Surgical vs medical treatment for isolated internal carotid artery elongation with coiling or kinking in symptomatic patients: A prospective randomized clinical study

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Background: **Whether surgically correcting symptomatic carotid elongation with coiling or kinking in the absence of an atherosclerotic lesion of the carotid bifurcation (isolated elongation) is effective in preventing stroke remains a controversial issue. The hypothesis behind this study was that surgical correction of symptomatic isolated carotid elongation with coiling or kinking could yield better results, in terms of stroke prevention and freedom from late stroke or carotid occlusion, than medical treatment.**

Methods: **We conducted a prospective clinical study randomly assigning symptomatic patients with isolated carotid elongation to undergo either elective surgery or medical treatment, with surgery reserved for any new onset or worsening of symptoms. The follow-up ranged from 1 month to 10 years (median, 5.9; mean, 6.2 years) and was obtained for all patients. The study end points were perioperative (30-day) stroke and mortality, late stroke, and stroke-related death and late carotid occlusions.**

Results: **Ninety-two patients were randomly assigned for surgery and 90 for medical treatment. Overall, 139 carotid surgical corrections were performed in 129 patients. All 92 patients in the surgical arm had an elective operation; 10 of these patients later developed symptoms on the opposite side (7 hemispheric and 3 retinal transient ischemic attacks) and had contralateral internal carotid artery surgery. An additional 37 patients (41.1%) randomly assigned to medical treatment crossed over to the surgical group within a mean of 16.8 months after randomization due to new hemispheric symptoms or worsening nonhemispheric complaints. There were no perioperative strokes or deaths. The incidence of late hemispheric and retinal transient ischemic attacks was significantly lower in the surgical than in the medical group, respectively, 7.6% (7 of 92) vs 21.1% (19 of 90) ($P = .01$) and 3.2% (3 of 92) vs 12.2% (11 of 90) ($P = .03$). Late strokes, 2 (2.2%) of which were fatal, occurred only in the medical group (6 of 90, 6.6%; $P = .01$). Late carotid occlusions also developed only in the medical group (5 of 90, 5.5%; $P = .02$). All surgically treated carotid elongations were analyzed histologically and 78 (56.%) of 139 showed atypical and typical patterns of fibromuscular dysplasia.**

Conclusions. **The overall results of this trial indicate that surgical correction of symptomatic isolated carotid elongations with coiling or kinking is better for stroke prevention than medical treatment. (J Vasc Surg 2005;42:838-46.)**

Although there are numerous studies in the literature on carotid elongation with coiling or kinking in the absence of atherosclerotic lesion of the carotid bulb (isolated elongation), many doubts remain as to its etiology, clinical role, and best management. The only aspect fully clarified concerns the terminology, introduced by Metz et al,[1] and Wiebel and Fields[2] in the 1960s: *coiling* is an elongation of the internal carotid artery (ICA) in a restricted space, causing tortuosity and resulting in a C- or S-shape curvature or a circular configuration, and *kinking* is a variant of coiling, that is, an angulation of one or more segments of the ICA often associated with a significant degree of stenosis.

These are relatively common angiographic findings, more frequently located in the lower rather than upper half of the ICA,[3] affecting up to 16% of subjects studied[1-2,4-5]; however, patients with hemispheric ischemic symptoms or aspecific neurologic complaints account for only a small percentage of these (approximately 4% to 20%).[6,7] A casual relationship between these anomalies and the clinical onset of neurologic signs, especially the nonhemispheric, is not easy to establish, also because of the frequently concomitant atherosclerotic occlusive disease at the site of the carotid bifurcation.[3,8-17]

The management of these conditions thus remains controversial, and differentiating between the therapeutic options and assuring the best care for these patients is still a challenge for neurosonographers and vascular surgeons.

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Competition of interest: none.

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We undertook a prospective, randomized, clinical trial to determine which treatment, surgical or medical, resulted in a higher stroke prevention rate, greater freedom from stroke, and a lower late ICA occlusion rate for patients with isolated carotid elongation with coil or kink (ICECK).

METHODS

Study design and objective. The hypothesis behind this single-center prospective randomized clinical study was that surgical correction of ICECK could yield better results, in terms of stroke prevention and freedom from late stroke or carotid occlusion, than medical treatment. The protocol was approved by the institutional review board of Padua University, Padova, Italy. All subjects provided written informed consent.

Patients. Over a 10-year period, all consecutive patients admitted to our institution with hemispheric and nonhemispheric ischemic neurologic signs and ICECK, as assessed by a duplex ultrasound (DUS) scan, were eligible for the study. Patients were ineligible if they had previously undergone ICA surgery or endovascular treatment, if they were on long-term anticoagulation or aspirin therapy, had aspirin intolerance, a life expectancy of <3 years, or DUS findings of nonisolated elongation, that is, the presence of an atherosclerotic lesion >50% at the carotid bifurcation associated with distal elongation, in which the distal tip of the plaque serves as fulcrum for the angulation.

Because the morphologic identification of ICECK is sometimes subjective at the DUS scan, assessment of frequency shifts and spectral analysis may be impeded by flow disturbances related to the geometry of the elongation, only ICECK causing significant blood flow changes with a peak systolic velocity of >150, but <240 cm/s, with spectral broadening, were considered.[18] Patients were examined in a neutral position. Head and neck postures identified by the patients as the origin of their symptoms were also reproduced.

Patients were all interviewed and evaluated by two experienced neurologists to establish whether there was a potential relationship between their symptoms and ICECK, having ruled out any neurologic mimics, concomitant underlying cardiac disease, untreated hypertensive and metabolic diseases, labyrinthine disorders, orthostatic hypotension, and even cervical spondylosis. Patients with nonhemispheric symptoms, such as dizziness, blurred vision, lateral homonymous hemianopsia, gait instability, transient syncopal episodes, and drop attacks, were enrolled only (1) if they had more than one symptom impairing daily activities, and only after at least 3 months of appropriate antiplatelet therapy, and (2) if, in the event of their having an ipsilateral hypoplastic vertebral artery, the compression test on the dominant vertebral artery was negative for the onset of complaints.

The aim of the compression test was to reproduce symptoms similar to those for which the patient complained. It consisted of direct vertebral artery compression using a Doppler probe with the patient standing. Each vertebral artery was compressed either at its V_1 segment (at the root of the neck, posterolaterally to the sternocleidomastoid muscle), or at the V_3 segment (at the suboccipital triangle, between the occipital bone and the transverse process of the atlas). The compression lasted from 5 to 20 seconds, but was immediately stopped when the first induced neurologic sign appeared.[19]

After clinical validation by the neurologists, all eligible patients were invited to take part in the study. They all had a cerebral computed tomography (CT) scan, and all DUS findings were confirmed by biplane carotid angiography (during the earlier part of the study), CT angiography, or magnetic resonance (MR) angiography, which also excluded significant intracranial arterial stenoses.

Patients were randomly assigned (using sealed opaque envelopes) to either surgical correction or aspirin therapy at 100 mg/day (dosages of aspirin available in Europe are 75, 100, 150, 325, and 500 mg). Patients randomized to receive medical treatment started taking aspirin immediately. Patients randomized to undergo surgery were scheduled for operation within 30 days of randomization.

Patients in the surgical group with nonhemispheric symptoms and bilateral ICA involvement were operated on the side where the peak systolic velocity was higher. All patients in the surgical group were also evaluated by two neurologists on reawakening from the anesthesia and immediately before discharge.

All patients were scheduled for regular clinical checkups after 1, 6, and 12 months, and then every 6 months during the follow-up. At each visit, subjects were examined by two neurologists, and a DUS scan was repeated. Patients, families, and physicians were instructed to contact the neurologist or one of the investigators on the surgical team in the event of any suspected new neurologic episode. Follow-up ranged from 1 month to 10 years (median, 5.9; mean, 6.2 years).

Surgical technique. All surgical procedures were performed by the same author (E. B.) with patients under deep general anesthesia and cerebral protection involving continuous perioperative electroencephalographic (EEG) monitoring for selective shunting. Shunting criteria were based exclusively on EEG changes consistent with cerebral ischemia. All operations included the following steps:

1. ICA transection at the bulb, with an incision almost longitudinal to the common carotid artery (CCA), taking a large patch and leaving a large hole in the CCA;
2. ICA straightening after all fibrous bands had been completely severed;
3. cephalad ICA intraluminal dilation using graduated olive-tipped metal dilators; and
4. caudal end-to-side ICA reimplantation on the lateral wall of the CCA (Fig 1).

At the end of the surgical procedure, the length of the corrected elongation was calculated in all patients by measuring the distance between the original bifurcation and the reimplantation site. Completion imaging studies were not performed.

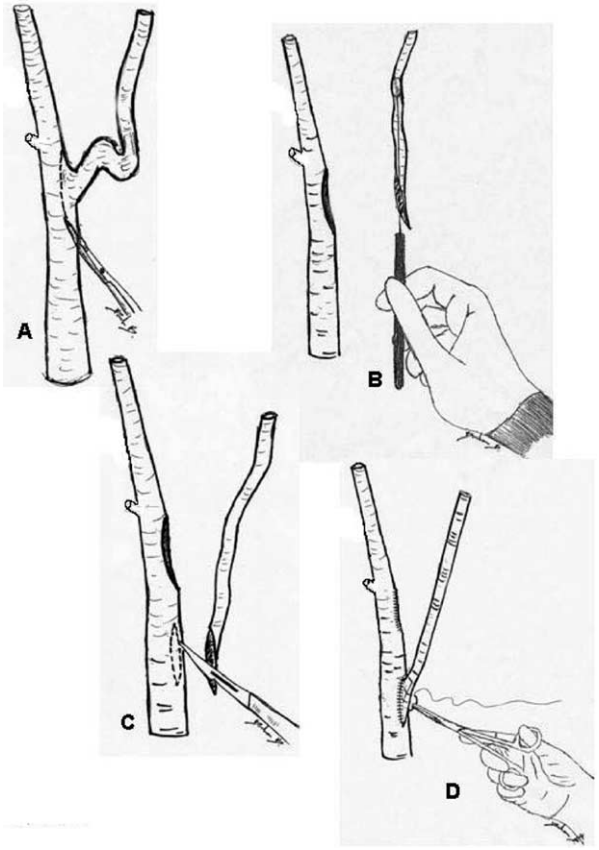

Fig 1. (A) The internal carotid artery is transected at the bulb with an incision almost longitudinal to the common carotid artery. **(B)** After its straightening, the internal carotid artery is cephalad dilated using graduated olive-tipped metal dilators. **(C)** A large matching elliptic longitudinal window is cut in the lateral wall of the common carotid artery at the level of the reimplantation site, and then, **(D)** the internal carotid artery is caudal end-to-side reimplanted in the common carotid artery.

All operated patients remained in the recovery room for 2 to 4 hours, until their blood pressure and neurologic status were considered acceptable, and then were transferred to the surgical ward. Patients with severe headache were monitored for hyperperfusion syndrome, and hypertension was treated aggressively. Most patients were discharged 24 to 48 hours after surgery.

Histologic examination. A large matching elliptic longitudinal window was always cut in the lateral CCA wall on a level with the ICA reimplantation site and examined histologically together with a circular histologic specimen 2 to 3 mm thick routinely obtained at the ICA origin after its transection. All arterial wall fragments were included in paraffin and sections 7 μm thick were cut and stained with haematoxylin and eosin, Weigert van Gieson and Alcian Pas. Immunohistochemistry was performed for smooth muscle cells (α-actin, 1:50; Dako, Glostrup, Denmark), leucocytes (CD 45, 1:20; Dako), T-lymphocytes (CD 3, 1:100; Novocastra, Newcastle upon Tyne, UK), B-lymphocytes (CD 20, 1:100, Dako), macrophages (CD 68, 1:50, Dako) and endothelial cells (CD 31, 1:30; Dako). All histopathologic tests were performed by two experienced pathologists dedicated to the study of cardiac and vascular diseases (G. T. and A. A.).

End points. The study end points were perioperative stroke and death, nonrecurrence or relief of nonhemispheric symptoms, late stroke, stroke-related death, and late ICA occlusion rates. *Minor stroke* was defined as a minimal, stabilized focal neurologic deficit of acute onset and persisting for >24 hours but not leading to disability or any significant impairment in activities of daily living. *Major stroke* was defined as a deficit lasting >30 days and inducing a change in lifestyle.

Cerebral CT or MR scans were performed in all patients presenting a new neurologic deficit. Other complications and events observed during the follow-up were recorded in accordance with the guidelines of the ad hoc committee on reporting standards for cerebrovascular disease.[20]

Statistical analysis. All values are expressed as mean ± SD. Continuous data were compared using Student's *t* test. Frequencies and categoric data were compared with the χ^2 or Fisher's exact test, as appropriate. All tests were two-tailed. Cumulative life-table analyses (Kaplan-Meier method) were performed to assess the freedom from stroke and late ICA occlusion in the two groups. Life-tables curves were compared with the log-rank test. For an estimated difference of 10% in the nonrecurrence of symptoms and stroke prevention between the two groups, with a power of 80% and a significance level of $P < .05$, it was calculated that each study group had to include 90 patients. Within each group, patients were stratified by the morphologic feature of the elongation in "coil" and "kink" patients.

RESULTS

Patient characteristics and assigned treatment. Between July 1994 and June 2004, 200 patients were eligible for the study. Three died before randomization (two in car accidents and one of pneumonia) and 15 refused randomization. The remaining 182 patients formed the treatment groups: 92 patients were assigned to surgery and 90 to medication.

The baseline characteristics of these patients are summarized in Table I. Demographic details, presence of coil or kink, coexisting conditions, cardiovascular risk profiles, features of contralateral ICA and vertebral arteries, and cerebral CT findings were comparable in the two groups. Overall, the elongation involved the ICA bilaterally in 94 patients (51.6%): 51 surgical (55.4%) and 43 medical patients (47.8%) (Table I). Cerebral CT showed ischemic lesions in 44 (31.4%) of 140 patients with hemispheric or retinal transient ischemic attacks (TIAs), in 20 (90.1%) of 22 patients with stroke, and in 4 (11.1%) of 36 patients with mixed or nonhemispheric symptoms.

Overall, 139 ICA surgical corrections were performed in 129 patients. All 92 patients in the surgical arm had elective operation; 10 patients later developed symptoms on the opposite side (7 hemispheric and 3 retinal TIAs) and

Table I. Patient characteristics

	Surgical group (n = 92) (%)	*Medical group (n = 90) (%)*
Age (yr)*	74 ± 5.9	73.8 ± 6.1
Male gender	34 (36.9)	29 (32.2)
Coiling	16 (17.4)	21 (23.3)
Kinking	76 (82.6)	69 (76.7)
Risk factors		
Hypertension†	74 (80.4)	80 (88.8)
Hyperlipidemia‡	57 (61.9)	63 (70)
Current smoker or history of smoking	77 (83.7)	71 (78.9)
Diabetes mellitus	44 (47.8)	49 (54.4)
Coronary artery disease§	31 (33.6)	24 (26.6)
Peripheral arterial disease/AAA	17 (18.4)	15 (16.7)
Symptomatic disease		
TIAs	57 (62)	51 (56.7)
Amaurosis fugax	15 (16.3)	17 (18.9)
Stroke	12 (13)	10 (11.1)
Nonhemispheric symptoms	8 (8.7)	12 (13.3)
Mixed (hemispheric + nonhemispheric) symptoms	10 (10.8)	6 (6.6)
Contralateral carotid artery		
occlusion	11 (11.9)	8 (8.9)
elongation	51 (55.4)	43 (47.8)
normal	21 (23)	26(28.9)
stenosis <50%	9 (9.7)	13 (14.4)
Ipsilateral vertebral artery		
hypoplastic	4 (4.3)	3 (3.3)
normal	57 (61.9)	64 (71.1)
elongated	27 (29.3)	21 (23.3)
stenotic >50%	1 (1.1)	0
stenotic <50%	3 (3.2)	2 (2.2)
Contralateral vertebral artery		
hypoplastic	2 (2.2)	1 (1.1)
normal	55 (59.8)	59 (65.6)
elongated	30 (32.6)	26 (28.9)
stenotic >50%	0	1 (1.1)
stenotic <50%	5 (5.4)	3 (3.3)
Ischemic lesion at cerebral CT	36 (39.1)	26 (28.8)
ipsilateral	31	21
contralateral	4	5

All differences between the groups were insignificant unless otherwise indicated.

AAA, Abdominal aortic aneurysm; *TIA,* transient ischemic attack; *CT,* computed tomography.

*Data are expressed as means ± SD.

†Defined as elevated blood pressure treated with medication.

‡Defined as elevated cholesterol or triglycerides treated with medication.

§Defined as a medical history, clinical symptoms, or electrocardiographic signs of myocardial ischemia.

Table II. Late results*

	Surgical group n = 92 (%)	*Medical group n = 90 (%)*	P
TIA	7 (7.6)	19 (21.1)	0.01
Ipsilateral	0	19	
Contralateral	7	0	
Stroke	0	6 (6.6)	0.01
Ipsilateral	0	6	
Contralateral	0	0	
Amaurosis fugax	3 (3.2)	11 (12.2)	0.03
Ipsilateral	0	7	
Contralateral	3	3	
Deaths	8 (8.7)	11 (12.2)	NS
Stroke-related death	0	2 (2.2)	NS
Carotid occlusion	0	5 (5.5)	0.02
Nonhemispheric symptoms	0	12 (13.3)	<.001

TIA, Transient ischemic attack; *NS,* not significant.

*1 month to 10 years (median, 5.9; mean, 6.2 years).

had contralateral ICA surgery (Table II). An additional 37 patients (41.1%) randomly assigned to medical treatment crossed over to the surgical group within a mean 16.8 months (range, 4 to 67 months) after randomization due to new hemispheric symptoms in 34 (4 strokes and 19 hemispheric and 11 retinal TIAs) or worsening non-hemispheric complaints in three, none of whom had a contralateral carotid occlusion or an ipsilateral hypoplastic vertebral artery (Table II). Nine (6.4%) intraoperative EEG changes consistent with cerebral ischemia and requiring the selective use of an intraluminal shunt were recorded. No intracranial aneurysms were diagnosed in patients of either group. The ICAs were shortened by a mean 2.8 cm (range, 1.9 to 5.7 cm).

End points and adverse events. There were no perioperative strokes or deaths. No hyperperfusion syndrome was observed in any patient. There were 11 hypoglossal nerve injuries (8 in the randomized surgical group and 3 in the group converting to surgery), all caused by nerve retraction or stretching, since nerve function was fully recovered in all patients ≤1 month. Other perioperative complications included two myocardial ischemic events, successfully managed with medical treatment, and one neck hematoma requiring operative evacuation, with no further complications.

None of the patients were lost to follow-up (Table II). The incidence of late hemispheric TIAs was 7.6% (7 of 92) in the surgical group and 21.1% (19 of 90) ($P = .01$) in the medical group. The incidence of retinal TIAs was 3.2% (3 of 92) in the surgical group and 12.2% (11 of 90) ($P = .03$) in the medical group. Patients with new hemispheric symptoms in the surgical group had bilateral ICA involvement with all symptoms contralateral to the revascularized hemisphere, so they underwent bilateral carotid surgery within a mean 26.2 months after the first operation.

All patients in the medical group who complained of recurrent hemispheric and retinal TIAs crossed over to the other group and underwent surgery. All patients in the surgical group with nonhemispheric symptoms had complete relief from their complaints, whereas all patients in the medical group with such symptoms reported persistent or worsening symptoms ($P < .001$) (Table II). Three of these patients crossed over to the surgical group and obtained full relief from their symptoms.

There were no late strokes in the surgical group, but these did affect 6.6% (6 of 90) in the medical group ($P = .01$). These events all occurred on awakening in the morning, the neurologist was contacted by telephone, and the patients were immediately admitted to the hospital. Two (2.2%) of the 90 patients had strokes that were major in

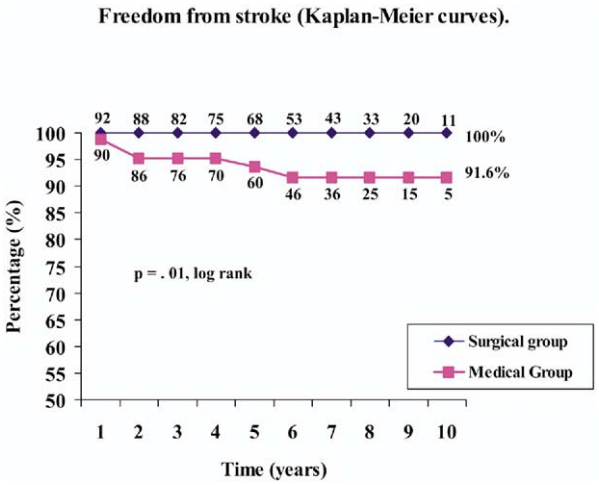

Fig 2. Kaplan-Meier life-table analysis of freedom from stroke between surgical and medical groups. Number of patients at risk for each interval is shown for each group. Percentages on the right represent freedom from stroke at 10 years for the groups: the difference was significant (p=0.01). Range of standard error for medical group is 0% to 4%.

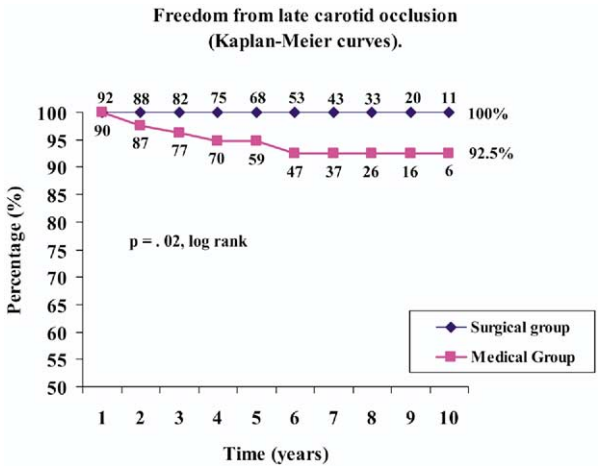

Fig 3. Kaplan-Meier life-table analysis of freedom from late carotid occlusion between surgical and medical groups. Number of patients at risk for each interval is shown for each group. Percentages on the right represent freedom from stroke at 10 years for the groups: the difference was significant (p=0.02). Range of standard error for medical group is 0% to 4%.

severity—29 and 24 points on the National Institutes of Health (NIH) stroke scale—and proved fatal. The strokes occurred 14 and 18 months after randomization and were associated with ICA occlusion, diagnosed by DUS scan, and confirmed by arteriography, despite a last control DUS scan performed, respectively, 49 and 8 days before the stroke that showed a patent artery. In both cases, cerebral CT showed a large area of infarction in the elongated ICA territory. The other four strokes were minor (4, 4, 5, and 6 points on the NIH stroke scale), all related to the hemisphere pertinent to the elongated ICA and DUS findings were no different from those observed at the baseline DUS scan. No ischemic lesions were evidenced on cerebral CT or MR scans. The patients were monitored until their neurologic recovery reached a plateau and then underwent uneventful ICA correction.

Kaplan-Meier analysis showed that the respective freedom from stroke at 1, 3, 5, 7, and 10 years was 100%, 100%, 100%, 100%, and 100% for the surgical group and 98.9%, 95.3%, 93.7%, 91.6%, and 91.6% for the medical group (P = .01) (Fig. 2).

No carotid restenoses were detected after surgical repair during the follow-up. In addition, late ICA occlusions were only observed 5 (5.5%) of 90 in the medical group (P = .02): two caused fatal strokes, whereas the other three occurred asymptomatically and were detected at the last scheduled visit. Angiography confirmed the DUS finding. In all cases, prior DUS studies had shown no signs of progression to occlusion.

Kaplan-Meier analysis showed that the respective freedom from ICA occlusion at 1, 3, 5, 7, and 10 years was 100%, 100%, 100%, 100%, and 100% for the surgical group and 100%, 96.3%, 94.8%, 92.5%, and 92.5% for the medical group (P = .02) (Fig. 3). No significant statistical difference was found in the incidence of late strokes or ICA occlusions between coil and kink patients within the medical group.

Nineteen late deaths (10.4%) occurred in the series as a whole. Although two stroke-related deaths occurred in the medical group (2.2%), the late mortality rate was similar in the surgical (8.7%, 8 of 92) and medical groups (12.2%, 11 of 90). The cause of late death was primarily cardiac-related (42%, 8 of 19).

Histopathologic findings in carotid specimens. All examined arterial specimens disclosed histologic abnormalities. These were nonatherosclerotic and noninflammatory alterations primarily involving the media and intima of the arterial wall. Three main types of lesion could be identified in the tissue obtained at the origin of the ICA:

1. aspecific degeneration in the tunica media, consisting either of elastic fragmentation and disorganization, fibrosis, cystic medial necrosis, and/or medionecrosis, observed in 61 specimens (43.9%) (Fig 4);
2. tunica media hyperplasia with increased extracellular mucoid Alcian-Pas-positive matrix surrounding variously oriented smooth muscle cells, accounting for the tunica media thickening, detected in 54 vessels (38.9%) (Fig 5); and
3. a specific pattern of classic fibromuscular dysplasia, namely thickened fibromuscular hyperplasia alternating with areas of pronounced thinning of the media and superimposed intimal fibromuscular hyperplasia, diagnosed in the remaining 24 cases (17.2%) (Fig 6).

The same histologic findings as in the ICA were also found in the elliptical area removed from the CCA. The same histologic findings were found in both sides in pa-

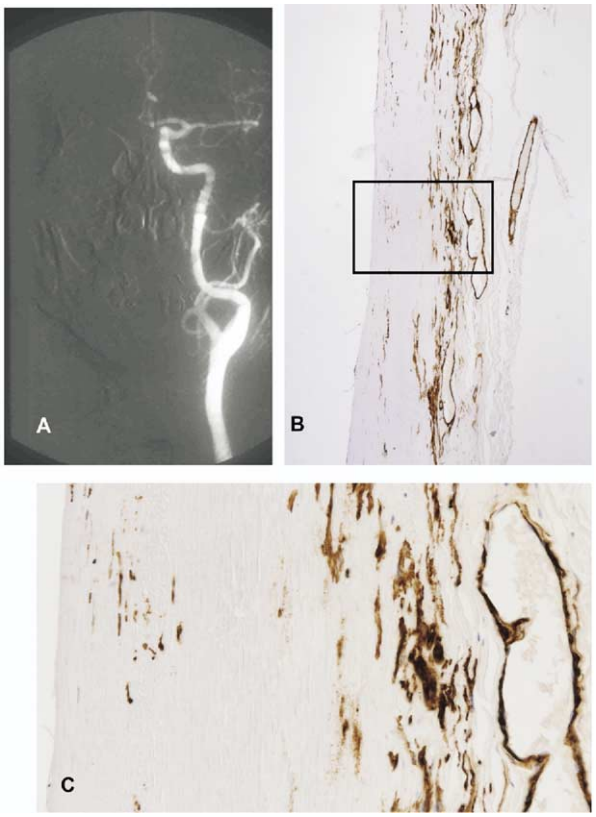

Fig 4. **(A)** Angiographic picture of a left carotid elongation with kinking causing hemispheric symptoms. **(B)** Tranparietal section of the carotid artery at its origin showing degenerative findings in the tunica media, characterized by medionecrosis. Immunohistochemical staining with anti-α actin antibody for the identification of smooth muscle cells (in brown). Note the massive loss of smooth muscle cells within the tunica media. **(C)** Close-up of B. Original magnifications: B = x 8; C = x 31.

tients who underwent bilateral carotid correction. No relationship was observed between the morphologic feature of the elongation or the nature of the symptoms and the type of histologic finding.

DISCUSSION

Although the thromboembolic mechanism, secondary to endothelial lesions due to local flow alterations at the site of arterial bending, has been judged responsible for the occurrence of many ischemic symptoms in patients with ICECK,[3,7,21] the hemodynamic mechanism seems to play an important part, when the elongation is narrow, in both neutral and dynamic conditions.[7,21,22] This theory is supported by experimental studies demonstrating that blood flow may be reduced by >40% with an angle of 60° on the onside of the curve along the ICA and by >60% with an angle of 30°,[23] so that the smaller the angle, the more hemodynamically significant the kink and, consequently, the greater the blood flow reduction.

Transient hypotension, such as occurs during sleep, on neck extension, or bending or turning the head from side to

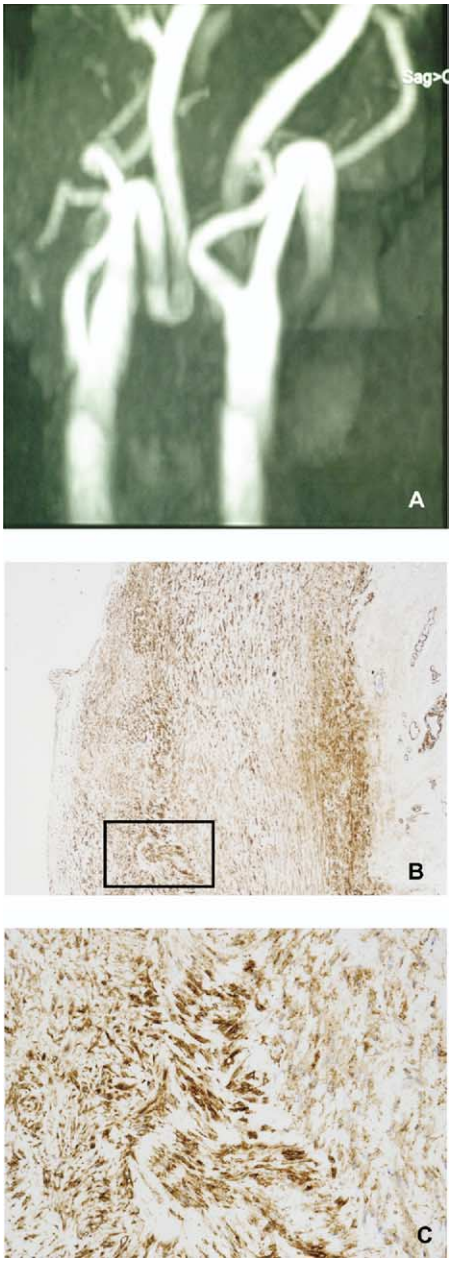

Fig 5. **(A)** Angiographic picture of bilateral carotid elongation with kinking causing right hemispheric symptoms. **(B)** Transparietal section of the carotid artery at its origin showing the tunica media hyperplasia characterized by increased extracellular matrix surrounding variously-oriented smooth muscle cells. Immunohistochemical staining with anti-α actin antibody for the identification of smooth muscle cells (in brown). Note the high number of variously-oriented smooth muscle cells within the tunica media. **(C)** Close-up of B. Original magnifications: B = x 8; C = x 31.

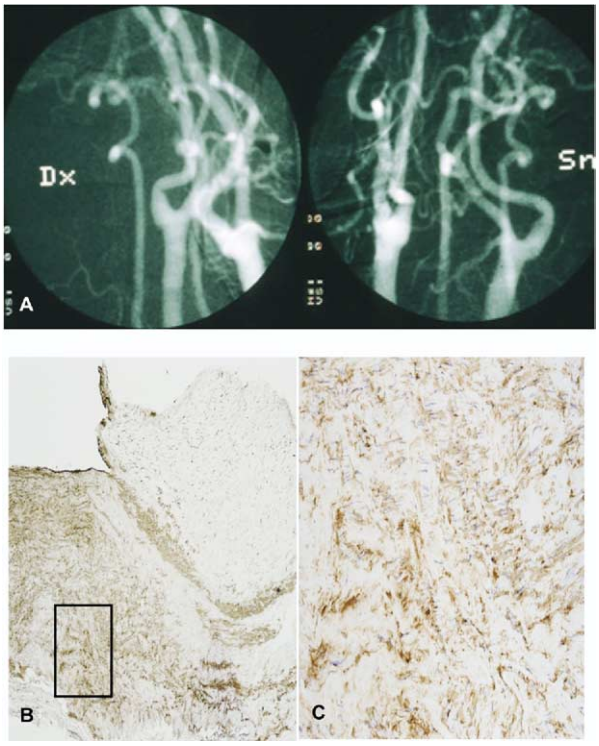

Fig 6. (A) Angiographic picture of bilateral carotid elongation with coiling causing right hemispheric symptoms. **(B)** Transparietal section of the carotid artery at its origin showing a classic fibromuscular displasia characterized by thickened fibromuscular hyperplasia alternating with thinning of the media and superimposed intimal hyperplasia. Immunohistochemical staining with anti-α actin antibody for the identification of smooth muscle cells (in brown). Note the thinning of the media with superimposed intimal smooth muscle cell hyperplasia. **(C)** Close-up of B. Original magnifications: B = x 8; C = x 31.

side, can make the ICA collapse at the point of maximal angulation and reduce the blood flow, causing hemispheric or global ischemia, despite the absence of fixed mural disease.[1,22,24] In most cases, however, such symptoms are promptly relieved by resuming a neutral head position.

The distinction between carotid coiling and kinking is usually based on traditional or CT and MR angiograms. Each of these anatomic varieties, however, can trespass one into another in relation of the imaging projection, so mixed forms can be observed.[6] In addition, there is often a marked discrepancy between angiographic/imaging features and intraoperative findings, with the angiographic/imaging feature consistently under-reading the degree of the angulation,[3] the hemodynamic importance of which may be clearly assessed only by DUS evaluation.[8] This is why we considered in this study only ICECK with ultrasound evidence of significant blood flow changes.

The outcome of this study on the safety and effectiveness of surgical ICECK correction in affording lasting protection against recurrent symptoms correlates well with the findings in many previously reported series.[4-8,10-17,21,22,25] All such earlier studies were retrospective, however, either forming part of larger series[6,11,16,17] or dealing with smaller series concerned exclusively with the surgical management of such anomalies.[5,12-15,22,25] None of these earlier studies were randomized, and the small sample sizes and anecdotal nature of the data made it impossible to draw any definitive conclusions.

Although a correlation between ICEKC and ischemic stroke has been suggested in some studies,[4,11,15,16,26] the lack of a group of unoperated patients serving as controls prevented any valid comparison between the two management strategies, so no conclusive proof emerged on the superiority of surgical treatment for stroke prevention. Data emerging from this trial, on the other hand, confirm the effectiveness of surgery in terms of stroke prevention, a finding further emphasized by the fact that four of the six patients in the medical group who experienced a stroke during the follow-up period crossed over to the other group, had surgery, and then reportedly had no new minor or major neurologic events. Late mortality was related more to cardiac than to cerebrovascular events in both groups, however, so the operated patients' freedom from stroke was not translated into a longer survival.

We are unable to explain why some patients with ICECK have hemispheric symptoms while others have nonhemispheric complaints. In the case of the latter, we might expect an involvement of the vertebral artery, but this does not seem to be the case in our study. Most of the ipsilateral vertebral artery lesions were mild ostial atherosclerotic stenoses (3 of 92, 3.2%) or a nonstenotic elongation of a dominant vertebral artery (27 of 92, 29.3%), and the remaining (4 of 92, 4.3%) were hypoplastic vertebral arteries not requiring surgical treatment. Furthermore, none of the patients underwent revascularization of the ipsilateral or contralateral vertebral artery before or after ICA revascularization. Even though a connection between ICECK and nonhemispheric complaints is difficult to hypothesize, the total and persistent symptom relief obtained in all surgical patients, including those crossing over from the medical group, remains an indisputable result, warranting a careful consideration of surgical correction for patients with nonhemispheric complaints.

The finding that no carotid restenoses were detected during the follow-up period correlates well with the recently published report on eversion carotid endarterectomies performed in patients with severe symptomatic and asymptomatic carotid stenosis.[27] This is probably related to the reimplantation technique of the ICA in the CCA (two large arteries that serve to patch each other) that simplifies the arteriotomy closure and prevents potential ICA narrowing secondary to a longitudinal primary or patched closure through or just beyond the critical distal endpoint, which seems to be the main cause of recurrent carotid disease after a traditional carotid endarterectomy procedure.

That late ICA occlusions only developed in the medical group suggests that untreated ICECK, like atherosclerotic lesions, may progress to sudden occlusion, and this represents an important addition to our understanding of the

anatomic and clinical history of this anomaly. However, although ICA thrombosis secondary to the progression of an atherosclerotic plaque at the bifurcation affects the whole ICA, from the bifurcation to the origin of the ophthalmic artery, thrombosis secondary to the occlusion of an elongation seems to spare the first few centimeters of the ICA, as if the first stretch of the ICA could serve as a stiff stent.

A correlation between ICECK and occlusion has already been reported,[10,28] but no information is available on the potential onset of neurologic warning signs. In this trial, late occlusion seemed to follow the *all or nothing* law: two of the five occlusions occurred during sleep and resulted in fatal strokes, whereas the other three developed asymptomatically and were discovered during routine DUS scans. This may be of clinical relevance in the management of asymptomatic patients.

Indeed, since the elongation usually involves the ICA bilaterally (>50% in this series), in the case of ICA elongation and contralateral carotid occlusion, it may be supposed that this latter event occurred in an ICA with a morphology and spatial configuration similar to the elongated patent vessel. Therefore, surgery could be extended to asymptomatic patients with ICECK and contralateral occlusion or to asymptomatic patients with ICECK whose imaging features or DUS findings support the presence of a partial obstruction in stable condition[4]: it may be that a certain head position causes a subocclusion of the ICA lumen and remaining longer in such a position, as in sleep, can give rise to complete ICA thrombosis.

This study unequivocally proved that 56.1% of elongated ICAs show atypical (tunica media hyperplasia with increased extracellular mucoid Alcian-Pas-positive matrix surrounding variously oriented smooth muscle cells, accounting for the tunica media thickening in 38.9%) (Fig 5) and typical patterns of fibromuscular dysplasia (thickened fibromuscular hyperplasia alternating with areas of pronounced thinning of the media and superimposed intimal fibromuscular hyperplasia in 17.2%) (Fig 6) on histologic examination.

Fibromuscular dysplasia is defined as a segmental angiopathy of uncertain origin affecting medium-sized vessels.[29-32] In the carotid district, this condition was first reported as an angiographic finding, with the typical "string of beads" pattern,[29] and then described histologically.[33] Concomitant intracranial aneurysms have also been documented in approximately 25% of patients with fibromuscular dysplasia.[34] Contrary to the common belief that fibromuscular dysplasia involves only the middle and upper segments of the ICA while the CCA and the proximal 2 to 2.5 cm of the ICA are almost always spared,[8,34] we found the CCA and the first few centimeters of the ICA were also involved.

No concomitant intracranial aneurysms were observed in our patients, confirming the suggestion that ICA elongation is dysplastic in nature,[6,11,17,35] possibly representing a different morphologic pattern of the same histologic substrate, and this could change the common attitude to this arterial anomaly. The age of our patients and the histologic observation of degenerative changes in the tunica media are consistent with an acquired arterial wall weakening (or "aging"), accounting for such elongation and angulation. It is worth noting, however, that in many cases, a classic histologic substrate of fibromuscular dysplasia was seen to result in elongation and angulation instead of stenosis and in the angiographic picture of a "string of beads".

CONCLUSION

The most important findings of this study are:

1. surgical correction of symptomatic ICECK prevents stroke better than medical treatment;
2. patients with nonhemispheric complaints reported total symptom relief after carotid surgery;
3. ICECK may progress to occlusion; and
4. the histologic examination of the ICA reveals nonatherosclerotic, noninflammatory changes in the arterial wall.

Although this is the first prospective randomized trial on this issue, it remains a single-institution series. We believe that the issue is so important that before making any definite conclusions and indicating potential guidelines for the best treatment for patients with ICECK, a multicenter, prospective, randomized study with adequate power would be appropriate.

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INVITED COMMENTARY

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It is unusual to see symptomatic patients with isolated internal carotid artery (ICA) coils or kinks but no evidence of atherosclerosis. It is unclear whether this problem is more prevalent in Italy, goes unrecognized because of the absence of atherosclerotic disease in the carotid bulb during duplex ultrasound screening, or simply is not addressed by vascular surgeons because of the absence of data to support intervention combined with the controversial nature of the problem. The current article provides data from a large number of patients about the potential value of surgical reconstruction. One hundred forty-six (81%) of the 182 patients had hemispheric symptoms, and two thirds were female. The absence of early and late postoperative stroke or stenosis/occlusion in the 92 surgical arm patients is highly significantly better than the 7% stroke, 37% continued symptoms, and 5% ICA occlusion rates in the 90 medical arm patients. Histopathologic examination of all surgical specimens confirmed the absence of atherosclerotic changes and showed one or more of three types of noninflammatory changes: fibrosis, cystic medial necrosis, or fibromuscular dysplasia. The operative procedure used (as illustrated in their figure 1) is straightforward: transection of the ICA at the bulb, ICA shortening, ICA intraluminal dilation, and end-to-side ICA reimplantation onto the more proximal common carotid artery. Most atherosclerotic coils and kinks cannot be treated this way because of the axial tongue of plaque that runs through them, which requires endarterectomy and patching. The authors are to be congratulated on a well-planned and -executed study with landmark results. Now that we are confident that surgical intervention is advisable, it will be interesting to see whether more patients with this seemingly rare problem are identified.