

Outcome Analysis of Carotid Artery Occlusion

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The outcome of carotid artery occlusion was studied through the retrospective identification of 115 affected patients. The majority were white (77%) males (61%) with multiple atherogenic risk factors and suffering ipsilateral stroke (57%). Those patients presenting with stroke were not distinguished by demographic features, risk factors, lipid profile, medical regimen, or subsequent mortality when compared with those without. Overall, 36 patients (31%) required contralateral carotid endarterectomy (CEA), with one (2.8%) perioperative stroke, whereas 4 (3%) underwent ipsilateral external CEA without incident. With 81% follow-up

(mean 3.9 years), the overall mortality of the group was 46%; the annualized risk of ipsilateral stroke was 1.6%. This study documents a significant risk of stroke and contralateral occlusive disease with ipsilateral carotid artery occlusion, which cannot be reliably predicted by clinical criteria. Duplex surveillance is valuable, but flow velocity measurements alone may be misleading. Surgical endarterectomy can be performed with an acceptable rate of perioperative stroke.

Keywords: carotid occlusion; outcomes; stroke; death; risk

Spontaneous occlusion of the cervical carotid artery was first described by Moniz et al in 1937 following Moniz's development of cerebral angiography.¹ During the subsequent decade, numerous case reports of this finding were published, but it was not until 1951 that Fisher provided a definitive review that linked this anatomic lesion with symptoms of stroke and transient ischemic neurological events.² It was concluded from this study that extracranial occlusion was more common than previously suspected and that it was, in most cases, the terminal result of atherosclerotic disease. Its diverse clinical features were attributed primarily to differences in intracranial collateral circulation. Since that time, refinements of diagnostic imaging, including duplex ultrasound scanning,^{3,4} magnetic resonance angiography,^{5,6} and computerized tomographic⁷ angiography, have allowed the reliable identification of carotid occlusion in a broader

population of patients, which has permitted an examination of its natural history. Despite this capability, controversies persist regarding the associated risks and outcomes of carotid occlusion. This study was performed to describe its presentation and to identify factors that might influence its various manifestations.

Patients and Methods

Following a 14-year-period retrospective review of an Intersocietal Commission for the Accreditation of Vascular Laboratories registry, 115 patients were identified with carotid artery occlusion, representing 3.1% of all individuals undergoing carotid scanning during that time. The diagnosis of carotid occlusion was based on findings of echogenic material within the arterial lumen, lack of pulsation and intra-arterial Doppler signals, evidence of reversal of flow near the origin of the internal carotid artery (ICA), and loss of diastolic flow in the ipsilateral common carotid artery (CCA). It was confirmed in all equivocal cases (32%) by alternative studies including magnetic resonance imaging (46%), computerized tomography (8%), and catheter-directed

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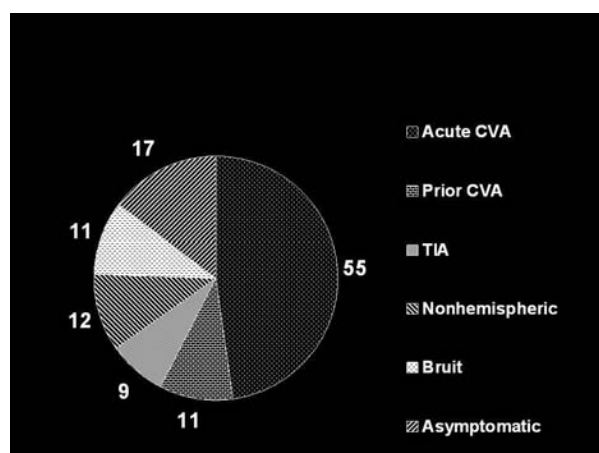


Figure 1. Clinical presentation of carotid artery occlusion. CVA = cerebrovascular accident; TIA = transient ischemic attack.

angiography (46%). In this study group, there was a predominance of males (61%) and white (77%), with an age range of 37 to 89 years (mean 65.4 ± 11.4 years) (Table 1). Primary risk factors were a history of smoking (80%), hypertension (79%), diabetes (40%), peripheral vascular disease (39%), and coronary arterial occlusive disease with myocardial infarction (26%) and coronary intervention (24%). A family history of stroke was not common (14%). At the time of examination, the following were used in the pharmacological management of patients: aspirin (70%), β -adrenergic blockers (60%), statins (52%), and angiotensin-converting enzyme inhibitors (38%). The principal clinical indication for carotid scanning was ipsilateral stroke in 66 (57%) patients (28 acute left, 27 acute right, 11 previous) and ipsilateral transient ischemic attack in 9 (8%) patients (6 hemispheric, 3 amaurosis fugax). The remaining 39 patients (34%) had either nonspecific or nonlateralizing symptoms (11) or had no neurological symptoms (28) (Figure 1).

Duplex examination of the carotid artery demonstrated ICA occlusion in 104 patients (90%), CCA occlusion in 4 (3%), combined ICA and CCA occlusion in 4 (3%), and complete system occlusion (CCA, ICA, and external carotid artery [ECA]) in 3 (3%). The contralateral carotid showed no appreciable disease in 40 (35%) patients, of whom 8 had undergone previous contralateral endarterectomy. It was mildly diseased (16% to 49% stenosis) in 28 (24%), moderately diseased (50% to 79% stenosis) in 22 (19%), severely diseased (80% to 99% stenosis) in 18 (16%), occluded in 6 (5%), and congenitally absent in 1 (1%) (Figure 2). In 4 cases, carotid occlusion followed previous carotid endarterectomy

(CEA) at a mean interval of 7.5 years.

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS, Chicago, Illinois) software for Windows with a P value of $<.05$ being considered significant for all analyses. Between-group comparisons of continuous data were performed using the two-sided Student's t test, and categorical data were compared using the Pearson chi-square or the Fisher exact statistic.

Results

With an 81% follow-up to a mean of 3.9 ± 3.3 years (range, .5-14 years), there were 45 verified deaths (48%) within the study group. Of these, 37 (82%) occurred within 5 years of the diagnosed occlusion, with the average time to death being 3.1 ± 3.0 years. This represented a mean annualized mortality of 10.0% or an equivalent one death per each 3.1 person-years. One patient (2.8%) died as an immediate consequence of their primary stroke. However, an additional 6 patients died subsequently as a direct result of stroke and 8 others from complications attributed to their neurological event. Mortality in the remainder of the group was ascribed to cardiac disease (6), cancer (5), and to other causes (3). In 16 cases, the exact cause of death could not be ascertained. Recurrent stroke was identified in 8 patients (7%), of which 1 case involved the contralateral hemisphere. The mean annualized risk of stroke ipsilateral to a carotid occlusion was 1.6%, equivalent to one event per 3.2 person-years. Those with recurrent ipsilateral stroke had demographic features similar to those without it, although with a mild trend toward greater risk in diabetics and in those with an absence of disease in the contralateral artery. Contralateral CEA was performed in 36 patients (31%) and was associated with 1 (2.8%) perioperative stroke. Four patients (3%) underwent ipsilateral external CEA without incident.

Patients suffering from stroke as a result of their carotid occlusion were compared with those who did not. There were no demographic differences found in these groups, although trends were noted for age less than 60 years ($P = .09$) and for white patients ($P = .08$). Risk factor profiles were also similar. However, those with chronic renal failure were found to have a lower risk of stroke ($P = .03$), whereas those with peripheral vascular or coronary occlusive disease had a higher risk ($P = .03$). Comparison of lipid profiles did not show any difference between the groups except for C-reactive

Table 1. Demographics and Risk Factors of Study Groups

	Total (N = 115)	Stroke (n = 65)	Recurrent (n = 7)	Death (n = 45)
Age (years)	65.5	62.9	60.0	69.5
Male	.60	.62	.57	.47
White	.76	.75	.71	.80
Smoking	.80	.81	1.00	.69
Htp	.79	.78	.86	.71
DM	.40	.40	.71	.38
PVD	.39	.34	.14	.36
MI	.26	.26	.28	.22
CRF	.09	.03*	.14	.36
ASA	.70	.77	.71	.67
β -Blocker	.60	.62	.43	.62
Statin	.52	.48	.43	.44

Note: ASA = aspirin; CRF = chronic renal failure; DM = diabetes mellitus; Htp = hypertension; MI = myocardial infarction; PVD = peripheral vascular disease.

* $P < .05$.

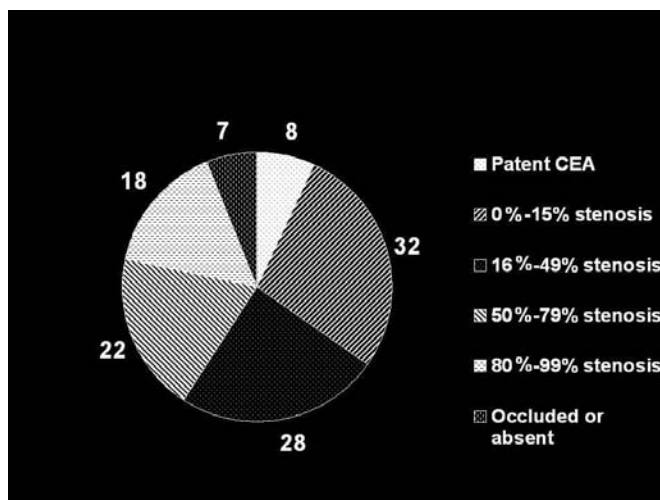


Figure 2. Status of the carotid artery contralateral to the occlusion. CEA = carotid endarterectomy.

protein, which tended to be higher in those with stroke ($P = .08$). It was also found that there was a higher frequency of significant contralateral carotid stenosis in whites ($P = .03$) and in those taking aspirin ($P = .02$), and a trend toward a greater incidence of contralateral stenosis in those with coronary occlusive disease ($P = .08$). Similarly, the need for contralateral endarterectomy was greater in whites ($P = .04$). No other risk factor or pharmacological agent was found to be related. Contralateral occlusion was correlated only with a history of myocardial infarction ($P = .04$).

To assess the effect of unilateral carotid occlusion on Doppler flow parameters, patients with ICA

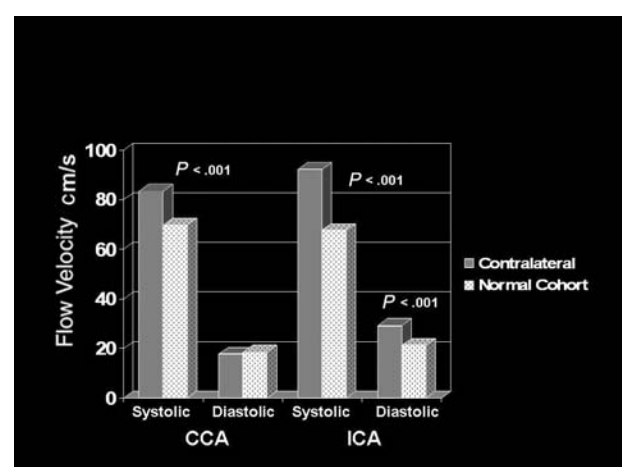


Figure 3. Arterial flow velocities in the normal contralateral internal carotid artery (ICA) versus a normal cohort (common carotid artery [CCA]).

occlusion and a normal contralateral carotid (39) were compared with an age-, gender-, and ethnicity-matched normal cohort (1:2). Normalcy of the contralateral carotid and of the cohort arteries was based on the absence of mural plaque on B-mode scanning and an absence of flow turbulence on color-flow examination. Measurements of both peak systolic and diastolic flow velocities were taken from the mid-CCA and the mid-ICA, and the ratio of ICA to CCA systolic velocity was calculated. In the control group, there were no differences found between the right and left velocity measurements. The CCA ($P < .001$) and ICA ($P < .001$) systolic velocities were significantly greater in the artery opposite the occlusion

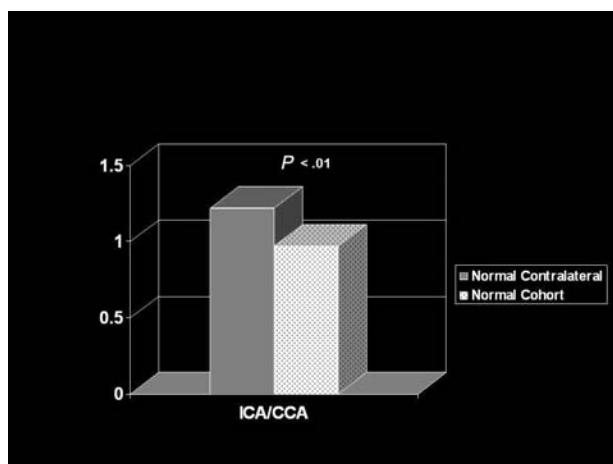


Figure 4. Internal carotid artery/common carotid artery (ICA/CCA) flow velocity ratio: normal contralateral artery versus a normal cohort.

than in the normal, control artery (Figure 3). The ICA diastolic ($P = .001$), but not the CCA diastolic, velocity was also greater, as was the ICA/CCA ratio ($P = .001$) (Figure 4). This latter finding indicated a greater relative increase in the ICA velocities as compared with those of the CCA. On the occluded side, the CCA systolic velocity tended to be less than that for the nonoccluded CCA ($P = .06$) and was comparable to the normal CCA (Figure 5). However, the diastolic flow velocity of the CCA on the occluded side was significantly lower than that of either the nonoccluded side ($P < .0001$) or the normal artery ($P < .0001$).

Discussion

Occlusion of the carotid artery has been most commonly linked to atherosclerosis and its known risks, including smoking, dyslipidemia, hypertension, and diabetes.⁸ Other recognized etiologies are cardioembolism, dissection, trauma, and arteritis.⁹ Because many minimally affected or asymptomatic individuals may not undergo formal evaluation, the true incidence of this disease is likely to be underestimated. However, several postmortem series have indicated a prevalence of 2.9% to 6.5%.^{8,10-12} In a recent population-based study of carotid artery occlusion, Flaherty et al have demonstrated an age- and gender-adjusted incidence of 6 per 100 000 (95% CI = 4.6-7.3), which has been conservatively equated to 15 000 to 20 000 events occurring annually in the United States.¹³ To date, investigations of the natural history of carotid

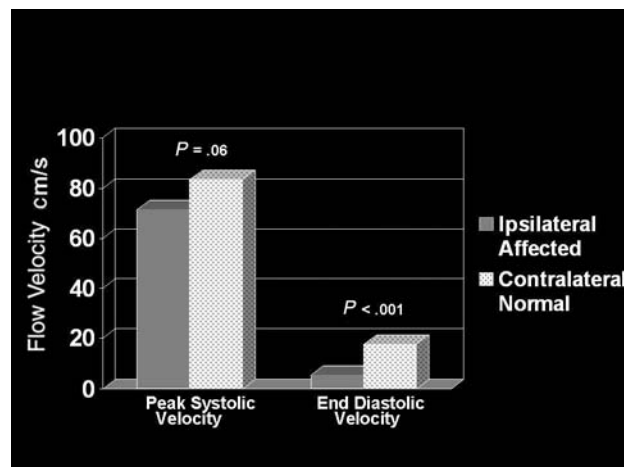


Figure 5. Effect of internal carotid artery (ICA) occlusion on common carotid artery (CCA) flow velocities.

artery occlusion have failed to provide a reliable means of predicting either its clinical presentation or its risk of subsequent neurological events. The Joint Study of Extracranial Arterial Occlusion, which included angiographic evaluations of nearly 3800 patients experiencing signs or symptoms of ischemic cerebrovascular disease, verified that 72% of their registry enrollees with carotid occlusion had some degree of neurological deficit on initial evaluation.¹⁴ Heilbrun¹⁵ suggested that the risk of significant stroke was considerably lower, with only 27% of his occluded group experiencing severe complicated stroke, whereas Fritz placed this figure at 38%.¹⁶ The factors that determine the immediate outcome of carotid occlusion are not clear. In the Joint Study, African-American ancestry, the presence of intracranial vascular occlusive disease, and a normal contralateral carotid artery were all associated with more severe impairment,¹⁷ but other studies have been unable to confirm these findings.

It has been postulated by numerous investigators that the variability in clinical outcome of carotid occlusion may be due more directly to regional patterns of cerebral circulation, which are defined by the extent of intracranial occlusive disease and by intrinsic anatomical variations of the cerebral vasculature.^{2,14,18} Other systemic factors such as cardiac output, blood pressure, blood volume, oxygen content, and viscosity have also been implicated,¹⁷ although conclusive evidence for their role in influencing morbidity has been lacking. Similarly, some studies have cited an increased risk of stroke with hypotension as occurring with hemorrhage, cardiac

failure, or postural change.¹⁹ These same elements may have an impact on the risk of subsequent or recurrent neurological events. It has been shown repeatedly that patients with carotid occlusion are at continued risk for both stroke and transient ischemic neurological events. Following a review of 20 observational studies, Klijn found a combined annual risk for ipsilateral stroke of 2.1% (95% CI = 1.6-2.8) and for all strokes of 5.5% (95% CI = 5-6).¹⁸ This risk appears to be lower for those with asymptomatic disease and higher for those presenting initially with a neurological deficit.²⁰⁻²³ A meta-analysis of this data has identified the presence of hypertension and intracranial disease as possible risks for postocclusive events, whereas bilateral occlusion and the use of oral anticoagulants appeared to reduce this risk.²⁴ It has been suggested that the event rate may be greater near the time of occlusion with later neurological stabilization, at which time cardiac disease assumes a greater role in determining morbidity and mortality.^{13,16,20,23} This was not confirmed in the Canadian Cooperative study, in which there appeared to be no period of either increased or reduced risk.²²

It is believed that the mechanism by which post-occlusive events occur is either embolic or flow related, and it may be enhanced further by the extension of a thrombus into the intracranial circulation. Examination of autopsy specimens has demonstrated clot propagation into the middle cerebral artery in 50% to 80% of patients suffering stroke, correlating with the principal involvement of the middle cerebral artery territory as compared with the anterior or posterior cerebral areas.^{3,25} It was previously believed that embolic episodes could not be the cause of ipsilateral neurological events in view of the fact that the occluded ICA could no longer transmit material distally. However, more recent observations indicate that emboli can originate from the blind stump,²⁶ from the ECA,²⁷ or from a diseased contralateral carotid artery and travel through the external circulation, the ascending pharyngeal branch,²⁸ or by means of trans-hemispheric microembolization.²⁹ The hypothesis that recurrent stroke is an embolic event is further supported by the demonstration of a cessation of symptoms after excision of the proximal stump, following endarterectomy of the external carotid or of a stenotic contralateral carotid artery, and the initiation of antithrombotic agents.^{26,29-31}

Hemodynamic failure is an equally compelling theory of the cause of postocclusive events. Under normal conditions, cerebral blood flow is maintained

despite changes in cardiovascular hemodynamics because of intrinsic autoregulation of the cerebral vasculature. In cases of proximal large vessel obstruction, maximal vasodilatation may result from ischemia-induced loss of autoregulatory activity. In this setting, a vasodilatory stimulus can lead to a decrease in regional cerebral blood flow through the shunting of blood to peripheral areas that have maintained their reactivity. This can enhance cerebral ischemia in unresponsive areas and cause border-zone infarcts.^{32,33} Alterations in vasoreactivity through breath holding, carbogen, or acetazolamide have been shown to occur in the presence of severe carotid stenosis or occlusion.³³⁻³⁶ Based on these studies, it has been estimated that 12% of those with ICA occlusion have "exhausted" reactivity and another 29% reduced reactivity in response to hypercapnea, as measured by transcranial Doppler.³⁷ These findings have been associated with a worse clinical prognosis: Klijn has shown that those with impaired hemodynamics have an annual rate of subsequent ipsilateral stroke of 9.5% (95% CI = 6.4-14) and of all strokes of 12.5% (95% CI = 8.9-17), whereas those with severe hemodynamic impairment of 31% (16.2-59.7) and 41.1% (23.5-72.9), respectively.¹⁸ Similarly, Kuroda et al quantitated regional blood flow and cerebrovascular reactivity in response to acetazolamide using ¹³³Xe SPECT and found that patients with reductions in both had a significantly higher risk of both ipsilateral (relative risk = 8.0; 95% CI = 1.9-34.4) and all total stroke (relative risk = 3.6; 95% CI = 1.4-9.3).³⁸ Grubb et al have concluded that hemodynamic failure distal to a symptomatic occluded carotid artery is an independent predictor of subsequent ischemic stroke but has stated that hemodynamic failure should not imply that subsequent stroke is necessarily hemodynamically mediated, as low flow states may also predispose to thromboemboli, which may lead to infarction in areas of poor collateral circulation.³⁹

Mortality associated with carotid occlusion has been largely attributed to either neurological or cardiovascular complications. The overall annual mortality of this group of patients has been reported to be 1.4% to 18% per year,^{18,20,22,23,40} being greatest within the first several months following carotid occlusion and declining more gradually thereafter.⁴¹ Early mortality has been linked to cerebrovascular events, whereas cardiac mortality increases in prevalence over time^{21,22}; that related to stroke may reach 77%, although more immediate neurological mortality

has been commonly estimated at 20% to 28%.^{17,42} Fields attempted to stratify this risk: a mortality of 50% with recurrent events, 46% with unilateral occlusion, and 60% with bilateral occlusion.¹⁷ It is noteworthy that in this series, asymptomatic occlusion carried an overall mortality of 43%. Although no consistent predictors of mortality have been identified, some investigators have suggested an increased risk with diabetes, hypertension, and age.^{9,20,42,43}

In this study, patients discovered to have carotid occlusion demonstrated an atherosclerotic profile with an older, male demographic and with associated risk factors, including smoking, hypertension, diabetes, and concurrent coronary and peripheral arterial occlusive disease. A significant number of these patients presented with a neurological deficit, but they did not distinguish themselves from their asymptomatic cohort other than showing trends for age, Caucasian race, and concurrent peripheral vascular disease. There were no differences in their lipid profiles, but those with stroke demonstrated a tendency for higher C-reactive protein levels. The overall incidence of latent neurological events was found to be similar to that reported elsewhere and was found to have no clear clinical discriminating features other than a mild trend toward increased risk in diabetics ($P = .12$) and in those without significant contralateral disease ($P = .18$). Moderate to severe disease of the contralateral carotid artery was either found at presentation or required previous endarterectomy in 54 members (47%) of this group, of which more than one third ultimately required surgical treatment. Other investigators have also noted a high incidence of contralateral disease and of disease progression.^{23,43} The role and associated risks of endarterectomy in this setting have been debated. Subgroup analysis of the Asymptomatic Carotid Atherosclerosis Study group suggested increased longer-term incidence of ipsilateral stroke in asymptomatic patients with unilateral carotid occlusion undergoing contralateral endarterectomy and indicated lack of long-term surgical benefit for this group.⁴⁴ Additional limitations were suggested by Jordan et al, who concluded that endarterectomy, although successful in reducing the neurological morbidity of carotid occlusion, provided no survival benefit.⁴⁵ However, numerous other studies have demonstrated that endarterectomy can be performed with comparable early and late stroke rates reported for those with a patent contralateral artery.^{46,47} Because there appears to be a greater risk of both ipsilateral and all strokes in patients with

combined carotid stenosis and contralateral occlusion, it has been recommended that a decision for endarterectomy be based on the same criteria established by the Asymptomatic Carotid Atherosclerosis Study group for the surgical treatment of asymptomatic carotid disease.⁴⁸ It should be noted, as suggested previously⁴⁹ and confirmed by this study, that contralateral occlusion is associated with elevation of the ipsilateral arterial flow velocities as measured by duplex scanning. This finding should be considered if the interpretation of noninvasive diagnostic imaging and subsequent clinical decisions are based primarily on flow criteria. Finally, following a review of 20 published studies, Gertler and Cambria have also verified the safety and potential benefits of external CEA. This procedure has improved both morbidity and mortality rates in patients with persistent ipsilateral hemispheric or retinal symptoms, presumed to be because of continued embolization from a diseased ipsilateral ECA, and should be recognized as a valuable treatment option for selected patients.⁵⁰

Conclusion

The present study confirms a significant risk of acute stroke as a result of carotid artery occlusion and an ongoing threat of recurrent, ipsilateral stroke despite obstruction to flow. Neither initial presentation nor subsequent outcome can be reliably predicted by clinical criteria. There is a high incidence of contralateral carotid occlusive disease in this patient population, which is amenable to surgical therapy, with an acceptable perioperative morbidity. Because of this, continued surveillance of these patients is warranted. However, the effect of carotid occlusion on contralateral flow velocities must be considered if a clinical decision is based primarily on these measurements.

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