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Urgent Carotid Endarterectomy in Patients with Acute Neurological Symptoms

The Results of a Single Center Prospective Nonrandomized Study

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Abstract

Background: **To evaluate the feasibility and the safety of performing urgent (within 24 hours) carotid endarterectomy in patients with carotid stenosis presenting with repetitive transient ischemic attacks or progressing stroke.** ***Methods:*** **Thirty consecutive patients underwent urgent carotid endarterectomy for repetitive transient ischemic attacks (N = 12) or progressing stroke (N = 18) according to the following criteria: two or more transient ischemic attacks or a fluctuating neurological deficit over a period of less than 24 hours (progressing stroke), no impairment of consciousness, no cerebral infarct larger than 1.5 cm in diameter on computed tomography and a carotid artery stenosis of 70% or more on the appropriate side, diagnosed by echodoppler ultrasonography and/or arteriography. Patients with cerebral hemorrhage were excluded. All patients were examined pre- and postoperatively by the same neurologist and surgery was performed by the same vascular surgeon. All the patients underwent a cerebral CT scan within 5 days after surgery.** ***Results:*** **There were 19 men and 11 women. The mean age was 71 ± 7.6 years. The time delay of surgery after the onset of transient ischemic attacks or progressing stroke averaged 19.4 ± 11.5 hours. For patients suffering progressive stroke, one developed a fatal ischemic stroke 24 hours after surgery, five showed no improvement of their neurological status after surgery, but none worsened. Twelve patients experienced significant improvement of their neurological status with an European Stroke Scale of 77.9 ± 25.2 at admission and 95.8 ± 4.6 at discharge, and all but one of those patients had a Barthel's index value over 85/100 at discharge. The 12 patients with repetitive transient ischemic attacks had an uneventful postoperative outcome. The mean duration of follow-up was 3.4 ± 1.2 years. No patient developed another transient ischemic attack or ischemic stroke during the follow-up period.** ***Conclusions:*** **The results of our series documented the feasibility and the safety of performing urgent (within 24 hours) carotid endarterectomy in patients presenting with repetitive transient ischemic attacks or progressing stroke. This procedure seems to us to be justified by the fact that waiting for surgery may lead to the development of a more profound deficit or another stroke in these neurologically unstable patients whose only chance for neurological recovery is in the early phase.**

Key Words

Carotid endarterectomy · Transient ischemic attacks · Stroke in evolution

Introduction

Carotid endarterectomy (CEA), first performed in 1953 by DeBakey [1], is an effective and recognized

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vascular elective procedure for symptomatic patients with moderate or severe (≥70%) carotid stenosis and in patients with severe asymptomatic stenosis [2,3]. But the best timing to perform CEA in patients with acute neurological symptoms (repetitive transient ischemic attacks, minor stroke or stroke-in-evolution) has for a long time been subject to controversy and is still a source of debate. In fact, to our knowledge, there are no prospective randomized trials to determine which neurologically unstable patient (presenting repetitive transient ischemic attacks or stroke-in-evolution), might safely undergo urgent or delayed CEA.

In the past, the increased risks of reperfusion injury and conversion to hemorrhagic infarction have led to the historical recommendation of delayed CEA in patients with acute neurological symptoms. But, in recent years, most published data demonstrated that the risk of recurrent stroke in the first few days after a transient ischemic attack (TIA) or minor stroke appears to be much higher than previously estimated. Rothwell et al. [4], assessed the risk of stroke at 7, 30, and 90 days first after TIA as 8, 11.5, and 17.3% respectively and after a minor stroke as 11.5, 15, and 18.5%. On the other hand, some centers report the safety and efficacy of urgent CEA (before two weeks) after acute minor stroke, repetitive TIAs, or stroke-in-evolution (SIE) [5–13]. A subanalysis of NASCET results [14,15] illustrates a rapid decline of the benefit of CEA over time in terms of stroke prevention after the index focal neurological deficit (TIA or minor stroke). Recent guidelines document that early surgery is associated with increased benefits compared with delayed surgery for secondary stroke prevention and recommend CEA within two weeks for patients presenting with a TIA or minor stroke [16].

We performed a prospective nonrandomized protocol for urgent (within 24 h) CEA in neurologically unstable patients (presenting with repetitive TIA or progressing stroke) with a symptomatic carotid stenosis of more than 70% in order to assess the safety of this therapeutic approach.

Methods

During a five year period, we performed a single center, prospective, nonrandomized consecutive series of urgent CEA. In accordance with the NASCET and ECST studies [3,2] and the Charing Cross series results [17], the following inclusion criteria have been used: symptomatic carotid stenosis of 70% or more, with unstable neurological status consisting in repetitive TIA or progressive stroke evolving no longer than 24 hour, no impairment of consciousness, and no cerebral infarct larger than 1.5 cm in diameter on preoperative CT scan (Table 1). There were no exclusion criteria except for age over 80 years. Hemorrhage seen on the initial CT-scan eliminated the patient from the study. The term "progressing stroke" is applied to patients with a neurological deficit that has progressed or fluctuated over a period of at least 24 hours. The diagnosis of carotid stenosis was based on echodoppler ultrasonography and/or selective carotid angiography. The degree of stenosis was determined by means of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. All patients were examined by the same neurologist pre- and postoperatively (PD). Neurological evaluation of the patients was blinded from the surgeon's clinical examination to avoid under or overestimation in the patient's clinical status.

Table 1. Inclusion Criteria for Patient Enrollment

Inclusion criteria
Symptomatic carotid stenosis of 70% or more
Unstable neurological status consisting in repetitive TIA or progressive stroke evolving no longer than 24 h
No impairment of consciousness
No cerebral infarct larger than 1.5 cm in diameter on preoperative CT-scan

All patients were scored by the European Stroke Scale (ESS) [18] at admission and at discharge (maximum ESS score is 100 and indicates a patient without any neurological deficit). Barthel's index [19] was only evaluated at hospital discharge because it is impossible to determine preoperatively patient's autonomies. It is considered that a patient is independent at home if his score (Barthel's index) exceeds 85. The preoperative investigation included in all cases: blood sample analysis, ECG and/or cardiac echography, chest X-ray, carotid echo color Doppler ultrasonography, selective angiography of the carotid arteries, and cerebral CT-scan. No MRI was performed because MRI was not accessible on an emergency basis. From the day of the admission to the discharge from hospital, all patients received heparin at a prophylactic dose, along with statin therapy. As CEA was performed on an emergency basis (within the first 24 hours), no aspirin was administred preoperatively.

A standard surgical open endarterectomy, with Javid shunt (to maintain cerebral circulation during surgery) and prosthetic patching, was performed under general anesthesia by the same vascular surgeon (NS) in all cases. The postoperative care was performed in a stroke unit, with ECG, noninvasive arterial blood pressure monitoring, and transcutaneous oxygen saturation monitoring for at least 48 hours. All the patients underwent a cerebral CT scan before discharge, within the five days after surgery. In the postoperative period, patients were maintained on a low dose of heparin (4000 IU) and statin therapy together with their scheduled medications. At discharge from the hospital, antiplatelet therapy (acetylsalicylic acid 100 mg daily) was started. During regular follow-up, all patients were

Table 2. Patient's Characteristics and Medical History

	No. of patients (%)
Demography	
Mean age (y)	71
Men: Women	19 (63): 11 (37)
Neurologic clinical presentation	
Repetitive TIA (≥ 2/24h)	12 (40)
Progressive stroke	18 (60)
Comorbidities	
Hypertension	6
Diabetes	3
Hypercholesterolemia	19
Smoking history	14
Previous myocardial infarction	3
Previous TIA and/or stroke	0

reviewed by the same neurologist (PD) and the same surgeon (NS) independently from each other at six weeks after surgery and every six months during the first year, and every 12 months thereafter. Assessment of outcome was based on follow-up control examination.

Statistical Analysis Patient details, including age, gender, and comorbidities were collected in an Excel database (Microsoft Ltd). Categorical data were presented as absolute frequencies and percent values. Quantitative measurements were expressed as mean ± SD. Data on survival, neurological events, and patency was studied directly.

Results

Patients Characteristics The study concerns 30 consecutive patients included out of a series of 638 patients admitted to the emergency department for acute TIA or progressive stroke during a five year period. In these 30 patients, CEA was performed within 24 hours following the neurological event (repetitive TIA or progressive stroke). Of these, there were 12 patients presenting with repetitive TIA and 18 progressive strokes. There were 19 men and 11 women with a mean age of 71 ± 7.6 years. No patient had any neurological deficit before the onset of repetitive TIA or progressing stroke. Baseline patient characteristics and medical history are presented in Table 2.

Perioperative Characteristics All patients had documented internal carotid artery stenosis of 70% or more. For patients suffering progressive stroke (n = 18), the degree of carotid artery stenosis was 85% or more. The mean delay of surgery after onset of the first TIA or progressive stroke was 19.4 (±11.5) hours (range, 6–48 hours). At operation, the macroscopic examination of the internal carotid artery in all 30 patients showed a complex ulcerated plaque and/or an intraplaque hemorrhage.

Outcomes One patient (5%) with initial progressive stroke developed a fatal ischemic stroke within 24 hours after the operation, and Doppler ultrasonography performed immediately showed very good patency of the operated carotid artery. Five (28%) of the 18 patients with progressive stroke had an incomplete recovery with limited residual neurological deficit and experienced no clinical improvement but none of them worsened after the operation, whereas the 12 other patients (67%) with residual neurological deficit (as a result of their progressive stroke) showed significant improvement of their clinical status. The 12 patients with repetitive TIA remained free of neurological deficit after the operation. All but one of the 18 patients with progressive stroke had a Barthel's index over 85 at hospital discharge. The mean ESS of the 18 patients with progressive stroke was 77.9 ± 25 at admission, and was 95.8 ± 4.6 at discharge. All the patients underwent a cerebral CT scan within five days after surgery. No hemorrhagic transformation of cerebral infarcts was detected. No new lesion on postoperative CT scan was found in the 12 cases of TIA. All of the 18 progressive stroke patients had a lacunar size lesion (<15 mm); there had been no enlargement of the lesion postoperatively except in one case in which there was a large infarction (>2 cm). There was no reoperation for cervical hemorrhage or wound infection. No patients developed vocal cord paralysis due to nerve injury. Patients were discharged after a median of four days (range, 4–10 days). The mean duration of follow-up was 3.4 years (±1.2) and was 100% complete in all patients. No residual or recurrent stenosis was documented on echo color Doppler ultrasonography follow-up. No recurrent stroke and/or TIA, no cardiac event, and no death occurred in this series during follow-up.

Discussion

Timing of CEA in patients with acute neurological symptoms still remains a challenging but unresolved problem [5–7,20]. The management uncertainty can be explained by the inability to predict who is at higher early risk of a recurrent stroke after a cerebrovascular

Table 3. Results of Urgent CEA (within 15 d) Reported Recently in the Literature

Author and year	No. of patients	Mean interval between symptom and CEA	In-Hospital mortality rate	Complications (stroke rate)
Gertler et al., 1994 [21]*	52	<24 h	0%	2.0%
Schneider et al., 1999 [22][a]	43	≤72 h	0%	0%
Brandl et al., 2001 [23][a]	16	<24 h	0%	–
Gay et al., 2002 [11]*	21	<24 h	9.5%	–
Huber et al., 2003 [24]*	67	2 d	3.0%	13%
Sbariga et al., 2006 [10][a]	96	1.5 d	2%	0%
Karkos et al., 2007 [8][b]	42	3 d	4.8%	4.8%/19%
Bazan et al., 2008 [6]*	764	–	2.0%	2.88%/3.1%
Ballotta et al., 2008 [25][a]	102	8 d	0%	0%
Gorlitzer et al., 2009 [9]*	28	4 d	0%	0%
Leseche et al., 2011 [12, 13][a,b]	91	5 d	0%	0%
Dorigo et al., 2011 [26]*	75	<24 h	2.7%	–
Capoccia et al., 2012 [27]*	48	<24 h	2.0%	2.0%
*Present study**	30	<24 h	3.3%	3.3%

*Mixed study including patients with acute stroke and TIA.

[a]Study concerns patients with acute ischemic stroke.

[b]Study concerns patients with crescendo TIA.

event (TIA or stroke). Interestingly, a subanalysis of the NASCET results has revealed that the benefit of CEA versus medical treatment is greatest if the symptomatic carotid artery stenosis is operated within two weeks following the index neurological event [14,15]. Among the medically treated patients, the risk of ipsilateral stroke is highest immediately after the initial ischemic event and subsequently drops dramatically [17].

In recent years, several studies (Table 3) have shown very good results and outcomes for urgent CEA procedures. In the Charing Cross series [17], 19 patients suffering from progressing stroke and 14 patients presenting with repetitive TIA underwent urgent CEA (all patients were operated within 48 hours after the onset of symptoms). There was a good evolution in all but three cases. All the patients had a small infarct size (<2.0 cm) on preoperative CT scan, were conscious, and had a mild neurological deficit. The criteria for the selection of our patients have been chosen in the light of the results of the Charing Cross series. The choice of these criteria was based on the assumption that a severe neurological deficit or impaired consciousness often implies a large infarction in progress, eventually but not yet visualized on early cerebral CT scan, leading to a higher risk of postoperative bleeding because of hyperperfusion in a large ischemic brain area. In our study, using these criteria, all but one patient had a good outcome. One patient suffered a fatal stroke due to postoperative enlargement of the existing small cerebral infarction. Intraoperative embolization was probably the cause because Doppler ultrasonography performed immediately showed very good patency of the operated carotid artery.

Gertler et al. [21] reported their experience in neurologically unstable patients with carotid stenosis presenting with crescendo TIA and SIE, of whom only one patient (2.7%) worsened his neurological deficit after CEA within 24 hours. Based on these good results, they recommend urgent CEA. Most recently, Leseche et al. [12,13] reported excellent outcome of urgent CEA in the acute phase of SIE and crescendo TIA, with no perioperative stroke or death. The mean delay to surgery from initial examination was five days. For patients operated for SIE, a complete neurological recovery was observed in 81% of patients, while 19% maintained a residual deficit. No patient presented a worsening of his deficit following urgent CEA. In a meta-analysis of 47 studies on carotid surgery published between 1980 and 2008, Rerkasem et al. [20] found no excess operative risk for early (urgent) CEA versus delayed CEA.

However, less favorable outcome after urgent CEA in neurologically unstable patients has been reported by other investigators. These studies demonstrated a higher rate of perioperative complications after

urgent CEA in neurologically unstable patients (presenting crescendo TIA and SIE) compared with delayed CEA. Karkos et al., [7] in a meta-analysis, reported a 16.9% perioperative stroke rate and a 20% combined stroke/death rate for urgent CEA after stroke-in-evolution. Considering crescendo TIA, the analysis revealed a more favorable outcome (6.5% perioperative stroke rate and a 9% combined stroke/death). In a meta-analysis done by Bond et al. [28] and Halm et al. [29], the operative risk of CEA increases when it is performed after stroke-in-evolution (a 14.0% 30-day stroke/death rate), compared to a 2.8% 30-day stroke/death rate after CEA for asymptomatic carotid artery stenosis.

This rather elevated morbidity-mortality should be balanced against the stroke risk in these neurologically unstable patients if surgery had not been performed. Actually, no randomized controlled trial has been done comparing the outcome of crescendo TIA and stroke-in-evolution treated medically versus urgently operated.

Early CEA for symptomatic severe carotid stenosis ($\geq$70%) in neurologically unstable patients may be justified by the instability of the lesion, in order to prevent a subsequent complete or more severe stroke. In all of our patients, an ulcerative or hemorrhagic plaque was discovered intraoperatively. Urgent removal of this unstable embolic source has some logic. An arbitrary 2-week delay for CEA probably exceeds the risk of urgent CEA and may expose the neurologically unstable patient to a risk of recurrent or more disabling stroke, or to an occlusion of the internal carotid artery. Before starting our prospective study, in some cases with a small cerebral lesion, we had chosen medical treatment before performing urgent surgery. Unfortunately in some cases, we observed fatal neurological events a few days later, after the first neurological events (unpublished data).

In contemporary literature, there exists consensus that a patient presenting with an acute, nondisabling neurological deficit with complete or partial recovery should benefit from a carotid endarterectomy without delay. For the high-risk group of neurologically unstable patients (crescendo TIA and SIE), who often present with subocclusive stenosis with friable ulcerated plaque, the current available literature data are less conclusive. Some series reporting a rather high perioperative morbidity-mortality seem to discourage urgent CEA in this setting. However, in our small experience, and in some centers of excellence, the operative outcome of urgent CEA in neurologically unstable patients was favorable. The creation of a "Stroke Unit" could favor the management and development of urgent CEA while allowing better selection and management of these unstable patients.

Limitations of the Study Our results should be interpreted in light of several limitations. First, the number of patients enrolled in this single center prospective study is too small to give definite conclusions. This was the reason why a formal statistical analysis was not performed. However, due to the heterogeneity and paucity of data in the literature, subject to controversy and still a source of debate, our experience may add to the management of these unstable neurological patients. Second, it is important to note that our study is not randomized. Although randomized trials are certainly the gold standard in clinical study, in neurologically unstable patients, such a trial is difficult for ethical reasons.

Conclusion

Our consecutive series shows that urgent CEA can be performed safely in selected patients with an evolving or unstable neurological deficit. It also confirms the relevance of some previously noticed criteria for the prognosis of urgent CEA, such as a normal level of consciousness, the absence of large cerebral infarction on preoperative cerebral CT scan, and the limited severity of the neurological deficit before the operation. We may recommend surgery within 24 hours for all symptomatic patients with unstable plaques diagnosed by imaging tools. Urgent CEA seems to us to be justified by the fact that a symptomatic carotid stenosis is an unstable lesion and waiting may lead to the development of another stroke that is more disabling for the patient. The perioperative risk can be reduced with better diagnostic strategies and must be balanced against the natural history if surgery is not performed. Only a large randomized multicenter prospective trial will be able to conclusively assess the effectiveness and outcome of urgent CEA in neurologically unstable patients.

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EDITOR'S COMMENTS

Dr. Sakalihasan and colleagues show us that prompt open surgical therapy for recurrent TIAs or unstable stroke in evolution can lead to excellent clinical outcomes and apparent salvage of at-risk cerebral tissue. They have taken a courageous posture. While not a large-scale randomized study, this report gives an important "real world" glimpse at what can be accomplished with aggressive, non-timid surgical care. We look forward to watching their experience grow based on these very favorable institutional results. It is important to note that the operated patients were selected from among hundreds of patients presenting during the time interval of this study; clinical judgment in patient selection, in addition to the stated inclusion and exclusion criteria, likely was an important factor in attaining favorable results.