



# Urgent Carotid Endarterectomy in Patients with Recent/Crescendo Transient Ischaemic Attacks or Acute Stroke **CME**

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## KEYWORDS

Urgent carotid endarterectomy;  
Recent TIA;  
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Acute stroke

**Abstract Objectives:** Objective of this study was to review the results of urgent carotid endarterectomy (CEA) performed in patients with recent (<24 h) or crescendo (at least 2 episodes in 24 h) transient ischaemic attack (TIA) or with acute stroke in a single centre experience.

**Materials and methods:** From January 2000 to December 2008, 75 patients underwent urgent CEA for severe internal carotid artery stenosis and recent/crescendo TIA (51 patients, TIA group) or acute stroke (24 patients, stroke group). In patients with acute stroke the intervention was proposed on the basis of clinical and instrumental features (patient conscious, patency of middle cerebral artery, no lesions or limited brain infarction at CT scan) according to neurologists' suggestion. Data from all the interventions were prospectively collected in a dedicated database, which included main pre-, intra- and postoperative parameters. Independent neurological assessment with National Institute of Health Stroke Scale (NIHSS) score calculation was performed before the operation and within the 30th postoperative day.

Early (<30 days) results were evaluated in terms of mortality, modifications in NIHSS values and stroke and death rates. The surveillance program consisted of clinical and ultrasonographic examinations at 1, 6 and 12 months and yearly thereafter. Follow-up results (survival, occurrence of ipsilateral stroke in TIA group, recurrence of stroke in stroke group) were analysed by Kaplan–Meier curves.

**Results:** Among patients presenting with TIA, 28 had crescendo TIAs and 23 had a recent TIA; in stroke group, two patients had a stroke in evolution, eight patients had a recent major non-disabling stroke and 14 patients had a recent minor stroke.

Preoperative mean value of NIHSS score in stroke group was 4.7 (SD 3.2).

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There were 2 perioperative (<30 days) deaths, both in stroke group, in one case due to acute respiratory failure and to fatal stroke in the other one (preoperative NIHSS value 9, postoperative 17), with a cumulative 30-day mortality rate of 2.7%, significantly higher in stroke group (8.3%) than in TIA group (no death,  $p = 0.03$ ). No postoperative cerebral haemorrhage occurred.

In TIA group one postoperative major stroke occurred, with a 30-day stroke and death rate of 1.9%.

In surviving patients of stroke group NIHSS value improved in 13 cases, with a mean improvement of 2 points (SD 0.9); in 8 cases the value remained unchanged, while in the remaining case it increased from 2 to 4. Mean postoperative NIHSS score in stroke group was 3.9 (SD 3.7), significantly reduced in comparison with preoperative value ( $p < 0.001$ ).

Mean duration of follow-up was 34 months (SD 28.1). No ipsilateral stroke in patients of TIA group occurred; in stroke group a recurrent fatal stroke at 1 postoperative month was recorded. Estimated 48-month stroke-free survival rate TIA group was 95% and 79% in stroke group ( $p = 0.02$ ).

**Conclusions:** Urgent CEA in patients with recent/crescendo TIA provided in our experience excellent results, with low rates of perioperative and late stroke. In selected patients with acute stroke early surgery seems to provide acceptable results.

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## 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.<sup>1–3</sup> By contrast, there is no evidence from randomised trials to support the use of emergent or urgent CEA in patients presenting with unstable neurological status. Recent systematic reviews have demonstrated increased perioperative risk with the use of early CEA in patients with recent/crescendo transient ischaemic attacks (TIAs) and, to a greater extent, in patients with stroke in evolution or acute fixed stroke.<sup>4,5</sup>

From our group,<sup>6</sup> a previous study on early CEA in patients with recent/crescendo TIA reported that although satisfactory perioperative and long-term results may be obtained, outcome in this urgent subgroup of patients was slightly worse than in symptomatic patients with a stable neurological status.

The aim of this study was to retrospectively update our results in this subgroup of patients, including in the analysis also patients with stroke in evolution and recent major non-disabling stroke.

## Materials and Methods

From January 2000 to December 2008, 3335 consecutive CEAs in 2797 patients were performed at the University of Florence. Data concerning these interventions were prospectively collected in a dedicated database containing 150 fields, including anatomical, clinical, diagnostic and technical variables. This database also contains perioperative (<30 days) results in terms of mortality and neurological morbidity, and all relevant clinical and diagnostic data collected during follow-up. A *post hoc* analysis of this database was performed and 75 urgent interventions carried out in 75 patients with severe internal carotid artery stenosis; and acute neurological event were identified: in 51 cases, the intervention was performed for recent/crescendo TIA (TIA group), while, in the remaining

patients, the intervention was performed in patients with stroke in evolution or recent major non-disabling or minor stroke (stroke group).

Recent TIA was defined as a single episode of TIA, which occurred within 24 h, while crescendo TIAs were defined as two or more episodes within 24 h, with complete recovery after each episode. Stroke in evolution was defined the progression of a neurological deficit that had occurred over at least 24 h, and recent stroke was defined as a fixed neurological deficit occurring within the past 5 days. Minor stroke was defined as any neurological event lasting more than 24 h with recovery in several days without residual functional impairment. Major non-disabling stroke was defined as any neurological event lasting more than 24 h with minimal residual neurological deficit.

All the patients underwent preoperative duplex scanning of extracranial vessels and angio-computed tomography (CT) scan for the evaluation of cerebral parenchyma and supra-aortic vessels. The degree of stenosis was determined by means of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method.<sup>1</sup> The status of the vertebral arteries and intracranial vessels was also examined during the preoperative assessment with angio-CT scan. All the patients were preoperatively evaluated by a consultant neurologist using the National Institute of Health Stroke Scale (NIHSS) score assessment. In patients with neurological deficit, the presence of impaired consciousness, of fluctuating symptoms without complete recovery between different episodes, of severe neurological impairment (major disabling stroke), of middle cerebral artery occlusion, of ischaemic lesions larger than 1 cm at CT scan and of a NIHSS score higher than 15 were considered as contraindication for surgical intervention. Patients not selected for surgery were admitted to a stroke unit and then medically managed.

Patients' characteristics were analysed in terms of demographic data, common risk factors for atherosclerosis and co-morbidities. Risk factors and co-morbidities included arterial hypertension (defined as blood pressure greater than 130/85 mmHg or the need for anti-hypertensive medications), diabetes, defined as the need for specific drugs to

maintain metabolic control, (hyperlipaemia (defined as triglycerides and cholesterol values  $> 200 \text{ mg/dl}^{-1}$ ), coronary artery disease (history of myocardial infarction, angina and previous coronary revascularisation) and peripheral arterial disease (ankle/brachial index  $< 0.9$ ).

Intra-operative data included type of anaesthesia, cerebral monitoring and protection and technique of carotid reconstruction. The choice of anaesthetic method was at the discretion of the operating surgeon and anaesthesiologist. Patients undergoing CEA under general anaesthesia had cerebral monitoring with somatosensory evoked potentials (SEPs) and selective shunt insertion on the basis of SEP abnormalities.<sup>7</sup> With local anaesthesia or our previously described Cooperative Patient General Anaesthesia (CoPaGeA)<sup>8</sup> technique, a carotid shunt was inserted on the basis of clinical neurologic monitoring during carotid clamping. At the end of the intervention routine, completion angiography was performed.

Demographics, risk factors, co-morbidities, anatomical indications for surgery and intra-operative technical features were analysed and compared in both groups with the  $\chi^2$  test and Fisher's exact test, when necessary. Neurological status was assessed daily in the immediate postoperative period. Any postoperative death was recorded; also, postoperative acute myocardial infarction (MI) rate was assessed: the criteria for the diagnosis of MI were the presence of cardiac enzymes' elevations associated with electrocardiographic and echocardiographic signs of infarction. Cardiac enzymes were routinely checked on the first postoperative day. After discharge, a 1-month follow-up neurological evaluation was performed and new neurological events were assessed and defined and NIHSS values were calculated.

Perioperative results were evaluated in terms of mortality and 30-day stroke and death rate in the TIA group and of mortality and NIHSS values' modifications in the stroke group; pre- and post-operative NIHSS values in the stroke group were compared with the *t*-test for paired variables. Univariate analysis for 30-day stroke and death rate in the TIA group was performed. The analysis included the following risk factors: sex, age greater than 79 years, coronary artery disease, peripheral arterial disease, arterial hypertension, diabetes, presence of contralateral carotid occlusion, type of anaesthesia and cerebral monitoring, shunt insertion, type of arterial reconstruction, characteristics of the TIA (recent or crescendo) and interventions performed within or beyond 24 h from the onset of symptoms. Multivariate analysis (stepwise logistic regression analysis) for the same outcome with the inclusion of the factors noted to be significant at univariate analysis was performed. In the stroke group, univariate analysis for improvement in NIHSS values at 30 days was performed. The analysis included the following risk factors: sex, age greater than 79 years, coronary artery disease, peripheral arterial disease, arterial hypertension, diabetes, presence of contralateral carotid occlusion, type of anaesthesia and cerebral monitoring, shunt insertion, type of arterial reconstruction, stroke characteristics (in evolution, major or minor), preoperative NIHSS score higher or lower than 5 and interventions performed within or beyond 48 h from the onset of symptoms. Multivariate analysis (stepwise logistic regression analysis) for the same outcome with the

inclusion of the factors noted to be significant at univariate analysis was performed. Statistical significance was defined as a *p* value less than 0.05.

Follow-up was performed at 1, 6, 12 months and yearly thereafter, by clinical exam and duplex scan. All studies were performed using an Acuson Sequoia 512 Ultrasound System (Acuson Corporation, Mountain View, CA, USA). Patients who did not complete follow-up examinations had a telephone interview. During the telephone interview, the following outcomes were assessed: patient's survival and cause of death, if known; and neurological events and their time of appearance. Additional data regarding long-term survival and major cardiovascular events were obtained from the Regional Health Care database.

Follow-up data were analysed by life-table analysis (Kaplan–Meier test) in terms of death, ipsilateral stroke in TIA patients and recurrence of stroke in stroke patients. Stroke-free survival rates in the TIA group and recurrence-free survival rates in the stroke group were assessed. Statistical analysis was performed by means of Statistical Package for Social Sciences (SPSS) 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

## Results

### Demographic data, risk factors, co-morbidities and anatomical status

There were not significant differences between the two groups of patients in terms of demographic data, risk factors and co-morbidities, except for a higher percentage of octogenarians in the TIA group (Table 1). There were no differences in terms of degree of carotid stenosis at the operated side, of status of the contralateral internal carotid artery and of type of intervention (primary or secondary, Table 2).

### Clinical details

Among patients presenting with TIA, 28 had crescendo TIAs and 23 had a recent TIA. In 40 cases, only one neurological symptom was present (contralateral upper extremity weakness in 14 cases, contralateral hemiplegia in 12 cases, contralateral lower extremity weakness in two cases, amaurosis fugax in eight cases, disturbance of language in three cases and central facial nerve paralysis in the remaining case). In 11 cases, two of the above-mentioned symptoms were present. Mean time interval between the onset of symptoms and the intervention was 22.6 h (SD 13.7).

In the stroke group, two patients had a stroke in evolution, eight patients had a recent major non-disabling stroke and 14 patients had a recent minor stroke. In 14 cases, only one neurological symptom was present (contralateral hemiplegia in six cases, contralateral upper limb paralysis in five cases, contralateral lower limb paralysis in one case and disturbance of language in three cases). In eight cases, two of above-mentioned symptoms were present, while the remaining two patients had three associated neurological symptoms. Mean preoperative NIHSS score was 4.7 (SD 3.2).

**Table 1** Patients' demographic data, risk factors and co-morbidities.

	TIA group (pts. 51)	Stroke group (pts. 24)	<i>p</i>
Female sex	9 (17.5%)	9 (37.5%)	0.06
Median age (years)	73.5	71.3	0.4
Age > 79 yrs.	10 (25%)	—	0.01
Hypercholesterolemia	11 (21.5%)	6 (25%)	0.7
Hypertriglyceridemia	7 (13.5%)	4 (17%)	0.7
Diabetes mellitus	8 (15.5%)	7 (29%)	0.7
Arterial hypertension	26 (51%)	16 (66%)	0.2
Coronary artery disease	7 (13.5%)	3 (12.5%)	0.8
Peripheral artery disease	7 (13.5%)	6 (25%)	0.2
Smoker or past smoker	29 (57%)	19 (79%)	0.07

The mean time interval between the onset of symptoms and the intervention was 52.5 h (SD 28.7).

### Intra-operative details

Local anaesthesia or CoPaGeA with clinical monitoring were used in 13 interventions in the TIA group (25%) and in seven cases in the stroke group (29%;  $p = 0.7$ ). Shunt insertion rates were similar between the two groups (33% TIA group and 41% stroke group,  $p = 0.4$ ), with no differences in the type of anaesthesia. In the TIA group, the shunt insertion rate was 23% in patients undergoing local anaesthesia or CoPaGeA and 37% in patients undergoing general anaesthesia ( $p = 0.3$ ); the corresponding values in the stroke group were 28% and 41%, respectively ( $p = 0.4$ ). For arterial reconstruction, a wide use of patch closure was noted in both groups (84% in the TIA group and 83% in the stroke group,  $p = 0.3$ ); the remaining patients had primary closure.

### Early results

Two perioperative deaths occurred, both in the stroke group, in one case in a patient operated on for minor stroke who died in first postoperative day of an acute respiratory failure, and in the other case due to a fatal stroke (preoperative NIHSS score 9, postoperative 17) in a patient operated on for a tight carotid stenosis with intra-operative finding of fresh thrombosis at the carotid bifurcation.

The cumulative 30-day mortality rate was 2.7%, significantly higher in the stroke group (8.3%) than in the TIA group (no death,  $p = 0.03$ ). No postoperative cerebral haemorrhage or MI occurred.

In the TIA group, one perioperative major stroke occurred in a patient with crescendo TIAs operated on for

left internal carotid artery near occlusion. The intervention was performed under local anaesthesia with shunt insertion due to the occurrence of a neurological deficit after 11 min of carotid clamping, and complete recovery after shunting. Patch closure was performed, and intra-operative completion angiography demonstrated patency of the operated internal carotid artery and intracranial vessels. On first postoperative day, the patient developed severe aphasia (NIHSS 4) despite the patency of extra and intracranial internal carotid artery assessed by angio-CT scan. At discharge on the 10th postoperative day, the patient's clinical status was unchanged, and a new CT scan showed the presence of limited, left-cortical brain infarction.

Cumulative 30-day stroke and death rate in TIA group was 1.9%.

At univariate analysis for 30-day stroke and death rate in TIA group, none of the examined factors were found to be significant.

In the stroke group, the mean postoperative NIHSS score was 3.9 (SD 3.7), significantly reduced in comparison with preoperative values ( $p < 0.001$ ; 95% confidence interval (CI) 0.1–1.7). In surviving patients in the stroke group, NIHSS value improved in 13 cases, with a mean improvement of 2 points (SD 0.9); in eight cases, the value remained unchanged, while in the remaining case, it declined from 2 to 4.

At univariate analysis for factors affecting NIHSS score improvement at 30 days, none of the examined factors were found to significantly affect this outcome (Table 3).

### Follow-up results

The mean duration of follow-up was 34 months (SD 28.1); 71 patients (94.5%) had their follow-up completed. During follow-up, five deaths occurred, three in the stroke group and two in the TIA group. The causes of deaths in the stroke

**Table 2** Anatomical features.

	TIA group (Pts. 51)	Stroke group (Pts. 24)	<i>p</i>
Degree of stenosis			
60–80%	10 (19.5%)	6 (25%)	0.3
>80%	37 (72.5%)	12 (50%)	0.07
Near-occlusion	3 (6%)	2 (8%)	0.5
Thrombosis	1 (2%)	4 (16.5%)	0.07
Contralateral occlusion	3 (6%)	—	0.2

group were recurrence of stroke in one case and acute MI in two cases; in the TIA group, one patient died of a bladder cancer and the other patient from a fatal cerebral haemorrhage.

In the TIA group, neither ipsilateral nor contralateral stroke was recorded. One patient had a new ipsilateral TIA at 9 months, and significant restenosis of the operated internal carotid artery was found and re-intervention was planned, but the patient suffered from a fatal cerebral haemorrhage prior to the scheduled procedure. Another patient had a TIA from a mild-to-moderate stenosis of the contralateral internal carotid artery at 20 months, and underwent elective contralateral CEA.

In the stroke group, as previously noted, one patient suffered from a fatal recurrent ipsilateral stroke at 1 month.

Cumulative estimated stroke-free survival rate at 48 months was 89.7%; the corresponding figures in the TIA and stroke groups were 95.1% (standard error (SE) 0.03) and 79.2% (SE 0.08), respectively ( $p = 0.02$ ; log rank 5.1; Fig. 1).

## 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.<sup>9–11</sup> As a consequence, in the following 20 years, the avoidance of urgent CEA was commonly accepted worldwide, and the intervention was generally delayed up to 6 weeks after the clinical event.<sup>12</sup>

In recent years, however, significant improvements in medical, surgical and anaesthesiological techniques and

the creation of territorial care networks for the treatment of acute stroke has raised interest in the surgical treatment of patients with unstable neurological symptoms.

In this study, we have analysed our experience in the treatment of acute carotid artery stenosis, both in patients with recent/crescendo TIAs and in patients with acute stroke.

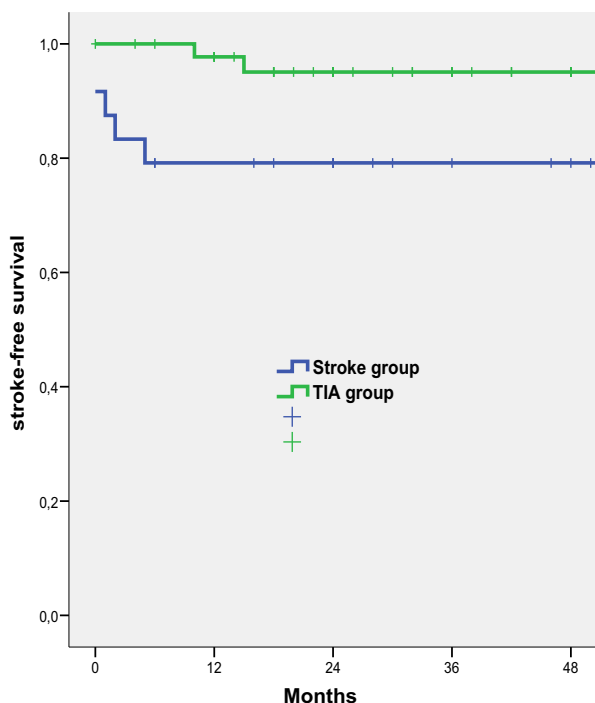
In the presence of recent or crescendo TIA, the role of surgical intervention has already been described by several studies. TIA represents a significant warning sign for further, severe neurological events, with a risk of stroke of 5% in the first 48 h and 10% within 3 months.<sup>13</sup> In patients with severe or moderate carotid stenosis in the affected hemisphere, the risk increases to 6% in the first 48 h and to 20% within 3 months,<sup>14</sup> and becomes even higher in the presence of crescendo TIAs.

On the basis of these data, the indication for urgent CEA in patients with recent/crescendo TIAs seems compelling considering that in most patients the ischaemic episode is caused by a high-grade unstable stenosis, with morphologic features of high risk for intracranial embolisation. These were our criteria of the feasibility for surgical intervention, similar to those adopted in many clinical studies,<sup>15–17</sup> which report good results in this selected subgroup of patients at high risk for early recurrent neurological events.

Our results in the TIA group were good, with a satisfactory 30-day stroke and death rate of 1.9% and only one postoperative stroke that occurred in a patient operated on for internal carotid artery near occlusion. The role of surgery in stroke prevention in patients with this pattern of carotid disease is still controversial: while the NASCET trial<sup>18</sup> reported a significant advantage for surgical intervention in these patients, a meta-analysis of pooled data

**Table 3** Univariate analysis for NIHSS score improvement at 30 day in stroke group.

Risk factor	NIHSS improvement	<i>p</i>
Female gender	5/9 (55%)	
Male gender	9/15 (60%)	0.8
CAD	2/3 (66%)	
No CAD	12/21 (57%)	0.7
PAD	5/6 (83%)	
No PAD	9/18 (50%)	0.1
Arterial hypertension	10/16 (62%)	
No arterial hypertension	4/8 (50%)	0.5
Diabetes	6/7 (85%)	
No diabetes	8/17 (47%)	0.08
Preop. NIHSS < 5	7/15 (46%)	
Preop. NIHSS > 5	7/9 (77%)	0.1
Symptoms' onset < 48 h	6/10 (60%)	
Symptoms' onset > 48 h	8/14 (53%)	0.8
Stroke in evolution	2/2 (100%)	
Minor stroke	9/14 (65%)	
Major stroke	3/8 (39%)	0.07
Local or CoPaGeA anaesthesia	4/7 (57%)	
General anaesthesia	10/17 (58%)	0.9
Shunt insertion	4/10 (40%)	
No shunt insertion	10/14 (71%)	0.1
Patch closure	13/22 (59%)	
Primary closure	1/2 (50%)	0.8



Months	0	12	24	36	48
TIA group (n. at risk)	23	17	14	9	7
with SE (%)	5%	8%	8%	8%	8%
Stroke group (n. at risk) with SE	43	42	29	18	12
	2%	2%	3%	3%	3%

#### Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	5,157	1	.023

Test of equality of survival distributions for the different levels of tia.

**Figure 1** Estimated stroke-free survival rate at 48 months in TIA group and stroke group with number of patients at risk.

from randomised trials in symptomatic patients<sup>1</sup> demonstrated that the risk of stroke for medically treated patients with near occlusion was lower than in patients with severe stenosis, and the analysis of the long-term effect of surgery in this group showed no significant benefit. In our experience, we usually operate on patients with near occlusion only in the presence of neurological symptoms; however, the lack of data, particularly concerning the role of CEA in patients with near occlusion and acute neurological events, makes any recommendation difficult.

Recent studies have reported that the stroke and death rate in patients with crescendo TIA seems to be higher than in patients operated on for a single, recent episode of TIA<sup>4</sup>; also, in our series, the only postoperative stroke in the TIA group occurred in a patient with crescendo TIA; however, the limited number of events makes any further evaluation unreliable.

As expected, our results in stroke patients were poorer than those obtained in TIA patients, with a mortality rate of 8.3%, confirming the increased perioperative risk in this subgroup of patients already described in other studies and reviews.<sup>4,5</sup> However we found a significant and encouraging

improvement in postoperative NIHSS score in more than 50% of our surviving population, and only in one case was there a slight impairment. One must consider that some improvements in neurological status, particularly in patients with minor or major non-disabling stroke, can be expected in many patients, and the absence of a control group (patients medically treated) in our series could make these results less significant. Moreover, conclusions may have been affected by the relatively small number of patients with stroke in evolution in stroke population, while most patients in this group had recent fixed neurological deficit. The risk of CEA in patients with stroke in evolution in contemporary series has been reported to be significant, with a threefold higher operative risk in comparison with patients operated on for recent stable stroke<sup>5</sup>; however, in our series, the two patients with stroke in evolution had a favourable outcome, significantly improving their NIHSS score values in the postoperative period.

There was no postoperative intracranial haemorrhage, possibly explained by the careful preoperative diagnostic assessment of patients and particularly by the evaluation of the status of cerebral parenchyma, with the exclusion from surgery of patients with large (>1 cm) new ischaemic areas.<sup>19,20</sup>

We analysed also long-term results, and we are not aware of a previous study describing the fate of acute patients during follow-up. We found a significant difference between the TIA and stroke groups in terms of long-term survival, both related to the higher perioperative mortality in the stroke group, suggesting these patients to have a more severe systemic disease. Follow-up results in terms of neurological outcomes were satisfactory, with low rates of new events in both groups, confirming the long-term effectiveness of CEA also in these subgroups of patients.

A crucial point in the management of unstable neurological patients is the strict collaboration with the neurologist who should be, in our opinion, the team leader in the decision-making process. This was also our strategy, and it was supported by an effective network between the local health-care system and our hospital. This is further demonstrated by the reduced delay between symptom onset and surgical intervention, ranging from 22 h in the TIA group to 52 h in the stroke group, different from what is reported in contemporary series, where unacceptable delays in diagnosis and intervention are described in most patients.<sup>21</sup>

This study has several limitations: it is a non-randomised, retrospective study with a limited number of cases and of events, and a relative heterogeneity of the study population, particularly in stroke patients. However, due to the paucity of data on this issue in the literature, our study may add to the management of these complex patients.

## Conclusions

Urgent CEA in patients with recent/crescendo TIA provided, in our experience, excellent results, with low rates of perioperative and late stroke. In selected patients with acute stroke, early surgery seems to provide acceptable results.

Careful patients' selection, with close collaboration of different specialists (neurologists, neuroradiologists and

vascular surgeons in a multidisciplinary unit), is critical to improve the results of surgical intervention and to reduce the incidence and the severity of early and late complications.

## Funding

None.

## Conflict of Interest

None.

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