Interactive CardioVascular and Thoracic Surgery

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*Interact CardioVasc Thorac Surg* 2007;6:369-373; originally published online Feb 9, 2007;
DOI: 10.1510/icvts.2006.137547

doi:10.1510/icvts.2006.137547

INTERACTIVE CARDIOVASCULAR AND THORACIC SURGERY

Interactive CardioVascular and Thoracic Surgery 6 (2007) 369–373

www.icvts.org

ESCVS article - Vascular thoracic

# Carotid endarterectomy in patients with acute neurological symptoms: a case-control study☆

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Received 31 May 2006; received in revised form 15 January 2007; accepted 22 January 2007

**Abstract**

**Objective:** The aim of this study was to retrospectively evaluate our experience in urgent carotid endarterectomy (CEA) in patients with acute neurological symptoms comparing them with results obtained in stable symptomatic patients in a case-control study. **Materials and methods:** From January 1996 to December 2005, 3336 consecutive CEAs were performed at our department. In 70 cases CEA was carried out in patients with acute neurological deficit; in all these patients, clinical presentations were recent (<24 h) or crescendo (defined as two or more episodes in 24 h, with complete recovery after each episode) TIAs (group 1). The control group was randomly obtained from our historical database and consisted of 352 stable symptomatic patients operated on in the same period (group 2). Early (30-day) results in the two groups were compared by $\chi^2$ and Fisher exact tests; follow-up data were analysed by life-table analysis (Kaplan–Meier test) and results in subgroups were compared by means of log-rank test. **Results:** Considering mortality and any neurological morbidity, the patients of group 1 showed a cumulative rate of death and neurological complication significantly higher than those in group 2 (5.4% and 0.3%, respectively; $P=0.005$); however, when analysing 30-day disabling strokes and deaths, the patients of group 1 had a cumulative complication rate of 1.4%, whereas in group 2 the corresponding figure was 0.3% ($P$=n.s.). In patients of group 1, univariate analysis and logistic regression for multivariate analysis for 30-day risk of stroke and death did not show any influence of comorbidities, clinical status, anatomical and surgical features. Estimated cumulative 36-month survival was significantly better in group 2 than in group 1. Considering the absence of ipsilateral stroke at 36 months, there were no differences between the two groups; however, analysing the estimated absence of any neurological events, both ipsilateral and contralateral, at 36 months, patients of group 1 had a higher risk than those of group 2. **Conclusions:** Urgent CEA in patients with recent/crescendo TIA and appropriate carotid artery lesion, carries good early and long-term results, which, however, remain slightly poorer than those obtained in symptomatic patients with a stable neurological status.


*Keywords:* Carotid endarterectomy; Acute stroke; Crescendo TIA; Unstable neurological status

## 1. Introduction

Carotid endarterectomy (CEA) is a well-accepted method for stroke prevention both in patients with moderate or severe symptomatic carotid artery stenosis and in patients with severe asymptomatic stenoses [1–3].

However, there is no evidence concerning the benefit of CEA in patients with unstable neurological symptoms, depending on the lack of studies designed to evaluate this subgroup of patients, presenting with different clinical symptoms, instrumental features and anatomical characteristics, all comprised into the definition of 'patient with acute neurological deficit'.

Recent or crescendo transient ischaemic attack (TIA), stroke in evolution and acute stroke are considered emergent conditions under a neurological point of view; in some of these clinical situations urgent CEA can be indicated. Recent guidelines [4] stated that surgical treatment should be considered feasible only in the presence of appropriate carotid lesion, such as severe stenosis, near-occlusion, acute thrombosis, presence of floating thrombus into the lumen.

In spite of these concepts, several unsolved problems and unclear points are still present, mainly related to the definition of criteria for the selection of the patient with acute neurological deficit supposed to have some benefits from CEA, with a low rate of complications in perioperative period.

The aim of this study was to retrospectively evaluate our experience in urgent CEA in patients with acute neurological symptoms comparing them with those obtained in stable symptomatic patients in a case-control study.

## 2. Materials and methods

From January 1996 to December 2005, 3336 consecutive CEAs were performed at our department; data concerning these interventions were collected and prospectively

☆ Presented at the 55th International Congress of the European Society for Cardiovascular Surgery, St Petersburg, Russian Federation, May 11–14, 2006.

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inserted in a dedicated database, containing 150 fields concerning main anatomical, clinical, instrumental and technical variables. This database also contains early and 30-day results in terms of mortality and neurological morbidity and all the clinical and instrumental data collected during follow-up.

In the examined period, 1223 CEAs were performed in patients with symptomatic carotid artery stenosis; patients were defined symptomatic if they suffered at least a TIA episode in the six months prior to the intervention or if they showed cerebral lesions dependent on operated carotid artery at preoperative computed tomography (CT) scan.

In 70 cases CEA was carried out in patients with acute neurological deficit; in all these patients, the clinical presentations were recent ($<$24 h) or crescendo (defined as two or more episodes in 24 h, with complete recovery after each episode) TIAs (group 1). The control group was randomly obtained from our historical database and consisted of 352 stable symptomatic patients operated on in the same period (group 2).

All the patients underwent preoperative duplex-scanning of extracranial vessels and angio-computed tomography (CT) scan or digital subtraction angiography (DSA) in double projection for the evaluation of cerebral parenchyma and supra-aortic vessels. Degree of stenosis was determined by means of the NASCET method [1]. The status of vertebral arteries and of intracranial vessels was also examined during the preoperative assessment with angiography or angio-CT scan.

All the patients were preoperatively visited by a consultant neurologist; in patients with acute neurological symptoms, the presence of alterated consciousness, deep or fixed neurological deficit, middle cerebral artery occlusion or ischaemic lesions $>$1 cm at CT scan were considered as a contraindication for surgical intervention. Patients not selected for surgery were admitted to the stroke unit and then medically treated. Patients selected for surgery were operated on within 24 h from the last symptom.

All the interventions were performed under general anaesthesia: somatosensory evoked potentials (SEPs) were used to monitor cerebral status during surgical intervention and to indicate when the use of shunt was necessary. Criterion for shunt insertion was defined as a reduction of N20/P25 waves higher than 75% of baseline values [5]. Surgical strategy consisted of preliminary isolation and clamping of the distal internal carotid artery [6]. Standard longitudinal endarterectomy with a wide exposure of the proximal and distal limits of the plaque was then carried out. A policy of selective patching for carotid reconstruction on the basis of age, sex, size of internal carotid artery and distal extension of the plaque was used. At the end of intervention, completion study with digital subtraction angiography in double projection was routinely performed in acute patients. At discharge all the patients underwent a new neurological examination performed by a consultant neurologist. New central neurological focal events (TIA, minor stroke, major stroke) were assessed.

Clinical and ultrasonographic follow-up was performed at 1, 6 and 12 months and then once a year. All studies were performed using the Acuson Sequoia 512 Ultrasound System (Acuson Corporation, Mountain View, CA). A 8L5 linear array probe with an operating frequency of 8.0–5.0 MHz was used in all the cases.

Early (30-day) results in the two groups were compared by $\chi^2$ and Fisher exact tests; moreover, logistic regression for multivariate analysis was used for evaluation of 30-day stroke and mortality risks (SPSS 10.0 program for Windows; SPSS Inc., Chicago, IL). Follow-up data were analysed by life-table analysis (Kaplan–Meier test) and results in subgroups were compared by means of log rank test.

## 3. Results

There were no differences between the two groups in terms of age, comorbidities and common risk factors for atherosclerosis, except for a higher prevalence of coronary artery disease and diabetes mellitus in group 1 (Table 1). Considering degree of stenosis on the operated site, patients in group 1 had a significantly higher incidence of 80% stenosis than in group 2; moreover, in patients of group 1 a higher prevalence of near-occlusion was detected (Table 2). There were no differences between the two groups regarding contralateral preoperative neurological symptoms and degree of stenosis.

In group 1 there was a significant higher incidence of shunt insertion than in group 2 (Table 3); this was due both to a significant incidence of SEPs reduction at clamping and to a different adopted strategy (a higher number of shunts routinely applied in the patient with acute neurological deficit). There were no significant differences regarding carotid reconstruction, with a wide use of patch in both groups (70% in group 1 vs. 65% in group 2).

Early and 30-day results are shown in Table 4.

Considering mortality and any neurological morbidity, the patients of group 1 showed a cumulative rate of death and neurological complication significantly higher than those in

Table 1
General patient characteristics

| | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Median age | 73 | 74 | n.s. |
| Coronary artery disease | 23 (32.8%) | 54 (18.4%) | 0.05 |
| Peripheral artery disease | 19 (27.5%) | 110 (31.2%) | n.s. |
| Hypertension | 39 (55.5%) | 213 (60.1%) | n.s. |
| Hyperlipidaemia | 38 (54.2%) | 195 (55.3%) | n.s. |
| Diabetes mellitus | 21 (30%) | 70 (19.8%) | 0.05 |

Table 2
Degree of stenosis on the operated site

| | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Stenosis 60–80% | 13 (18.5%) | 134 (38%) | 0.02 |
| Stenosis 80–99% | 49 (70%) | 210 (58.5%) | 0.06 |
| Near-occlusion | 8 (11.5%) | 8 (2.2%) | 0.001 |

Table 3
Intraoperative cerebral status monitoring and shunt insertion

| | Group 1 | Group 2 | *P* |
|---|---|---|---|
| SEPs reduction | 8 (11.5%) | 25 (7%) | 0.02 |
| Routinely applied shunt | 17 (24.2%) | 11 (3.1%) | $<$0.001 |
| Total number of shunts | 25 (35.7%) | 36 (10.2%) | $<$0.001 |

Table 4
Early and 30-day results

| | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Neurological deficits at wakening | 3 (4%) | 0 | <0.001 |
| 30-day minor stroke | 3 (4%) | 0 | <0.001 |
| 30-day major stroke | 0 | 0 | n.s. |
| Death | 1 (1.4%) | 1 (0.3%) | n.s. |

group 2 (5.4% and 0.3%, respectively); however, when analysing 30-day disabling strokes and deaths, the patients of group 1 had a cumulative complication rate of 1.4%, whereas in group 2 the corresponding figure was 0.3%. The only death in group 1 was due to a myocardial infarction, occurring on the 3rd postoperative day in a woman who underwent urgent CEA for crescendo TIAs.

In patients of group 1, univariate analysis and logistic regression for multivariate analysis for 30-day risk of stroke and death did not show any influence of the examined parameters (sex, age, diabetes, arterial hypertension, coronary artery disease, hyperlipidaemia, contralateral carotid artery occlusion, shunt insertion, kind of reconstruction).

Follow-up was performed in 368 patients (88%), with a mean duration of 24 months (range 1–108). During follow-up there were 13 deaths (five in group 1 and eight in the other group) and seven ipsilateral neurological events.

Estimated cumulative 36-month survival was significantly better in group 2 than in group 1 (97% and 91%, respectively; $P=0.03$, log-rank 4.4; Fig. 1).

Considering the absence of ipsilateral stroke at 36 months, there were no differences between the two groups (100% in group 1 and 99% in group 2; $P=0.6$, log-rank 0.22); however, analysing the estimated absence of any neurological events, both ipsilateral and contralateral, at 36 months, patients of group 1 had a higher risk than those of group 2 (88% in group 1, and 97% in group 2; $P=0.006$, log-rank 11.7; Fig. 2).

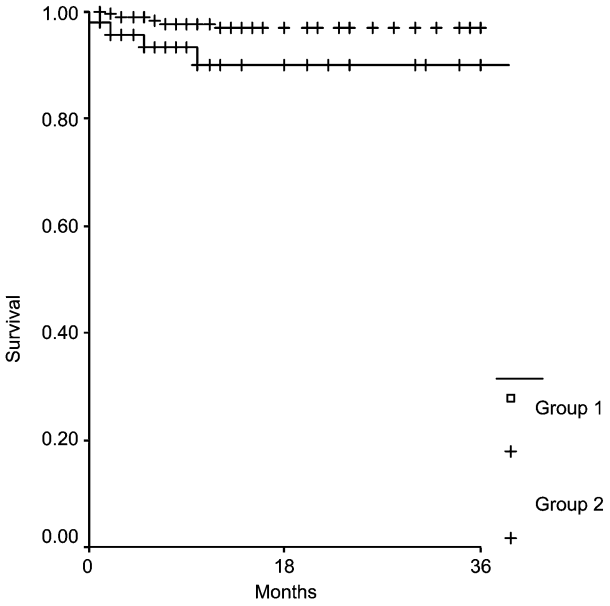
Moreover, there were no differences between the two groups in terms of 60% restenosis at 36 months (9% in group 1 and 10% in group 2; $P=0.1$, log-rank 2.2).

In patients of group 1, univariate analysis for the risk of ipsi- or contralateral neurological events during the follow-up did not show any correlation between the examined parameters (sex, age, diabetes, arterial hypertension, coronary artery disease, hyperlipidaemia, contralateral carotid occlusion, shunt insertion, kind of reconstruction) and long-term neurological events (Table 5).

## 4. Discussion

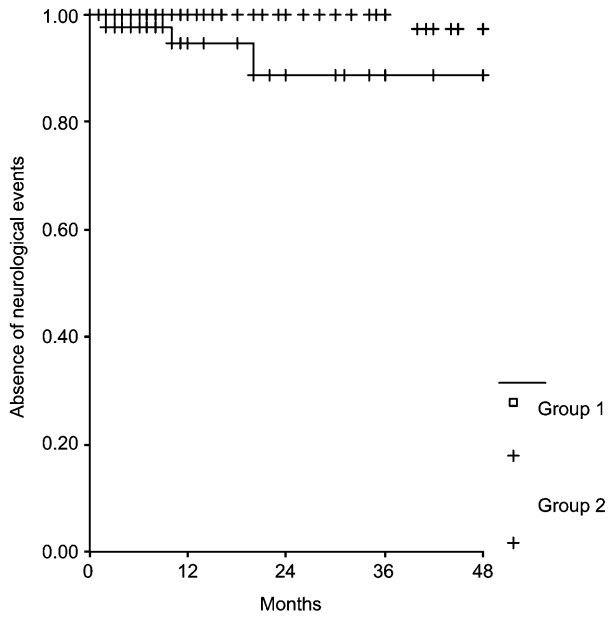
The first experiences in the treatment of ‘acute’ carotid artery stenosis were described in the early 1960s and were characterised by poor results, mainly due to postoperative intracranial haemorrhage [7–9]. As a consequence, in the following 20 years the avoidance of urgent CEA was commonly accepted worldwide and the intervention was generally delayed for up to six weeks after the clinical event [10].

In recent years, however, significant improvements in medical, surgical and anaesthesiological techniques, and the creation of territorial care networks for the treatment




| Months | 0 | 12 | 24 | 36 |
|---|---|---|---|---|
| Group 1 | 56 | 31 | 16 | 7 |
| Group 2 | 312 | 201 | 125 | 75 |

Fig. 1. Estimated cumulated 36-month survival in the two groups with number of patients at risk.




| Months | 0 | 12 | 24 | 36 |
|---|---|---|---|---|
| Group 1 | 56 | 30 | 17 | 7 |
| Group 2 | 312 | 197 | 119 | 67 |

Fig. 2. Estimated absence of any neurological events in the two groups during the follow-up with the number of patients at risk.

Table 5
Univariate analysis for neurological morbidity risk during follow-up in patients of group 1

| | Kaplan–Meier % at 2 years | Log-rank | *P* |
|---|---|---|---|
| Age | | | |
| ->79 years | 100 | 0.30 | 0.5 |
| -<79 years | 88 | | |
| Sex | | | |
| -Male | 90 | 0.45 | 0.5 |
| -Female | 80 | | |
| Patch closure | | | |
| -Yes | 86 | 0.13 | 0.9 |
| -No | 92 | | |
| Shunt insertion | | | |
| -Yes | 86 | 1.1 | 0.7 |
| -No | 80 | | |
| Coronary artery disease | | | |
| -Yes | 100 | 0.8 | 0.3 |
| -No | 93 | | |
| Arterial hypertension | | | |
| -Yes | 100 | 1.1 | 0.2 |
| -No | 90 | | |
| Diabetes mellitus | | | |
| -Yes | 100 | 1.8 | 0.1 |
| -No | 88 | | |
| Contralateral occlusion | | | |
| -Yes | 100 | 0.5 | 0.8 |
| -No | 88 | | |

of acute stroke has determined a new rising interest for the surgical treatment of patients with unstable neurological symptoms.

Particularly in the presence of recent or crescendo TIA, the role of surgical intervention seems to be really basic. TIA represents a substantial signal of danger for further, severe neurological events, with a risk of stroke of 5% in the first 48 h and of 10% within three months [11]; in patients with severe or moderate carotid stenosis on the affected hemisphere, the risk rises up to 6% in the first 48 h and to 20% within three months [12], and becomes even higher in the presence of crescendo TIAs, defined as two or more episodes in 24 h, with complete recovery after each episode [13].

On the basis of these data, the indication for urgent CEA in patients with recent/crescendo TIAs seems to be mandatory, also considering that, in most patients, the ischaemic episode is caused by a tight, unstable stenosis, with morphologic features of high-risk for intracranial embolisation, and that intracranial vessels are usually patent with no new cerebral lesions on CT examination. These were also our criteria of feasibility for surgical intervention, similar to those adopted in main clinical studies, which report good results of surgery in these selected subgroup of patients at high-risk for early recurrent neurological events [14–16].

As a consequence, the most recent Italian guidelines [4] recommend urgent TEA in patients with recent (<24 h)/crescendo TIA and severe carotid artery stenosis in experienced centres, with documented low complication rates in elective surgical treatment of extracranial carotid artery disease.

Also in our experience, results were fairly good, with no major strokes at 30 days; as expected, cumulative complication rate was significantly higher in the study group than in control group. These results suggest that acute carotid artery stenosis can be considered an end-stage atherosclerotic disease, and this hypothesis is confirmed by the significant differences between the two groups in terms of cardiovascular comorbidities and of severity of carotid stenosis. However, the aggressive medical treatment of cardiovascular disease and risk factors in our patients (statins, ACE inhibitors, β-blockers and antiplatelet drugs) allowed us to have a low rate of mortality and neurological events in patients with multiple cardiovascular disease (coronary artery disease, hypertension, diabetes). We had a higher shunt insertion rate in our experience, due both to surgeon's choice and to decreased tolerance to carotid clamping in our patients, which, however, did not affect our results. There were no postoperative intracranial haemorrhages, and it could be explained by the careful preoperative diagnostic assessment of patients and particularly by the evaluation of the status of cerebral parenchyma, with the exclusion from the intervention of patients with large (1 cm) new ischaemic areas [17, 18].

We performed a routine intraoperative completion study with DSA in all acute patients; in our experience, the use of routine DSA is not mandatory [19], but it is limited to selected patients (patients who had shunt insertion, in the presence of reintervention or carotid near-occlusion, when the surgeon uses a technique which he is not familiar with). Acute patients can be considered a subgroup requiring a careful intraoperative control, with evaluation of intracranial vessels' status. In recent years, the use of duplex scanning has been proposed as an alternative or adjunctive method for intraoperative completion study. Particularly in the detection of minor technical defects after CEA [20], duplex scanning has been reported to be more accurate than carotid angiography, and its routine use has been proposed; however, in acute patients DSA remains in our opinion worthwhile, due to the good visualisation of intracranial vessels.

We analysed also long-term results, and we are not aware of any previous study describing the fate of acute patients during follow-up. There were no significant differences between study group and control group in terms of ipsilateral neurological events during follow-up, confirming the long-term effectiveness of CEA; however, in the study group long-term survival and any (ipsi- and contralateral) neurological event-free rates were significantly lower than in the control group, thus reflecting the severity of atherosclerotic disease in these subgroups of patients.

There are no data in Literature concerning the use of carotid angioplasty and stenting (CAS) in patients with acute symptoms; recent studies [21] failed to demonstrate the non-inferiority of CAS against CEA in stable symptomatic patients, and it is reasonable to assume that results of CAS could be even poorer in the presence of unstable, complicated plaques, which are considered, at the moment, unsuitable for CAS.

In our series only patients without acute stroke were considered as candidates to surgical intervention; in Literature, little information exists about the efficacy of CEA in patients with acute ischaemic stroke, which is considered a high-risk procedure [22, 23]. Some studies reported a significant improvement following surgery among patients

with mild-to-moderate neurological impairment; still, the data are limited and the usefulness of urgent surgery among patients with severe neurological deficits is even less clear, thus contraindicating urgent CEA outside of a research setting [18].

However, encouraging results were reported in some recent studies [24, 25] analysing the effectiveness of urgent CEA in patients with stroke in evolution or fluctuating stroke. These few data in Literature confirm the feasibility of surgery in carefully selected patients, with encouraging results in terms of neurological recovery but no negligible rates of major complications.

## 5. Conclusions

Urgent CEA in patients with recent/crescendo TIA and appropriate carotid artery lesion seems to substantially modify the natural history of these patients who, if untreated, are at high risk for further, and more severe neurological and cardiovascular events. In these patients urgent CEA carries good early and long-term results, which, however, remain slightly poorer than those obtained in symptomatic patients with a stable neurological status.

For this reason, a careful patient selection, deriving from the close collaboration of different specialists (neurologists, neuroradiologists and vascular surgeons in a multidisciplinary unit), is the basic point in order to improve the results of surgical intervention and to reduce the number and the severity of early and late complications.

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