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Perioperative and Late Stroke Rates of Carotid Endarterectomy Contralateral to Carotid Artery Occlusion

Results From a Randomized Trial

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Background and Purpose—Several previous studies have reported the benefits of carotid endarterectomy (CEA) contralateral to carotid occlusion with mixed results, but none of these were randomized except for the North American Symptomatic Carotid Endarterectomy Trial. The purpose of this study was to analyze the results of surgery in patients with contralateral carotid artery occlusion in a randomized trial in which randomization was done according to the method of closure.

Methods—In 399 CEAs (357 patients) that were randomized into primary closure versus patching, 49 had contralateral occlusion. Strokes were designated as ipsilateral if they arose from the same CEA side and contralateral if they arose from the occluded side. A Kaplan-Meier analysis was used to estimate perioperative strokes and stroke-free survival in patients with contralateral occlusion (group A) versus those without contralateral occlusion (group B).

Results—Demographic characteristics and mean follow-up for both groups were similar (group A, 40 months; group B, 33 months). Group A had a higher incidence of contralateral transient ischemic attacks (TIAs) (12.2% versus 0.9%; $P<0.0001$), contralateral strokes (2% versus 0%; $P=0.025$), and combined contralateral TIAs/strokes (14.3% versus 0.9%; $P<0.0001$). The rates for perioperative and all strokes (operative and late) were 2% and 4.1% (2% ipsilateral and 2% contralateral strokes) for group A and 2.9% and 3.4% (all ipsilateral) for group B ($P=0.60$ and 0.85 , respectively). The rates for perioperative and all TIAs were 0% and 14.3% for group A versus 2.6% and 6.3% for group B ($P=0.918$ and $P=0.08$, respectively). The rates for perioperative and all neurological events (TIA and stroke) were 2% and 18.4% for group A and 5.4% and 9.7% for group B ($P=0.27$ and 0.113 , respectively). The cumulative stroke-free survival rates at 5 years were 84% for group A and 77% for group B ($P>0.1$). The cumulative stroke-free survival rates at 5 years for symptomatic and asymptomatic patients in group A and group B were also similar. The perioperative and late deaths were similar for both groups (group A, 8%; group B, 14%).

Conclusions—Group A had a higher incidence of contralateral TIAs and strokes than group B; however, the perioperative and all late stroke rates and survival rates of CEA were comparable in patients with and without contralateral occlusion. (*Stroke*. 2000;31:1566-1571.)

Key Words: carotid artery occlusion ■ carotid endarterectomy

Indications for carotid endarterectomy (CEA) for patients with carotid artery stenosis (symptomatic and asymptomatic) have been firmly established.^{1,2} However, patients with a contralateral occluded carotid artery have been considered high risk. Initial controversy existed regarding the benefit of CEA in patients with a contralateral occluded carotid artery. Reports before 1986 suggest that CEA in these patients involves higher morbidity.^{3,4} However, more recently, both retrospective and prospective studies have reported the benefits of CEA in these patients and confirmed that the indications for CEA should be similar.⁵⁻¹⁰ None of these studies were randomized except for the North American

Symptomatic Carotid Endarterectomy Trial (NASCET), which concluded that an occluded contralateral carotid artery significantly increased the risk of stroke associated with a severely stenosed ipsilateral carotid artery.¹¹

Therefore, the purpose of this study was to analyze results of surgery in patients with contralateral carotid artery occlusion in a randomized trial in which randomization was done according to the method of closure.

Subjects and Methods

In 399 CEAs (357 patients) that were randomized into primary closure versus patching, 49 had contralateral carotid occlusion.

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TABLE 1. Demographic Characteristics/Risk Factors and Indications for CEA

	Group A	Group B
No. of CEA	49	350
Sex		
Male	33 (67%)	187 (53%)
Female	16 (33%)	163 (47%)
Mean age (range), y	66.8 (41 to 88)	68.3 (35 to 90)
Smoking	29 (59%)	204 (58%)
Coronary artery disease	26 (53%)	207 (59%)
Hypertension	35 (71%)	274 (78%)
Diabetes mellitus	11 (22%)	88 (25%)
Mean preoperative cholesterol, mg/dL	209	218
Mean preoperative triglycerides, mg/dL	208	236
Preoperative antiplatelet medication	36 (73%)	253 (72%)
Mean diameter of ICA, mm	0.56	0.53
Indications for CEA		
Symptomatic (TIA/stroke)	24 (49%)	183 (52%)
Asymptomatic (and nonhemispheric symptoms)	25 (51%)	167 (48%)
No. with primary closure	17 (35%)	118 (34%)
No. with patching	32 (65%)	232 (66%)

These patients were asked to participate in this prospective randomized trial of CEA with primary closure versus polytetrafluoroethylene patching (W.L. Gore & Associates, Inc) versus vein patch closure, which was approved by the Institutional Review Board of the institution. Before surgery, all patients underwent carotid color duplex ultrasound and angiographic studies to determine preoperative stenoses. Preoperative risk factors including smoking, diabetes mellitus, hypertension, and coronary artery disease were determined for each patient, along with the use of preoperative antiplatelet therapy. Indications for surgery were categorized into hemispheric transient ischemic attack (TIA) symptoms, amaurosis fugax, hemispheric strokes, nonhemispheric TIA symptoms (classified with asymptomatic stenosis), and asymptomatic carotid bruits.

Randomization included 135 primary closures, 134 polytetrafluoroethylene patches, and 130 vein patch closures. All surgeries were done under general anesthesia with routine shunting.

All patients were administered aspirin therapy (325 mg daily within 24 hours after the operation). Details of the study protocol, patient characteristics, and operative techniques have been described previously.¹²

On the basis of their angiographic/duplex data, patients were divided into 2 groups. Group A (49 CEAs) consisted of patients who

TABLE 3. Perioperative and All Neurological Events and Mortality

	Group A (49)	Group B (350)	P
Perioperative TIAs	0	9 (2.6%)	0.918
All TIAs	7 (14.3%)	22 (6.3%)	0.084
Perioperative strokes	1 (2%)	10 (2.9%)	0.599
All strokes	2 (4.1%)	12 (3.4%)	0.85
Perioperative TIAs and strokes	1 (2%)	19 (5.4%)	0.269
All TIAs and strokes	9 (18.4%)	34 (9.7%)	0.113
Perioperative mortality	0	4 (1.1%)	>0.95
All mortality (perioperative and late)	4 (8%)	48 (13.7%)	0.393

underwent CEAs for significant ipsilateral internal carotid artery (ICA) stenosis (>50%) with a known contralateral ICA occlusion. Group B (350 CEAs) consisted of patients who underwent CEA of significant ipsilateral ICA stenosis without a contralateral occlusion. Both groups were similar in demographic characteristics and number of patching. Within each group, patients were separated into symptomatic (hemispheric TIA, amaurosis fugax, or stroke) versus asymptomatic subgroups. Strokes or TIAs were designated as ipsilateral if they arose from the same CEA side or contralateral if they arose from the occluded side.

Postoperative Follow-Up and Surveillance Protocol

Patients underwent clinical follow-up and immediate postoperative color duplex ultrasound scanning, which was repeated at 30 days, 6 months, 12 months, and every year thereafter with an ATL HDI system 3000 (Advanced Technology Laboratory, Inc). Reportable complications including death, TIA, stroke, and asymptomatic occlusive events were determined in accordance with the North American Chapter of the International Society of Cardiovascular Surgery/Society for Vascular Surgery Ad Hoc Suggested Standard for Reports Dealing with Cerebrovascular Disease.¹³

Statistical Analysis

Comparative data between groups A and B were evaluated with χ^2 analysis, Fisher's exact test, or the Student's *t* test. Cumulative life-table analyses were performed to assess stroke-free and late

TABLE 2. All Neurological Events: Ipsilateral vs Contralateral

	Group A (n=49)	Group B (n=350)	P
All TIAs	7 (14.3%)	22 (6.3%)	0.0843
Contralateral TIAs	6 (12.2%)	3 (0.9%)	<0.0001
Ipsilateral TIAs	1 (2%)	19 (5.4%)	>0.5
All strokes	2 (4.1%)	12 (3.4%)	0.85
Contralateral strokes	1 (2%)	0	0.025
Ipsilateral strokes	1 (2%)	12 (3.4%)	>0.9
All neurological TIA/stroke	9 (18.4%)	34 (9.7%)	0.113
Contralateral	7 (14.3%)	3 (0.9%)	<0.0001
Ipsilateral	2 (4.1%)	31 (8.9%)	>0.3

Time to Stroke or Death in Patients With or Without Pre-Operative Contralateral Occlusion

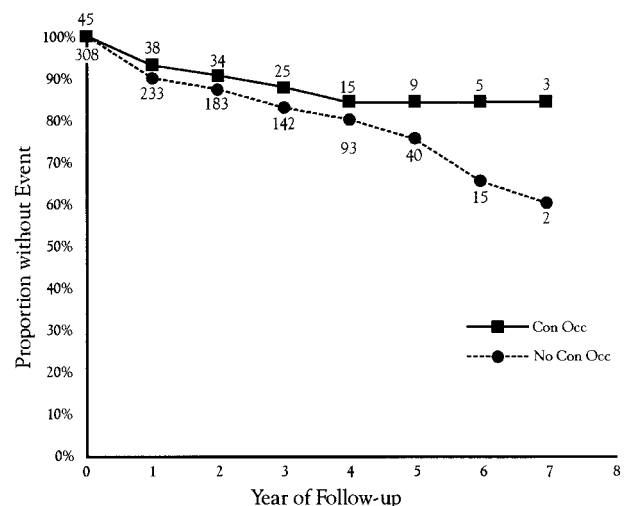
**Figure 1.** Kaplan-Meier curve: stroke-free survival according to contralateral occlusion (Con Occ).

TABLE 4. Correlation of All Strokes or Deaths to Contralateral Occlusion and Preoperative Symptoms

Preoperative Symptoms	Group A	Group B	P
Symptomatic	5/24 (21%)	36/183 (20%)	>0.80
Asymptomatic	1/25 (4%)	24/167 (14%)	>0.2
Total	6/49 (12%)	60/350 (17%)	>0.5

Values are number with stroke or death. There were no significant differences between symptomatic patients (as indication for CEA) and the presence or absence of contralateral carotid occlusion.

survival rates. Life-table data were compared with the log-rank test. Statistical significance was assumed for $P<0.05$.

Results

As noted in Table 1, the demographic characteristics, risk factors, and indications for CEA were similar in group A (patients with contralateral occlusion) and group B. The mean follow-up was also similar (group A, 40 months; group B, 33 months).

Table 2 summarizes all neurological events according to location (ipsilateral versus contralateral). Group A has a higher incidence of contralateral TIAs (12.2% versus 0.9%; $P<0.0001$), contralateral strokes (2% versus 0%; $P=0.025$),

TABLE 5. Life-Table Analysis of Stroke-Free Survival Rates for Groups A and B

Interval, mo	No. at Risk	No. of Strokes/Death	Withdrawn (Censored)	Interval Success	Cumulative Success (Stroke-Free Survival), %	SE, %
Group A						
Entry	45	0	0	1	100	0
0–6	39	3	4	0.97436	92.95	3.95
6–12	38	0	0	1	92.95	4.00
12–18	37	0	1	1	92.95	4.06
18–24	34	1	2	1	90.37	4.81
24–30	31	1	3	1	87.63	5.54
30–36	25	0	5	1	87.63	6.16
36–42	21	1	3	1	84.12	7.31
42–48	15	0	6	1	84.12	8.65
48–54	11	0	4	1	84.12	10.11
54–60	9	0	2	1	84.12	11.17
Group B						
Entry	308	0	0	1	100	0
0–6	254	21	33	1	92.88	1.56
6–12	233	8	14	1	89.83	1.88
12–18	205	2	26	1	89.00	2.06
18–24	181	4	20	1	87.21	2.32
24–30	159	4	17	1	85.20	2.60
30–36	142	4	14	0.99296	82.90	2.86
36–42	120	2	20	1	81.60	3.20
42–48	93	2	25	1	80.02	3.71
48–54	59	2	32	1	77.98	4.78
54–60	40	1	18	1	76.51	5.88

TABLE 6. Life-Table Analysis of Stroke-Free Survival Rates for Groups A and B (Symptomatic Subgroup)

Interval, mo	No. at Risk	No. of Strokes/Deaths	Withdrawn (Censored)	Interval Success	Cumulative Success (Stroke-Free Survival), %	SE, %
Group A						
Entry	23	0	0	1	100	0
0–6	21	3	0	0.952381	86.96	6.85
6–12	20	0	0	1	86.96	7.02
12–18	20	0	0	1	86.96	7.02
18–24	18	1	1	1	82.61	8.12
24–30	17	0	1	1	82.61	8.36
30–36	14	0	3	1	82.61	9.21
36–42	13	1	1	1	76.71	10.27
42–48	9	0	3	1	76.71	12.34
48–54	6	0	3	1	76.71	15.11
54–60	5	0	1	1	76.71	16.56
Group B						
Entry	170	0	0	1	100	0
0–6	133	13	24	1	91.95	2.26
6–12	122	4	8	1	89.05	2.67
12–18	106	1	15	1	88.28	2.94
18–24	96	1	9	1	87.42	3.16
24–30	87	3	6	1	84.59	3.56
30–36	80	3	4	0.9875	81.52	3.92
36–42	68	2	9	1	79.29	4.38
42–48	56	2	11	1	76.68	4.95
48–54	33	2	21	1	73.40	6.59
54–60	21	1	11	1	70.78	8.35

and combined contralateral TIAs/strokes (14.3% versus 0.9%; $P<0.0001$).

The perioperative stroke and all stroke (operative and late) rates were 2% and 4.1% for group A and 2.9% and 3.4% for group B ($P=0.60$ and 0.85 , respectively; Table 3). The perioperative TIA and all TIA rates were 0% and 14.3% for group A versus 2.6% and 6.3% for group B ($P=0.918$ and $P=0.08$, respectively; Table 3). The rates for perioperative and all neurological events (strokes and TIAs) were 2% and 18.4% for group A and 5.4% and 9.7% for group B ($P=0.27$ and 0.113 , respectively; Table 3). The perioperative mortality was similar in both groups: 0% in group A and 1.1% in group B (4/350; $P>0.95$). None of these deaths were stroke related. The overall mortality was also similar (Table 3). The overall stroke or death rates for symptomatic patients in groups A and B were also similar (Table 4).

The Kaplan-Meier analysis showed that the cumulative stroke-free survival rates at 5 years were 84% for group A and 77% for group B ($P>0.1$; Table 5, Figure 1). Similarly, a comparison of the subgroup of patients with and without symptoms in groups A and B revealed no significant differences in late stroke-free survival rates ($P>0.1$) (Tables 6 and 7, Figures 2 and 3). The late survival rates calculated by life-table methods are also shown in Table 8 and Figure 4. As

TABLE 7. Life-Table Analysis of Stroke-Free Survival Rates for Groups A and B (Asymptomatic Subgroup)

Interval, mo	No. at Risk	No. of Strokes/Deaths	Withdrawn (Censored)	Interval Success	Cumulative Success (Stroke-Free Survival, %)	SE, %
Group A						
Entry	22	0	0	1	100	0
0–6	18	0	4	1	100	0
6–12	18	0	0	1	100	0
12–18	17	0	1	1	100	0
18–24	16	0	1	1	100	0
24–30	13	1	2	1	93.75	6.50
30–36	11	0	2	1	93.75	7.09
36–42	8	0	3	1	93.75	8.29
42–48	6	0	2	1	93.75	9.57
48–54	5	0	1	1	93.75	10.48
54–60	4	0	1	1	93.75	11.72
Group B						
Entry	138	0	0	1	100	0
0–6	121	8	10	1	93.99	2.09
6–12	113	4	4	1	90.81	2.59
12–18	98	2	13	0.989796	88.99	2.98
18–24	86	2	10	1	87.09	3.37
24–30	72	1	13	1	86.04	3.79
30–36	63	1	8	1	84.73	4.17
36–42	52	0	11	1	84.73	4.59
42–48	38	0	14	1	84.73	5.37
48–54	27	0	11	1	84.73	6.37
54–60	20	0	7	1	84.73	7.40

noted, there were no significant differences in these rates between groups A and B ($P>0.1$).

The causes of late deaths in both groups are shown in Table 9, and they were somewhat similar. Again, none of these deaths were stroke related.

Discussion

Patients with contralateral carotid occlusion are intuitively considered a higher surgical risk for CEA for multiple reasons, eg, reduced collateral circulation during carotid clamping, cerebral hemorrhage secondary to hyperperfusion syndrome, and the overall advanced status of the vascular disease. Early literature has reported that patients with contralateral carotid artery occlusion who underwent CEA were at a higher risk for perioperative and late neurological events and/or received no benefit from surgery.^{3,4} Nicholls et al⁴ reported that CEA contralateral to carotid occlusion did not affect the overall survival or stroke rates. Fields and Lemak³ also concluded that surgical mortality was extremely high in patients with a carotid occlusion and that 34% of the surgically treated patients were alive at 66 months in contrast to 63% of medically treated patients. However, it is important to note that 71 of 108 patients with an occluded carotid artery underwent surgery on the side of the occlusion, and many

Time to Stroke or Death for Patients With Pre-op Sx: Contralateral Occlusion vs No Contralateral Occlusion

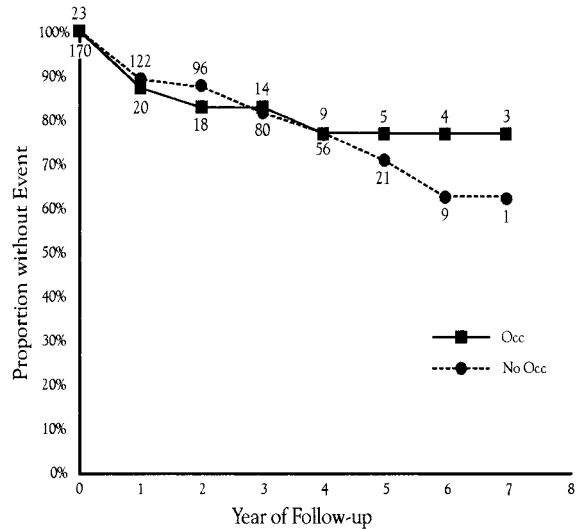


Figure 2. Kaplan-Meier curve: stroke-free survival for group A vs group B (symptomatic subgroup). Pre-op Sx indicates preoperative symptoms; Occ, occlusion.

were on the same day or within a few days of a recent stroke.³ This surgical approach is in contrast to what is practiced today.

More recent reviews^{5–10} have shown that indications for CEA in this subset of patients should not differ from the rest of the population. In fact, Mattos et al,⁵ in a study of 478 patients (66 of which had contralateral carotid artery occlusion), showed a perioperative stroke rate of 3% in patients with an occluded contralateral carotid artery versus 2.9% in patients with a patent contralateral carotid artery. Similarly, they found no differences in the late stroke rates of patients undergoing CEA with an occluded versus patent contralateral

Time to Stroke or Death in Patients, No Pre-Op Sx: Contralateral Occlusion vs No Contralateral Occlusion

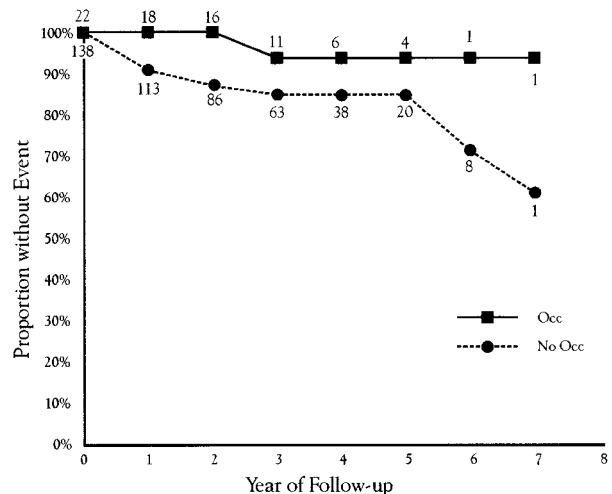


Figure 3. Kaplan-Meier curve: stroke-free survival for group A vs group B (asymptomatic subgroup). Abbreviations are as defined in Figure 2.

TABLE 8. Life-Table Survival Rates for Groups A and B

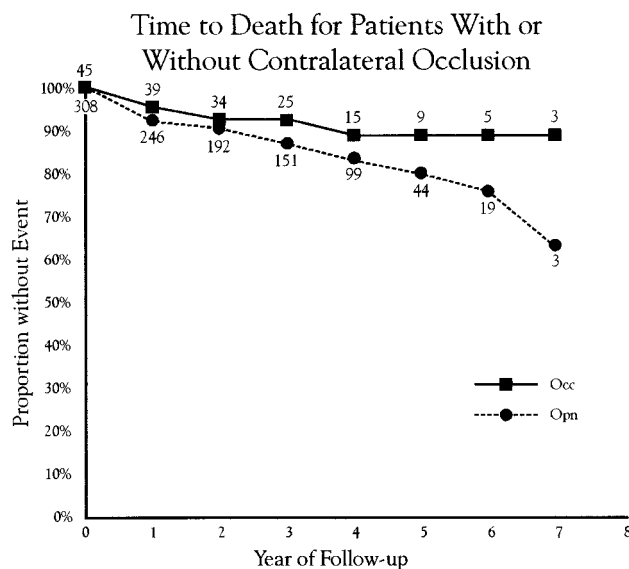
Interval, mo	No. at Risk	No. of Deaths	Withdrawn (Censored)	Interval Success	Cumulative Success (Survival Rates), %	SE, %
Group A						
Entry	45	0	0	1	100	0
0–6	40	2	4	0.975	95.18	3.30
6–12	39	0	0	1	95.18	3.35
12–18	37	0	2	1	95.18	3.44
18–24	34	1	2	1	92.53	4.34
24–30	31	0	3	1	92.53	4.54
30–36	25	0	6	1	92.53	5.06
36–42	21	1	3	1	88.83	6.48
42–48	15	0	6	1	88.83	7.88
48–54	11	0	4	1	88.83	8.95
54–60	9	0	2	1	88.83	9.90
Group B						
Entry	308	0	0	1	100	0
0–6	257	12	29	1	95.84	1.20
6–12	246	8	14	1	92.87	1.58
12–18	216	2	28	1	92.05	1.77
18–24	192	4	20	1	90.30	2.03
24–30	170	3	19	1	88.82	2.28
30–36	151	4	15	0.993377	86.57	2.58
36–42	130	2	19	1	85.36	2.86
42–48	99	3	28	1	83.14	3.43
48–54	68	2	29	1	81.18	4.27
54–60	44	1	23	1	79.80	5.41

carotid artery.⁵ Mackey et al⁶ reported similar results in 670 patients undergoing CEA, 63 of which had contralateral carotid occlusion. Their perioperative stroke rate of 5% in patients with an occluded ICA was similar to the control group (3%), and there was no difference in late stroke rates.⁶

Results from the NASCET study, which reviewed only recently symptomatic patients, demonstrated that medically treated patients with a contralateral occluded carotid artery were more than “twice as likely to have a stroke attributable to their stenotic lesion than patients with a patent contralateral artery.” However, when compared with medically treated patients, the overall risk of stroke contralateral to an occluded carotid artery was significantly reduced in the surgical patients. They showed that the risk of stroke in medically treated patients was 69% at 2 years versus 22% in patients treated surgically.¹¹

Our study demonstrated that patients with contralateral occlusion had a significantly higher incidence of contralateral TIAs (12% versus 1%; $P<0.0001$), contralateral strokes (2% versus 0%; $P=0.025$), and combined contralateral neurological events (both TIAs and strokes, 14% versus 1%; $P<0.0001$) after CEA.

Several studies of the natural history of carotid occlusion reported that the majority of strokes that occur in these patients are ipsilateral to the occluded vessel.^{4,14,15} This can

**Figure 4.** Kaplan-Meier curve: survival rates for group A vs group B. Opn indicates open.

be explained by the possibility of thrombus formation at the top of occlusion that may wash into the ipsilateral brain or can be secondary to embolization from the external carotid artery via collateral circulation. Cote et al¹⁶ reported that 64% of strokes in patients with an occluded ICA occur on the same side, with an annual stroke rate distal to an occluded ICA of 5% per year. Nichols et al⁴ also reported a similar number of patients (65%) suffering ipsilateral strokes, with an annual stroke rate of 3%. Jacobowitz et al¹⁷ and Hammacher et al¹⁸ believe that contralateral CEA provides long-term protection in both cerebral hemispheres. This can be explained by protecting a “functionally enlarged watershed area supplied by the remaining stenotic artery.”¹⁵ Although significant differences in contralateral TIAs, strokes, and all neurological event rates (TIA/stroke) were noted in patients with contralateral occlusion in our study, they were still much lower than the natural history of carotid artery occlusion.

Our study also demonstrated that CEA contralateral to a carotid occlusion can be done with overall perioperative and late stroke rates and mortality rates comparable to those seen in patients with a patent contralateral carotid artery. In fact, our perioperative and late stroke rates, 2% and 4%, respectively, in patients with contralateral occlusion of the carotid artery were similar to those found by Mattos et al⁵ and

TABLE 9. Causes of Late Deaths for Groups A and B

	Group A	Group B
Myocardial infarction	2 (50%)	25 (57%)
Congestive heart failure	0	2 (4%)
Pulmonary	0	3 (7%)
Cancer	0	3 (7%)
Renal	0	4 (9%)
Suicide	1 (25%)	0
Trauma	0	1 (2%)
Unknown	1 (25%)	6 (13%)

others.^{6–10} There were also no significant differences in the overall perioperative and late TIAs in both groups.

Aungst et al⁸ reviewed the findings from studies published since 1987 that have isolated the contralateral occluded groups. In their study, the perioperative stroke and death rates ranged from 0% to 8%, and the stroke-free rates at 5 years ranged from 88% to 95%. The 6 most recent studies^{5,6,8,9,17,19} found the perioperative stroke and death rates to be 5% or lower. These 6 studies demonstrated the same incidence of perioperative stroke or death rates as the NASCET and Asymptomatic Carotid Atherosclerosis Study (ACAS) (6% and 2%, respectively).^{1,2} Since the NASCET estimated the cumulative risk of any ipsilateral stroke at 2 years to be 26% for medically randomized patients, CEA is clearly indicated for patients with a contralateral occlusion.

The long-term effectiveness of CEA in these patients can be determined by the prevention of stroke on both the occluded side as well as the side of the endarterectomy. An earlier report by Nicholls et al⁴ concluded that CEA contralateral to an occluded carotid artery did not protect the contralateral hemisphere, but their finding of an 11% 5-year cumulative stroke rate for patients undergoing surgery was definitely less than the 22% rate in nonsurgical patients. Hammacher et al¹⁸ suggested that favorable results of CEA stem from the fact that the contralateral hemisphere (occluded ICA) “profits from revascularization through collateral pathways.” Mackey et al⁶ reported a cumulative stroke-free survival rate of 91% in patients with a contralateral occlusion at 5 years. Jacobowitz et al¹⁷ and Mattos et al⁵ noted similar results of 92% and 93%, respectively, at 5 years. Our 5-year stroke-free survival in these patients was also similar (84%).

Our study also concluded that the total perioperative and late death rates were similar for group A and group B (8% and 14%, respectively). Note that both groups had similar demographic characteristics, and patching was equally distributed among both groups. However, because of the sample size difference (49 versus 350) between these 2 groups, type I and/or II error in survival analysis should be considered. The cumulative survival rates at 1, 3, and 5 years were 95%, 93%, and 89% and 93%, 87%, and 80% for patients with and without contralateral occlusion, respectively ($P>0.1$). Mackey et al⁶ also found no significant differences in survival rates at 1, 5, and 10 years in patients with or without contralateral occlusion. Aungst et al⁸ similarly reported no differences for survival rates between these groups of patients. These findings were not surprising since most of the late deaths in patients with or without carotid occlusion were not stroke related.

In summary, patients with an occluded contralateral carotid artery have no increased risk in undergoing CEA. With no significant differences in perioperative and late stroke and late death rates, patients with contralateral carotid artery occlusion can expect beneficial and durable results from

CEA. CEA may also have a protective effect on the hemisphere ipsilateral to the carotid artery occlusion. Indication for CEA in these patients should be similar to that in the general population.

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