Internal Carotid Artery Occlusion: Association With Atherosclerotic Disease in Other Arterial Beds and Vascular Risk Factors

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Internal Carotid Artery Occlusion: Association With Atherosclerotic Disease in Other Arterial Beds and Vascular Risk Factors

Kosmas I. Paraskevas, MD, FASA,* Dimitri P. Mikhailidis, MD, FASA, FRCPath, FRCP,* and Christos D. Liapis, MD, FACS, FRCS,† *London, United Kingdom, and Athens, Greece*

The aim of this article is to investigate the association between internal carotid artery occlusion (ICAO) and the presence of atherosclerotic disease and vascular risk factors. The clinical characteristics and risk factors of 120 patients presenting with ICAO were retrospectively reviewed. All patients (n = 120) had at least 1 of the 4 vascular risk factor (diabetes, smoking, hypercholesterolemia, and hypertension); 2, 3, or all 4 risk factors were present in 14 to 82 of the patients (11.7% to 68.3%), 10 to 39 of the patients (8.3% to 32.5%), and 9 of the patients (7.5%), respectively. A total of 84 patients (70%) with ICAO had disease in at least 1 additional vascular bed (aorta, coronary or lower limb arteries). In addition to ICAO, vascular disease was present in 2 and all 3 of these arterial beds in 42 (35%) and 9 (7.5%) patients, respectively. Furthermore, stenosis or occlusion of the ipsilateral or contralateral vertebral arteries was recorded in 19 of 120 patients (15.8%). Regarding the contralateral carotid artery, 1 patient had bilateral ICAO. One patient had contralateral common carotid artery occlusion, and 1 patient was excluded from the analysis because of surgery to the contralateral carotid artery. Of the remaining 117 patients, 34 (29.0%) had less than 50% contralateral carotid artery stenosis. Thirty-two patients (27.4%) had 50% to 69%, and 51 (43.6%) had 70% to 99% stenosis. Ultrasonographic imaging of the carotid plaque of the contralateral carotid artery revealed that 52 of the 120 arteries (43.3%) were uniformly or predominantly echolucent (types I and II, respectively). Fifty-nine (49.2%) were predominantly or uniformly echogenic (types III and IV), and 9 (7.5%) could not be classified. A similar distribution of echomorphology was observed on the occluded side. ICAO is associated with widespread atherosclerotic disease and a high prevalence of vascular risk factors. Detection of ICAO should prompt the investigation of other arterial beds and treatment of risk factors.

Introduction

The annual incidence rate of symptomatic internal carotid artery occlusion (ICAO) in the general population is about 6 per 100 000 persons (age and gender adjusted to the US population).[1] The annual stroke and death rates of ICAO vary widely; a review summarized the results of 20 observational studies published between 1960 and 1995 and described the risk of recurrent stroke and death in patients with a transient ischemic attack (TIA) or stroke in the

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From the *Department of Clinical Biochemistry and Academic Department of Surgery, Royal Free Hospital, London, United Kingdom, and the †Department of Vascular Surgery, Athens University Medical School, Athens, Greece

Correspondence: Dimitri P. Mikhailidis, MD, FASA, FFPM, FRCPath, FRCP, Department of Clinical Biochemistry, Royal Free Hospital and Royal Free University College Medical School, Pond Street, London NW3 2QG, UK
E-mail: mikhailidis@aol.com.

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presence of ICAO.[2] The annual stroke rate in these studies varied between 0% and 20.1%[2]; the combined annual stroke risk of the 20 studies was 5.5% (95% confidence interval, 5.0% to 6.0%). The annual death rate similarly varied widely (between 0% and 14.2%). Approximately 55% of these deaths (over a median period of 33 months; range, 19-48 months) were due to a vascular cause. A recent study demonstrated that 45% of the patients with stroke associated with ICAO had died after a mean follow-up of 1.2 years.[3] In a study involving 65 patients with ICAO, the rate of ipsilateral cerebrovascular events was 18.5% over a period of 24 months.[4] The risk was greater when cerebral hemodynamics were impaired. There were also 3 events (4.6% of patients) on the contralateral side[4]; therefore, symptomatic ICAO is associated with high mortality and morbidity rates.

Previous studies have shown that a number of predisposing risk factors correlate with the severity of carotid artery stenosis. These include age,[5,6] hypertension,[6-9] smoking,[5-11] hypercholesterolemia,[9,11,12] ischemic heart disease,[9,12,13] diabetes mellitus,[12,14,15] and male gender.[5,13] In addition, carotid artery disease co-exists with vascular disease in other arterial beds, namely coronary artery disease (CAD),[16,17] peripheral arterial disease (PAD),[17] and aortic disease.[18]

Determining the association between ICAO with vascular disease in other arterial beds, as well as with traditional risk factors for vascular disease, holds strong implications for risk modification and improved patient management; therefore, we evaluated the extent of co-occurrence of vascular disease in other arterial beds in patients with ICAO, as well as the prevalence of established vascular risk factors.

Methods

The risk factors for vascular disease (diabetes, hypertension, hypercholesterolemia, and smoking) of 120 patients (106 men and 14 women; mean age, 64.9 years; range, 42-82) presenting to our department at the University of Athens with ICAO from October 1987 until April 2006 were recorded. All patients were symptomatic (amaurosis fugax, TIA, or stroke). The degree of co-existence of clinically evident vascular disease in other arterial beds besides the carotid vasculature was also investigated. Furthermore, the degree of contralateral carotid artery stenosis was recorded. Carotid plaque echomorphology was also assessed.

ICAO and Risk Factors for Vascular Disease

The presence of 4 vascular risk factors was noted: (1) hypertension, (2) diabetes mellitus, (3) smoking, and (4) hypercholesterolemia. A history of smoking was based on the information that the patient provided. Hypertension, diabetes mellitus, and hypercholesterolemia were considered to be present if the patient had been diagnosed with these conditions (whether on or off medication) before referral for a surgical opinion.

ICAO and Vascular Disease in Other Arterial Beds

The presence of clinically evident vascular disease in the aorta, coronary and peripheral arteries was recorded. The presence of CAD was not verified by stress electrocardiogram or angiography. For PAD, the Ankle Brachial Pressure Index (ABPI) was measured for most patients. For aortic disease, all patients underwent a physical examination, and in the case of suspicion of abdominal aortic aneurysm, an ultrasound examination was performed. In addition, the ipsilateral and contralateral vertebral arteries were examined by Duplex ultrasonography.

Investigation of the Contralateral Internal Carotid Artery

The contralateral carotid artery was examined by Duplex ultrasonography. In order to calculate a mean contralateral carotid artery stenosis percentage for the entire study population, the following values were assigned to each degree of stenosis: (1) for less than 50% stenosis, the actual recorded percentage of stenosis was assigned; (2) for 50% to 69% stenosis, an average value of 59.5% was assigned; (3) for 70% to 99% stenosis, an average value of 84.5% was assigned; and (4) for total occlusion, a value of 100% was assigned. These values in all contralateral carotid arteries were then added and divided by the number of patients to derive the overall mean percentage of stenosis.

Ultrasonographic Grading of the Ipsilateral and Contralateral Carotid Plaques

The carotid plaques on the occluded and contralateral side were evaluated by ultrasonography.

The following plaque categories were considered: uniformly echolucent (type I), predominantly echolucent (type II), predominantly echogenic (type III), uniformly echogenic (type IV), unclassified, and thrombotic. Echolucent plaques are more likely to progress and to be associated with cerebrovascular events.[19,20]

Results

Of 120 patients with ICAO, the right side was affected in 62 patients and the left side in 57. One patient had bilateral ICAO.

ICAO and Vascular Risk Factors

Thirty-eight individuals were diabetic, 89 received medical treatment for hypercholesterolemia, 108 were on antihypertensive medication, and 52 were smokers. All patients (N = 120) had at least 1 risk factor present, whereas 14 to 82 (11.7% to 68.3%), 10 to 39 (8.3% to 32.5%), and 9 patients (7.5%) had at least 2, 3, and all 4 risk factors, respectively. The distribution of at least 2, 3 and all 4 risk factors is shown in Tables I and II.

ICAO and Vascular Disease in Other Arterial Beds

The patient distribution with clinically evident vascular disease in other arterial beds besides the carotids is shown in Table III. Of the 120 patients, 84 (70%) had concomitant vascular disease in another noncarotid, nonvertebral arterial bed; 18 patients had aortic disease (9 abdominal aortic aneurysms and 9 diffuse aortic stenoses). Sixty-six had CAD, whereas 62 had PAD.

In the PAD group, 9 patients had previous lower limb surgery, and 12 patients had intermittent claudication but did not have their ABPI measured. Of the remaining 41 patients in the PAD group, the right- and left-side mean ABPI ± SD was 0.63 ± 0.21 and 0.61 ± 0.20, respectively. The ABPI in the right and left leg did not differ significantly, but these values correlated significantly (r = 0.31, 2-tailed $P = .049$). A normal ABPI (≥0.90) was recorded in 58 patients.

Besides ICAO, vascular disease was present in at least 2 other of these arterial beds (CAD and aortic, CAD and PAD, or aortic and PAD) in 42 of 120 patients (35%). In addition to ICAO, 9 patients (7.5%) had vascular disease in all 3 of these arterial beds.

Examination of the ipsilateral and contralateral vertebral arteries showed stenosis or occlusion in 19 of the 120 patients (15.8%).

Table I. Number of patients with at least 2 established risk factors for internal carotid artery occlusion.

Risk Factors Evaluated	Number of Patients (%)
Diabetes + hypercholesterolemia	29 (24.2)
Diabetes + hypertension	33 (27.5)
Diabetes + smoking	14 (11.7)
Hypercholesterolemia + hypertension	82 (68.3)
Hypercholesterolemia + smoking	40 (33.3)
Hypertension + smoking	43 (35.8)

The percentages do not add to 100% because many patients had more than 2 risk factors, and as a result, they are included in more than 1 subcategory.

Table II. Number of patients with 3 of 4 and all 4 established vascular risk factors for internal carotid artery occlusion.

Risk Factors Evaluated	Number of Patients (%)
Diabetes + hypercholesterolemia + hypertension	24 (20)
Diabetes + hypertension + smoking	10 (8.3)
Diabetes + hypercholesterolemia + smoking	11 (9.2)
Hypercholesterolemia + hypertension + smoking	39 (32.5)
All 4	9 (7.5)

The percentages do not add to 100% because some patients had less than 3 risk factors.

Investigation of the Contralateral Internal Carotid Artery

One patient was excluded from the analysis because of previous operation. One patient

Table III. Distribution of vascular disease in additional arterial beds (coronary artery disease, peripheral arterial disease, and/or aortic) in patients with internal carotid artery occlusion.

Vascular Beds	Number of Patients (%)
In at least 1 additional arterial bed	84 (70)
Aorta + PAD	14 (11.7)
Aorta + CAD	13 (10.8)
CAD + PAD	36 (30)
In any 2 arterial beds	42 (35)
In all 3 arterial beds	9 (7.5)

CAD, coronary artery disease; PAD, peripheral arterial disease.

This may represent an underestimation because not all patients were extensively investigated. Most patients had vascular disease in more than 1 arterial bed. As a result, they are included in more than 1 subcategory; therefore, the percentages do not add up to 100%.

presented with occlusion of the contralateral common carotid artery, whereas another patient had bilateral ICAO. Of the remaining 117 patients, 34 (29.0%) had less than 50% contralateral carotid artery stenosis, 32 (27.4%) had 50% to 69%, and 51 (43.6%) had 70% to 99% stenosis. The average calculated contralateral internal carotid artery stenosis was 61.5%.

Ultrasonographic Grading of the Ipsilateral and Contralateral Carotid Plaques

Ultrasonographic imaging of the carotid plaques on the occluded side revealed that 46 plaques were uniformly or predominantly echolucent (types I + II); 56 plaques were predominantly or uniformly echogenic (types III + IV). A thrombus was detected in 18 plaques; therefore, 38.3% of the patients had an echolucent plaque on the occluded side.

Ultrasonographic imaging of the contralateral carotid artery revealed that 52 plaques were uniformly or predominantly echolucent (types I + II), and 59 plaques were predominantly or uniformly echogenic (types III + IV). Nine plaques could not be classified; therefore, 43.3% of the patients had an echolucent plaque on the contralateral side.

The distribution of echolucent/echogenic plaques did not differ significantly when the occluded and contralateral carotids were compared.

Discussion

We demonstrated that contralateral 70% to 99% internal carotid artery stenosis was present in almost half (42.5%, 51 of 120 patients) of the patients with ICAO. The average calculated stenosis of the contralateral internal carotid artery was more than 60%. These findings support the concept that carotid artery disease is a progressive atherosclerotic process affecting both sides.[21,22]

A significant number of patients with carotid artery occlusion will require endarterectomy of the patent contralateral carotid because the disease is likely to progress rapidly on that side.[21] Patients with 60% to 69% asymptomatic carotid artery stenosis and contralateral carotid occlusion, even with maximum medical therapy, have a high incidence of late (mean follow-up, 59.5 months) strokes and TIAs (33% and 27%, respectively).[22] It is therefore crucial to identify these patients and implement therapeutic measures.

The ultrasonographic appearance of the carotid plaques in both the occluded and the contralateral side was investigated because echomorphology predicts carotid stenosis progression and the occurrence of cerebrovascular events.[19,20,23] The distribution of echolucent/echogenic plaques did not differ significantly on the occluded and contralateral side. On the contralateral side, 43.3% of the plaques were echolucent, and the average calculated stenosis was 61.5%. These characteristics, together with an incidence of 15.8% vertebral artery stenosis, represent a population at high risk of cerebrovascular events.

Patients with ipsilateral ICAO should undergo routine investigation of the contralateral carotid artery more frequently than individuals without a history of ICAO.[21,22] Additionally, prophylactic carotid endarterectomy for 60% to 69% contralateral carotid artery stenosis has been advocated.[22] The results of other studies[24,25] also support the concept that in internal carotid arteries with a moderate degree of stenosis (defined as 50% or more[24] or 50% to 79%[25]) the risk of progression of carotid stenosis increases steadily with time to severe stenosis or even complete occlusion

(relative risk, 3.34).[24] Furthermore, as they progress, they become more symptomatic.[22,24,25]

Atherosclerotic disease of the vertebral artery is commonly associated with internal carotid stenosis.[26,27] Despite the possible differences in plaque appearance between extracranial vertebral and internal carotid artery stenosis,[28] stroke may result from formation of emboli at the site of atherosclerotic plaque in both arteries[29]; therefore, detection of ICAO justifies investigation of the ipsilateral and contralateral vertebral arteries.

Hypertension,[6-9,30,31] smoking,[5-11,30-32] hypercholesterolemia,[9,11,12,30,31,33] and diabetes[12,14,15] are well-established risk factors for vascular disease. These risk factors were also identified with increased prevalence in our retrospective survey. These factors require treatment. Additionally, patients with diagnosed (symptomatic or asymptomatic) carotid artery stenosis should be placed on an antiplatelet agent (eg, aspirin) to reduce the occurrence of cerebrovascular events.[34]

A total of 84 (70%) patients had vascular disease in at least one noncarotid, nonvertebral arterial bed (PAD, CAD, or aortic disease). One in 3 patients had vascular disease in 2 additional arterial beds. This finding has significant implications on long-term morbidity and mortality rates.

Detection of ICAO should be considered as a marker of systemic atherosclerosis[35-37] and thus initiate a number of diagnostic and therapeutic measures[38-44] to avoid vascular events.[45,46]

Limitations

Our study has several limitations. First, because of the long study period (approximately 20 years), several patients (mainly those enrolled early in the study) were lost to follow-up. This does not allow us to comment on event rates and ultrasonographically assessed disease progression. Second, all patients in our study were referred for a surgical opinion; therefore, our patients were highly selected. Third, the international guidelines on antihypertensive and cholesterol lowering changed markedly during the past 20 years. As a result, it is possible that some patients not on antihypertensive or cholesterol-lowering treatment 20 years ago would now be receiving treatment. Such a modification would make the association between these risk factors and ICAO even stronger. Moreover, the information regarding smoking habits was based on the information provided by the patients. It is likely that some withheld the truth. Additionally, information regarding the presence of hypertension, diabetes mellitus, and hypercholesterolemia were dependent on sources before referral. Furthermore, vascular disease in other arterial beds was not always defined by imaging; thus, its incidence may have been underestimated. Finally, the renal arterial system[47] or the aortic arch was not evaluated in our study.

Conclusions

A significant association of ICAO with vascular disease in the contralateral carotid artery, other arterial beds, and a high prevalence of established vascular risk factors was demonstrated in patients presenting with symptomatic ICAO. The detection of ICAO should prompt the investigation of other arterial beds. This initiative will require cooperation between specialties. Risk factor modification may not only reduce the risk of progression of internal carotid artery stenosis to ICAO but also lead to a significant reduction in vascular events in this high-risk population.

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