4.9 \times 10^{-15}$, Fisher exact test) and documented internal carotid occlusions ($p = 0.02$) were more common among patients receiving nonoperative therapy. In comparison, the incidence of subtotal lesions exceeding 90% stenosis was higher among patients selected for carotid endarterectomy ($p = 8.6 \times 10^{-14}$).

Carotid Bruits

The presence of asymptomatic carotid bruits clearly comprised the most common indication for DSA investigation in this series. A total of 252 (87%) of the 290 patients had bruits, including 163 (83%) of the nonoperated group and 89 (94%) of those who underwent carotid endarterectomy. Bruits were absent in only 38 patients (13%), and intravenous carotid imaging was obtained in most of these patients because they had other evidence of generalized vascular disease.

Figure 2 illustrates the correlation between carotid bruits and angiographic findings in the 252 patients who had bruits on physical examination. While carotid bruits reflected >50% angiographic stenosis on 70% of sides, the remaining 30% of bruit sides were associated either with lesser degrees of involvement (26%) or internal carotid occlusions (4%). Conversely, DSA revealed >50% stenosis on 22 (18%) of the sides without bruits, and another 18 silent sides (14%) had internal carotid occlusions. These data support two preliminary conclusions regarding the potential risk for neurologic complications represented by carotid bruits in this series: (1) subsequent TIA or strokes would not be anticipated on 26% of bruit sides having trivial angiographic involvement; and (2) neurologic events would not be inappropriate if they occurred on 32% of silent sides having >50% stenosis or internal carotid occlusions.

Management

Of the 195 patients in the nonoperated group, 104 (53%) were prescribed and complied with antiplatelet therapy (aspirin and/or dipyridamole), and nine others (5%) received formal anticoagulation with Coumadin®. No specific medical treatment was recommended for the remaining 82 patients (42%). A total of 116 carotid endarterectomies (21 bilateral) were performed in the 95 patients who underwent surgical treatment, including seven contralateral procedures in the subset with unilateral internal carotid occlusions. In addition, empiric medical management was continued throughout the follow-up period with the use of antiplatelet agents in 74 patients (78%) and with Coumadin anticoagulation in one.

Results

Surgical Complications

One (1.1%) of the 95 patients in the surgical group died with a postoperative myocardial infarction. Four others (4.2%) experienced operative strokes following 116 carotid endarterectomies (3.4%), and each of these events is entered into all appropriate life table calculations concerning the results of surgical treatment in this report. In comparison, 11 iatrogenic strokes (2.4%) occurred within the complete series of 466 carotid procedures performed by the authors for asymptomatic carotid stenosis during the same study period of 1980–1982, a figure that includes patients who received simultaneous myocardial revascularization (unpublished data).

Late Survival

During a mean follow-up interval of 35 months, there have been 43 late deaths (22%) in the nonoperated group and 13 late deaths (14%) in the surgical group. Late mortality was attributed to cardiac events in 30 patients (54%), to cancer in eight (14%), to fatal strokes in four (7%), and to all other causes in 14 (25%). Life table data were calculated according to Cutler and Ederer[25] and were analyzed for statistical significance using the method described by Lee and Desu.[26] Actuarial survival for men, women,

and the entire series is depicted in Figure 3, with 140 (48%) of the 290 patients eligible for consideration at least through 4 years. Despite one death among eight remaining patients in the final year of observation, overall 5-year survival in the surgical group (mean age: 64 years) was superior ($p = 0.01$) to nonoperated patients (mean age: 67 years). This difference attained significance in women ($p = 0.05$) but not in men ($p = 0.07$).

Additional comparisons suggested that associated coronary artery disease (CAD) had a substantial influence on late survival after carotid enderterectomy. Cumulative 5-year survival was 80% for 21 patients receiving surgical treatment who had no evidence of CAD either by history or by electrocardiographic findings. Another 38 patients in the surgical group were suspected to have CAD by these criteria, and 36 others have at some time required myocardial revascularization. Cumulative survival for these two respective subsets was 48% and 94%, but this difference was not statistically significant ($p = 0.1$).

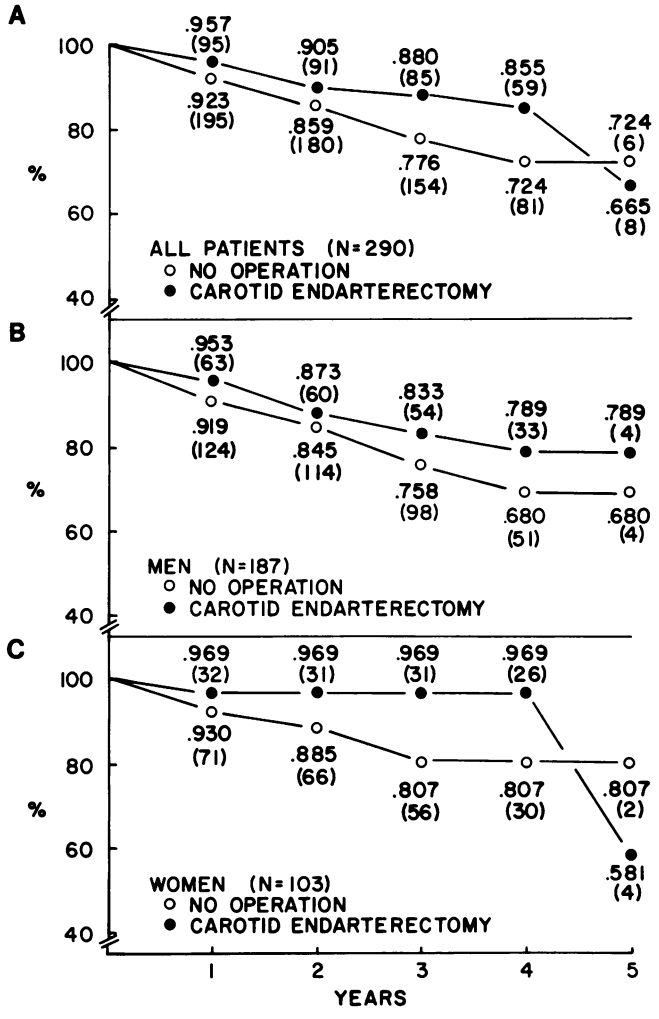

FIG. 3. Five-year cumulative survival for men, women, and the entire series. (Numbers in parentheses indicate patients who are still eligible for consideration.)

TABLE 3. *Comparison of the Crude Incidence of Late Stroke Occurring in the Nonoperated and Surgical Groups*

	No Operation (N = 195)		Carotid Endarterectomy (N = 95)	
Late Stroke	No.	%	No.	%
Total	18	9	7	7
Men	16	13	2	3
Women	2	3	5	16
Age				
Range	48–90		43–71	
Mean	65		62	
Risk factors				
Hypertension	10	8	6	9
Diabetes mellitus	4	11	3	16
Follow-up interval (mos.)				
Range	0–43		0–36	
Mean	15		11	

Neurologic Events

Crude incidence. Late neurologic events thus far have occurred in 17% of the 195 patients in the nonoperated group (16 TIA, 18 strokes) and, including four operative deficits, in 12% of the 95 patients who underwent carotid endarterectomy (4 TIA, 7 strokes). All but one of the 45 events were associated with hemispheric motor and/or sensory deficits or with monocular retinal ischemia, and 27 (79%) of the 34 patients who experienced neurologic symptoms during nonoperative management had their complications on the same side as uncorrected >50% carotid stenosis. A summary of the crude incidence of late stroke in both treatment cohorts is presented in Table 3. Five of the 18 strokes in the nonoperated group occurred at the time of open heart procedures or resection of a thoracoabdominal aortic aneurysm, and since the etiology of such events could be completely unrelated to incidental carotid stenosis, none of these five patients has been considered in the life table calculations comprising the remainder of this report.

Cumulative data. Figure 4 illustrates cumulative freedom from all neurologic events (TIA and strokes) and the incidence of late stroke in the nonoperated and surgical groups. During the 5 years following carotid endarterectomy, 91% of men have remained asymptomatic, and their cumulative stroke rate was only 4%. In comparison, 32% of men in the nonoperated group have experienced either transient or permanent deficits ($p = 0.05$), and nearly 18% have sustained late strokes ($p = 0.07$). Conversely, freedom from symptoms was not enhanced by surgical treatment in women. In fact, three (9.4%) of the 32 women who underwent carotid reconstruction had

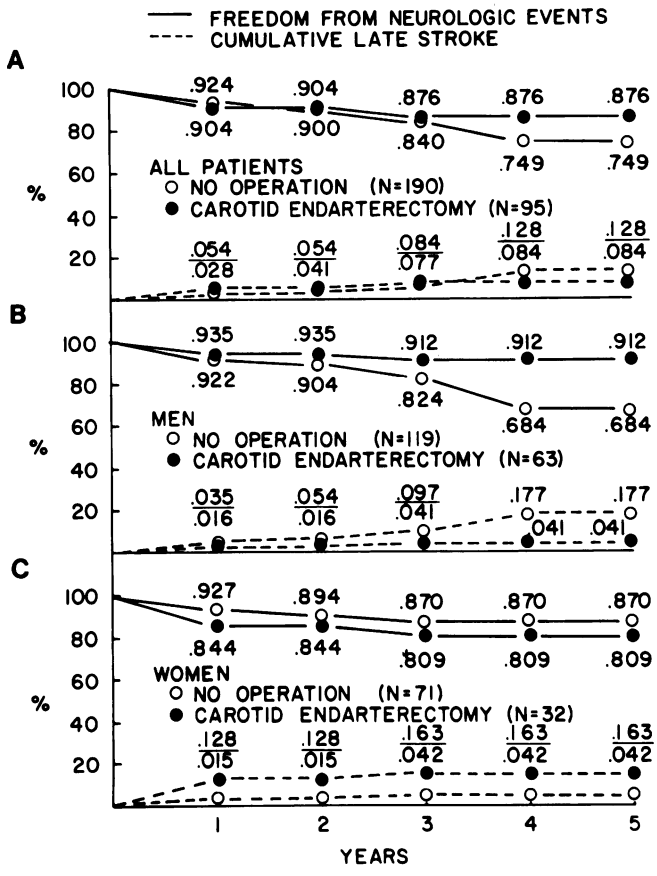

FIG. 4. Cumulative neurologic results for men, women, and the entire series.

iatrogenic deficits, and their 5-year stroke rate (16%) thus exceeded stroke risk in the nonoperated group ($p = 0.03$).

Clinical outcome is displayed according to age in Figure 5. Surgical intervention had no apparent effect on the incidence of TIA or stroke among 132 patients ranging from 60 to 69 years of age. In smaller subsets of patients less than 60 and over 70 years of age, 95% of those in the surgical group remained asymptomatic, and only 4% had strokes within 5 years of their operations. Although symptoms occurred in approximately 30% and strokes in 9–12% of patients of similar ages in the nonoperated group, none of these differences achieved statistical significance ($p \geq 0.09$).

Carotid stenosis. Since an unequivocal DSA examination was an entry requirement for this study, subsets of patients who might be at special risk for neurologic complications could be classified according to discrete angiographic criteria. In Figure 6, late results are stratified according to the maximum severity of carotid stenosis that either was corrected by endarterectomy or was placed under observation. This illustration represents 157 of the 190 follow-up patients in the nonoperated group because the remaining 33 only had stable internal carotid occlusions rather than patent, stenotic lesions.

A total of 96 patients had angiographic stenosis compromising the internal carotid lumen by 50–69%, but only eight received surgical management. While adequate statistical analysis was precluded by the small size of this subset, 84% of comparable nonoperated patients have remained asymptomatic, and late strokes have occurred in but 4%. Eighty-seven of the 95 patients in the surgical group underwent carotid endarterectomy to correct either 70–89% or >90% stenosis. The cumulative incidence of neurologic symptoms and late strokes in each of these two subsets was 8–12% and 7%, respectively. In comparison, 33–51% of nonoperated patients with higher grades of angiographic stenosis have experienced some type of neurologic complications, and 24–33% have had completed strokes. Nevertheless, none of these differences has yet attained statistical significance ($p \geq 0.23$).

Bilateral carotid involvement. The composite risk of bilateral carotid disease is illustrated in Figure 7. The nonoperated group contains a total of 33 patients who had internal carotid occlusions on one side, including 22 with trivial contralateral carotid changes (Fig. 7A) and 11 with >50% contralateral stenosis (Fig. 7B). Equivalent cumulative results were obtained among patients having unilateral lesions in both treatment cohorts. In the presence of bilateral >50% stenosis, 36% of patients in the

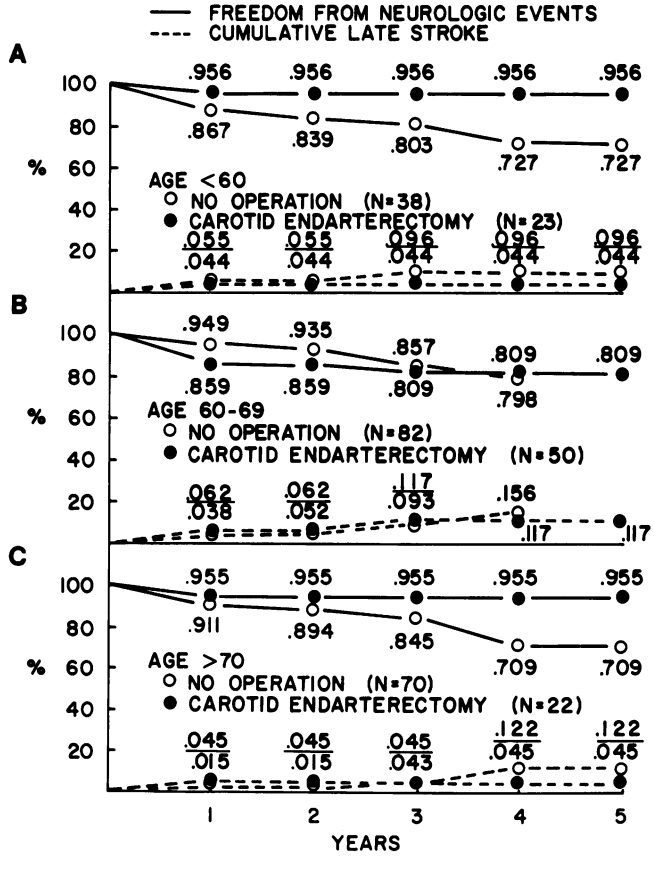

FIG. 5. Cumulative neurologic results according to age.

nonoperated group eventually experienced neurologic symptoms, and 20% have had completed strokes. In comparison, 91% of those with bilateral carotid disease in the surgical group have remained asymptomatic, and the 5-year stroke rate in this subset was only 6%. None of these differences, however, was statistically significant ($p \geq 0.08$).

Other factors. Of the 190 patients in the nonoperated group for whom cumulative neurologic results were calculated, 111 received antiplatelet therapy (N = 102) or Coumadin anticoagulation (N = 9), while 79 had no medical treatment (Fig. 8A). Although the overall incidence of late neurologic events was similar in both subsets, 21% of untreated patients sustained strokes in comparison to 7% of those under some form of medical management. Neurologic events occurred in 34% and strokes in 15% of patients who had angiographic evidence of atheromatous ulceration, but none of these features attained statistical significance.

For several years, two angiographic criteria generally have been employed to select asymptomatic patients for prophylactic carotid reconstruction at the Cleveland Clinic: (1) >70% stenosis of either common or internal carotid artery; (2) >50% stenosis in conjunction with

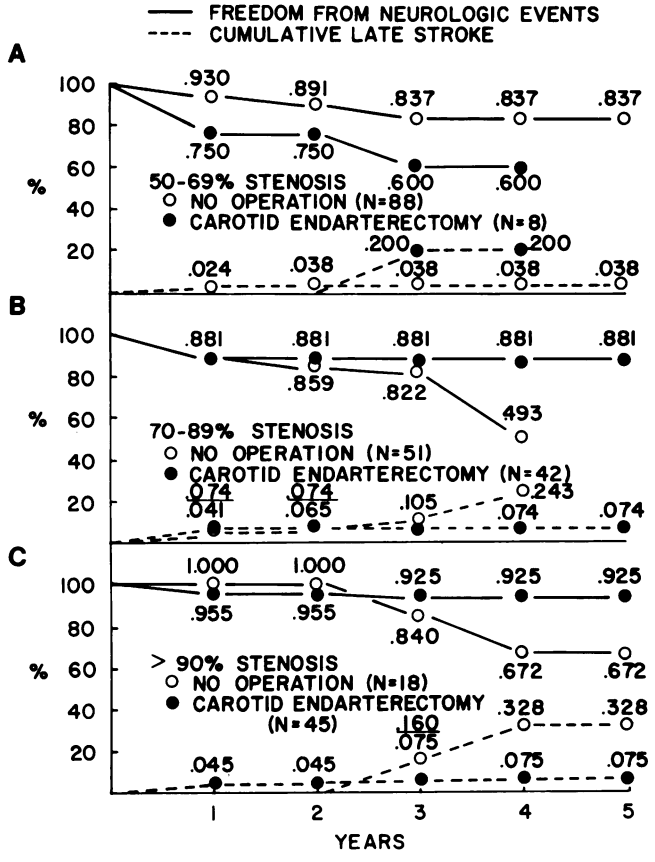

FIG. 6. Cumulative neurologic results according to the maximum severity of documented carotid stenosis.

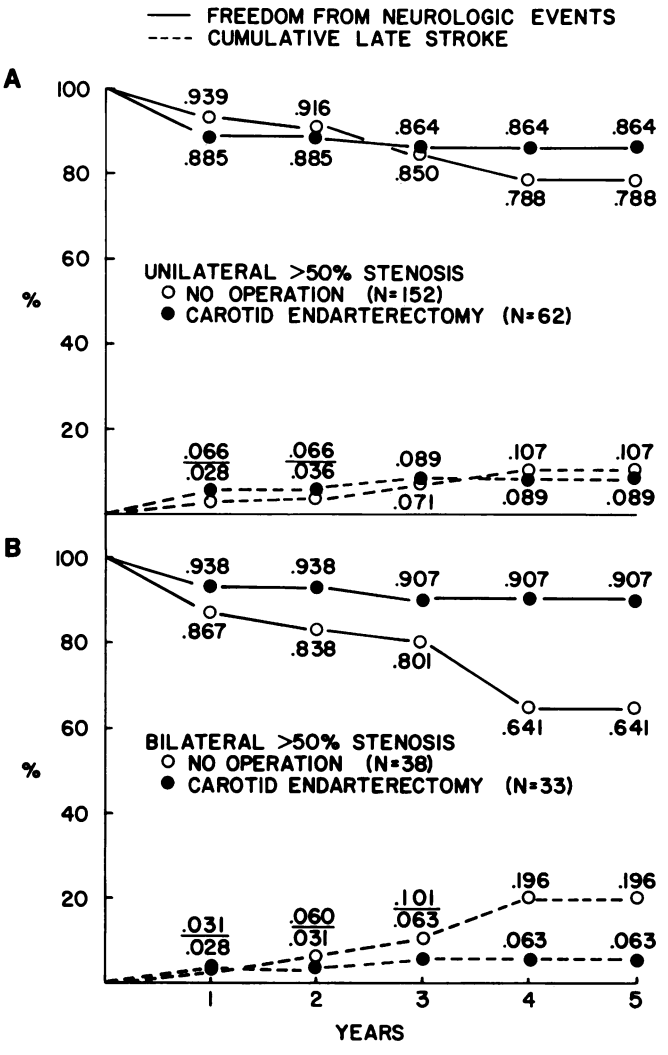

FIG. 7. Cumulative neurologic results for unilateral and bilateral carotid stenosis.

contralateral internal carotid occlusion. In this context, 106 of the patients in the nonoperated cohort did not have a surgical lesion at the time of their original DSA studies, while the remaining 84 had traditionally surgical disease for which carotid endarterectomy was not performed (Fig. 8B). During the 5 years comprising the follow-up investigation, 86% of the subset without surgical lesions have remained free of symptoms, and only 5% have had subsequent strokes. In comparison, neurologic events have occurred in 38% of the 84 patients with uncorrected surgical lesions, and 22% of this subset have experienced permanent strokes. At the present time, however, neither of these apparent trends is statistically significant ($p \geq 0.13$).

Discussion

Experienced surgeons recognize that stroke is not an inevitable outcome of carotid stenosis and that many

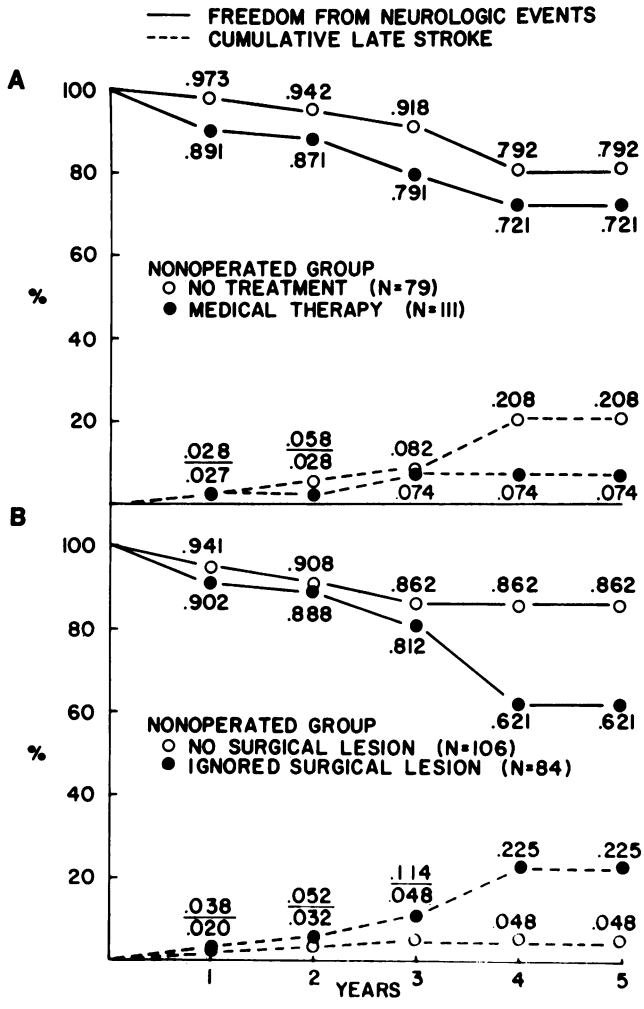

FIG. 8. Cumulative neurologic results in the nonoperated group according to whether medical therapy (antiplatelet agents or formal anticoagulation) was administered and whether a traditional surgical lesion was ignored (see text).

asymptomatic patients would never have neurologic complications even if prophylactic operations were not performed. Encouraged by the safety and successful late results of carotid endarterectomy for symptomatic lesions, however, most vascular centers in the United States offer surgical treatment to selected asymptomatic patients with severe carotid stenosis under the fundamental presumption that the risks of its natural history surpass those associated with elective reconstruction. Although surprisingly little information is available concerning the course of patients with asymptomatic lesions who are placed under observation or medical treatment, at least two recent reports indicate that the 5-year cumulative stroke rate for those having objective evidence of ≥50% carotid stenosis exceeds 20%. In a heterogeneous group of 125 peripheral vascular patients with asymptomatic bruits and/or abnormal Doppler ultrasound examinations, Barnes et al.[14] discovered that strokes occurred in 22% and TIA in another 34% during follow-up intervals of 2–44 months (mean: 22 months). Using similar diagnostic methods, Moore et al.[19] determined that 21% of patients with ≥50% stenosis sustained permanent deficits within 5 years and found that only one of the 36 strokes in this study was preceded by a herald TIA.

The composite 5-year incidence of completed strokes or delayed surgical intervention for TIA also was 22% among patients receiving nonoperative treatment in our series, and our data further suggest that stroke risk was concentrated among those who were documented to have at least 70% unilateral stenosis or bilateral 50% carotid involvement by digital angiography. The 5-year cumulative stroke rate ranged from 20 to 33% for unoperated patients in these specific angiographic subsets, and such results are consistent with the repeated observation that high-grade carotid lesions often undergo subintimal hemorrhage or plaque necrosis, which may precipitate either cerebral microembolization or sudden occlusion of the internal carotid artery.[27–30] Late strokes occurred in 22% of patients in the nonoperated group who otherwise had sufficient extracranial disease to merit traditionally their consideration as candidates for surgical treatment at this center. In comparison, the 5-year stroke rate in the surgical group was 8%, a figure that is identical to our previous experience with carotid endarterectomy.[31] Although several of the trends established in this study have not yet attained statistical significance, they clearly suggest that some asymptomatic lesions simply are more dangerous than others. Provided the severity of carotid stenosis is objectively documented, however, its risk appears to follow a logical pattern.

The incidence of perioperative stroke (9.4%) among 32 women in the surgical group does not accurately represent the complication rate (2.4%) for all 466 asymptomatic patients who underwent carotid reconstruction at the Cleveland Clinic from 1980 to 1982. Nevertheless, early results obviously influenced the late success of carotid reconstruction in this limited subset, and it must be conceded that an unacceptable operative risk would seriously jeopardize the benefit of surgical management if it were the rule rather than the exception. In two publicized community surveys, the combined morbidity and mortality of carotid endarterectomy was found to be 21% in Springfield, Illinois, and 9.5% in Cincinnati.[32,33] While those opposed to surgical treatment of asymptomatic extracranial disease have interpreted these data to reflect the results of carotid endarterectomy throughout the United States, similar reports have demonstrated that the combined risk of elective surgical management ranges from 2 to 4.4% in Cleveland, San Francisco, and Allentown, Pennsylvania.[34–36] Obviously, only one equitable conclusion may be drawn from such studies: the safety of carotid endarterectomy *must* be established at every hospital in which

it is conducted. Perhaps the most serious obligation of any prospectively randomized investigation regarding carotid endarterectomy for asymptomatic stenosis will be to measure the intrinsic merit of the operation, not the surgeons selected to perform it.

Acknowledgments

Marlene Goormastic, M.P.H., Department of Biostatistics and Epidemiology, and Miss Geri Locker, Research Division, performed the statistical analysis. Mrs. Frances Federico assisted with preparation of the manuscript.

References

1. Barnes RW, Archie JP Jr, Batson RC. Advocates in vascular controversies: prophylactic carotid endarterectomy. Surgery 1984; 95:739–748.
2. Dyken ML, Pokras R. The performance of endarterectomy for disease of the extracranial arteries of the head. Stroke 1984; 15:948–950.
3. Rutkow IM, Ernst CB. Vascular surgical manpower: Too much? Enough? Too little? Unknown? Arch Surg 1982; 117:1537–1542.
4. Rutkow IM, Ernst CB. An analysis of vascular surgical manpower requirements and vascular surgical rates in the United States. Journal of Vascular Surgery 1986; 3:74–83.
5. Barnett HJM, Plum F, Walton JN. Carotid endarterectomy: an expression of concern. Stroke 1984; 15:941–943.
6. Warlow C. Carotid endarterectomy: does it work? Stroke 1984; 15: 1068–1076.
7. Chambers BR, Norris JW. The case against surgery for asymptomatic carotid stenosis. Stroke 1984; 15:964–967.
8. Heyman A, Wilkinson WE, Heyden S, et al. Risk of stroke in asymptomatic persons with cervical arterial bruits: a population study in Evans County, Georgia. N Engl J Med 1980; 302:838–841.
9. Wolf PA, Kannel WB, Sorlie P, McNamara P. Asymptomatic carotid bruit and risk of stroke. JAMA 1981; 9245:1442–1445.
10. Thompson JE, Patman RD, Talkington CM. Asymptomatic carotid bruit: long-term outcome of patients having endarterectomy compared with unoperated controls. Ann Surg 1978; 188:308–316.
11. Cooperman M, Martin EW, Evans WE. Significance of asymptomatic carotid bruits. Arch Surg 1978; 113:1339–1340.
12. David TE, Humphries AW, Young JR, Beven EG. A correlation of neck bruits and arteriosclerotic carotid arteries. Arch Surg 1973; 107:729–731.
13. Riles TS, Lieberman A, Kopelman I, Imparato AM. Symptoms, stenosis, and bruit: interrelationships in carotid artery disease. Arch Surg 1981; 116:218–220.
14. Barnes RW, Nix ML, Sansonetti D, et al. Late outcome of untreated asymptomatic carotid disease following cardiovascular operations. Journal of Vascular Surgery 1985; 2:843–848.
15. Busuttil RW, Baker D, Davidson RK, Machleder HI. Carotid artery stenosis: hemodynamic significance and clinical course. JAMA 1981; 245:1438–1441.
16. Cullen SJ, Correa MC, Calderon-Ortez M, et al. Clinical sequelae in patients with asymptomatic carotid bruits. Circulation 1983; 68(suppl II):83–87.
17. Kartchner MM, McRae LP. Noninvasive evaluation and management of the "asymptomatic" carotid bruit. Surgery 1977; 82: 840–847.
18. Moore DJ, Sheehan MP, Kolm P, et al. Are strokes predictable with noninvasive methods: a five-year follow-up of 303 unoperated patients. Journal of Vascular Surgery 1985; 2:654–660.
19. Moore DJ, Miles RD, Gooley NA, Sumner DS. Noninvasive assessment of stroke risk in asymptomatic and nonhemispheric patients with suspected carotid disease: five-year follow-up of 294 unoperated and 81 operated patients. Ann Surg 1985; 202:491–504.
20. Roederer GO, Langlois YE, Jager KA, et al. The natural history of carotid arterial disease in asymptomatic patients with cervical bruits. Stroke 1984; 15:605–613.
21. Humphries AW, Young JR, Santilli PH, et al. Unoperated, asymptomatic significant carotid artery stenosis: a review of 182 instances. Surgery 1976; 80:695–698.
22. Durward QJ, Ferguson GG, Barr HWK. The natural history of asymptomatic carotid bifurcation plaques. Stroke 1982; 13:459–464.
23. Connolly JE, Brownell DA, Levine EF, McCart M. Accuracy and indications of diagnostic studies for extracranial carotid disease. Arch Surg 1985; 120:1229–1232.
24. Hertzer NR, Flanagan RA Jr, Beven EG, O'Hara PJ. Surgical versus nonoperative treatment of symptomatic carotid stenosis: 211 patients documented by intravenous angiography. Ann Surg 1986; 204:154–162.
25. Cutler SJ, Ederer F. Maximum utilization of the life table method in analyzing survival. J Chronic Dis 1958; 8:699–712.
26. Lee ET, Desu MM. A computer program for comparing K samples with right-censored data. Comput Programs Biomed 1972; 2: 315–321.
27. Imparato AM, Riles TS, Mintzer R, Baumann G. The importance of hemorrhage in the relationship between gross morphologic characteristics and cerebral symptoms in 376 carotid artery plaques. Ann Surg 1983; 197:195–203.
28. Lusby RJ, Ferrell LD, Ehrenfeld WK, et al. Carotid plaque hemorrhage: its role in production of cerebral ischemia. Arch Surg 1982; 117:1479–1488.
29. O'Donnell TF Jr, Erdoes L, Mackey WC, et al. Correlation of B-mode ultrasound imaging and arteriography with pathologic findings at carotid endarterectomy. Arch Surg 1985; 120:443–449.
30. Johnson JM, Kennelly MM, Decesare D, et al. Natural history of asymptomatic carotid plaque. Arch Surg 1985; 120:1010–1012.
31. Hertzer NR, Arison R. Cumulative stroke and survival ten years after carotid endarterectomy. Journal of Vascular Surgery 1985; 2:661–668.
32. Easton JD, Sherman DG. Stroke and mortality rate in carotid endarterectomy: 228 consecutive operations. Stroke 1977; 8:565–568.
33. Brott T, Thalinger K. The practice of carotid endarterectomy in a large metropolitan area. Stroke 1984; 15:950–955.
34. Hertzer NR, Avellone JC, Farrell CJ, et al. The risk of vascular surgery in a metropolitan community. Journal of Vascular Surgery 1984; 1:13–21.
35. Krupski WC, Effeney DJ, Goldstone J, et al. Carotid endarterectomy in a metropolitan community: comparison of results for three institutions. Surgery 1985; 98:492–498.
36. Slavish LG, Nicholas GG, Gee W. Review of a community hospital experience with carotid endarterectomy. Stroke 1984; 15:956–959.