Urgent carotid endarterectomy in patients with acute neurological ischemic events within six hours after symptoms onset

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Vascular published online 7 May 2013
DOI: 10.1177/1708538113478760

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What is This?
Urgent carotid endarterectomy in patients with acute neurological ischemic events within six hours after symptoms onset

P Gajin, Dj Radak, S Tanaskovic, S Babic and D Nenezic

To analyze the outcome of urgent carotid endarterectomy (CEA) performed within less than six hours in patients with crescendo transient ischemic attack (TIA) and stroke in progression. From January 1998 to December 2008, 58 urgent CEAs were done for acute neurological ischemic events – 46 patients with crescendo TIA and 12 patients with stroke in progression. Brain computed tomography (CT) was done prior and after the surgery. Disability level was assessed prior to and after urgent CEA using modified Rankin scale. Median follow-up was 42.1 ± 16.6 months. In the early postoperative period stroke rate was 0% for the patients in crescendo TIA group while in patients with stroke in progression group 3 patients (25%) had positive postoperative brain CT, yet neurological status significantly improved. Mid-term stroke rate was 2.2% in crescendo TIA group and 8.3% in stroke in progression group. In the early postoperative period there were no lethal outcomes, mid-term mortality was 8.3% in stroke in progression while in crescendo TIA group lethal outcomes were not observed. In conclusion, based on our results urgent CEA is a safe and effective treatment option for patients with crescendo TIA and stroke in progression with acceptable rate of postoperative complications.

Key words: urgent carotid endarterectomy; crescendo TIA; stroke

Introduction

After three large multicentric randomized trials have published their results, it became clear that carotid endarterectomy (CEA) is beneficial for stroke risk reduction in symptomatic and asymptomatic patients with high-grade internal carotid artery (ICA) stenosis. On the other hand, the indications for urgent CEA done in patients with acute neurological deficit have not yet been clearly defined.

The earliest studies have described adverse outcome of urgent CEA with a high rate of postoperative mortality (range 42–60%). Later studies reported that urgent CEA might be appropriate treatment for patients with recent neurological ischemic events and decreased rate of postoperative complications compared with earlier studies. Most recent studies demonstrated that urgent CEA performed in patients with ‘crescendo’ transient ischemic attack (TIA) as well as in patients with stroke in evolution could have favorable outcome.

Good evidence supporting the concept of a critical period of reversible ischemia during which compromised neurons may be salvaged have been described as well. Yet, after recent systematic literature reviews the outcome of urgent CEA is questioned since increased perioperative risk has been described in patients with crescendo TIA and stroke in evolution compared with the outcome after elective CEA.

After analyzing these studies we found that the timing of urgent CEA after recent neurological deficit was not precisely defined. The principle of ‘urgency’ after or during acute neurological ischemic events in patients with carotid disease has to be thoroughly investigated and outlined. Therefore the aim of our study was to analyze the outcome of urgent CEA done in patients with crescendo TIA and stroke in progression, which was performed within less than six hours after neurological ischemic events occurred.
Material and methods

From January 1998 to December 2008, a total of 5,192 elective CEsAs were done at our Institute and during the same period 58 urgent CEsAs were performed. All data were collected prospectively as part of our institution database. Patients admitted for elective CEA were followed for acute neurological ischemic events during the hospitalization and in these patients urgent CEA was done. These data were collected prospectively and in this study we wanted to present our data retrospective review.

All patients were admitted to our Institute for elective CEA. Following admission, after complete examination by attending neurologist, carotid stenosis was estimated by the means of computed tomography (CT) angiography and color duplex scan according to ESCT criteria and criteria described by AbuRahma et al. Carotid stenosis was considered significant (>70%) if peak systolic velocity (PSV) was >150 cm/s and end diastolic velocity (EDV) >90 cm/s.

On the basis of ultrasonographic findings we indicated ICA surgical treatment while multidetector CT (MDCT) angiography was done when ultrasound was not reliable enough: severe ICA stenosis with distal propagation, near to occlusion, diffuse common carotid artery lesions, accompanied supraaortic braches lesions or pathological elongations. All patients had brain CT done previously or upon admission on our Institute. Based on this findings ICA surgical treatment was indicated.

During the hospital stay and elective endarterectomy standard preparation sudden neurological deficit occurred in total of 67 patients. Crescendo TIA was defined as two or more episodes within 24 hours, with complete recovery after each episode, while stroke in progression was defined as gradual deterioration of neurological deficit that took place over at least six hours.

In all patients after symptoms onset neurological examination was done as well as repeated color duplex scan of carotid arteries followed by brain CT to exclude hemorrhage. Likewise, a middle cerebral artery (MCA) patency was assessed by transcranial Doppler (TCD). Contraindications for surgery were loss of consciousness (3 patients), cerebral hemorrhage (2 patients) and MCA occlusion (4 patients). After this exclusion criteria 58 patients underwent urgent CEA.

If extracranial ICA or bifurcation thrombosis was verified by color duplex scan we did CT angiography (6 patients, 10.7%) in order to evaluate distal ICA patency. Disability level was assessed prior to and after the surgery using the modified Rankin score scale (mRS), which ranged from 0 to 5, describing the degree of disability level. Urgent CEA was performed within a few hours (maximum of 6) after ischemic symptoms occurrence (for patients with crescendo TIA after last episode) during which time all diagnostic procedures were completed.

Surgical technique

All patients were operated on under general anesthesia. Operative technique was eversion CEA. Intraluminal shunt was used if patient had contralateral ICA occlusion (4 patients) or intraoperatively poor retrograde flow was noticed (1 patient). In all cases when fresh thrombus was found at the site of the distal ICA or bifurcation level, Fogarty catheter thrombectomy maneuver was performed, but only at the extracranial ICA level.

Plaque morphology was evaluated by visual inspection and histological analysis. Patients were observed in an intensive care unit setting for at least 24 hours following surgery. Neurological recovery were assessed as excellent if mRS was 0 or 1, improved if mRS was better than preoperatively and unaltered if mRS was unchanged. Brain CT was performed in all patients postoperatively. If the postoperative course was uneventful, the patients were discharged from our hospital by the third postoperative day.

Follow-up and statistical analysis

Follow-up consisted of a detailed history and physical examination with color duplex scan done at one month, six months, one year and annually afterwards, median follow up was 42.1 ± 16.6 months. Chi-square, ANOVA, Wald-Wolfwitz runs and t-test were used for comparison between the subgroups. The difference was assumed as statistically significant if $P < 0.05$. Patients’ groups were analyzed for demographic, clinical and surgical data, risk factors for atherosclerosis, co-morbidities, neurological recovery, postoperative complications and total hospital stay.

Results

Table 1 depicts patients’ demographic data, risk factors and co-morbidities.

Out of 58 patients, emergency CEA was done for crescendo TIA in 46 patients (group I; 5 patients had amaurosis fugax [10.9%], 5 patients had dysphasia [10.9%] and 36 patients [78.3%] had contralateral leg or arm weakness) while in 12 patients urgent CEA was done for stroke in progression (group II) (Table 1). There were no statistically significant differences between the two groups in terms of demographic data, risk factors and co-morbidities.
Upon admission only five patients (8.6%) were asymptomatic while 53 patients had previous TIA, stroke or silent brain CT ischemia (Table 2).

In crescendo TIA group there were statistically significant more patients with 70–90% ICA stenosis and patients with contralateral ICA occlusion (P < 0.01) (Table 2). With respect to the previous TIA or stroke presence as well as positive findings for brain CT ischemia, the difference noted was not significant (P > 0.05) (Table 2).

All patients had severe ICA stenosis, two patients had complete extracranial ICA thrombosis while four patients had secondary thrombosis on the basis of high-grade ICA stenosis only at the carotid bifurcation level (Table 3). In all of these patients we administrated low molecular weight heparin in the early postoperative period and Aspirin and Clopidogrel on discharge.

Four patients in crescendo TIA group (8.7%) had segmental bifurcation occlusion with patent distal ICA. Statistically significant difference was not registered regarding ICA clamping time (P = NS).

Table 1  Demographic data, risk factors and co-morbidities

<table>
<thead>
<tr>
<th></th>
<th>Group I ‘crescendo’ TIA (n = 46), n (%)</th>
<th>Group II stroke in progression (n = 12), n (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>27 (58.7)</td>
<td>8 (66.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Age (year ± SD)</td>
<td>65.74 ± 6.71</td>
<td>61.6 ± 3.84</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (67.4)</td>
<td>8 (66.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>29 (63.04)</td>
<td>10 (83.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (26.1)</td>
<td>3 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>28 (60.9)</td>
<td>8 (66.7)</td>
<td>NS</td>
</tr>
<tr>
<td>CAD</td>
<td>9 (19.6)</td>
<td>3 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2 (4.3)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>COPD</td>
<td>3 (6.5)</td>
<td>1 (8.3)</td>
<td>NS</td>
</tr>
<tr>
<td>PAOD</td>
<td>9 (19.5)</td>
<td>2 (16.7)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; PAOD, peripheral arterial occlusive disease; NS, non significant

Upon admission only five patients (8.6%) were asymptomatic while 53 patients had previous TIA, stroke or silent brain CT ischemia (Table 2).

In crescendo TIA group there were statistically significant more patients with 70–90% ICA stenosis and patients with contralateral ICA occlusion (P < 0.01) (Table 2). With respect to the previous TIA or stroke presence as well as positive findings for brain CT ischemia, the difference noted was not significant (P > 0.05) (Table 2).

All patients had severe ICA stenosis, two patients had complete extracranial ICA thrombosis while four patients had secondary thrombosis on the basis of high-grade ICA stenosis only at the carotid bifurcation level (Table 3). In all of these patients we administrated low molecular weight heparin in the early postoperative period and Aspirin and Clopidogrel on discharge.

Four patients in crescendo TIA group (8.7%) had segmental bifurcation occlusion with patent distal ICA. Statistically significant difference was not registered regarding ICA clamping time (P = NS).

Table 2  ICA stenosis and ischemic symptoms prior to surgery

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 46) (%)</th>
<th>Group II (n = 12) (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA stenosis &gt;90%</td>
<td>16 (34.8)</td>
<td>4 (41.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Contralateral occlusion</td>
<td>4 (8.7)</td>
<td>–</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Previous TIA</td>
<td>21 (45.6)</td>
<td>4 (33.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>12 (28.1)</td>
<td>3 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Brain CT ischemia</td>
<td>10 (21.7)</td>
<td>3 (25)</td>
<td>NS</td>
</tr>
</tbody>
</table>

ICA, internal carotid artery; TIA, transient ischemic event; CT, computerized tomography; NS, non-significant

In crescendo TIA group 32 patients had ulcerated plaque (69.6%, P < 0.01) while concerning other plaque characteristics significant difference was not observed, P = NS (Table 4).

In all patients of group I and 11 patients (91.7%) in group II we found excellent or good ICA retrograde flow. Comparing the ICA retrograde flow between two groups, we did not find statistically significant difference (P > 0.05).

In the early postoperative period (within 30 days) stroke rate was 0% for the patients in crescendo TIA group while in patients with stroke in progression group we accomplished to prevent stroke in 75% (9/12 pts) of the patients while three patients (25%) had positive postoperative brain CT, yet neurological status significantly improved (better mRS score after CEA). There were no lethal outcomes during the first 30 days following surgery in both groups (Table 5).

Comparing the outcome of urgent CEA between the crescendo TIA and stroke in progression group in the early postoperative period we found statistically significant difference regarding neurological recovery (P < 0.01) (Table 5). Postoperative brain ischemia was registered in three patients in group II and the difference was statistically significant (P < 0.01), yet these patients had improved neurological status (1 patient from mRS score 4 to 2 after urgent CEA, one patient from 4 to 3 and one patient from 4 to 2).

Table 3  Intraoperative findings

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 46) (%)</th>
<th>Group II (n = 12) (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmental ICA occlusion</td>
<td>4 (8.7)</td>
<td>–</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thrombus at carotid bifurcation level</td>
<td>–</td>
<td>4 (33.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Complete extracranial ICA thrombosis</td>
<td>–</td>
<td>2 (16.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Clamping time (min ± SD)</td>
<td>11.7 ± 2.7</td>
<td>12.8 ± 1.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

ICA, internal carotid artery; NS, non-significant

Table 4  Internal carotid artery plaque morphology

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 46) (%)</th>
<th>Group II (n = 12) (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrolipid</td>
<td>10 (21.7)</td>
<td>2 (16.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Intraplaque hemorrhage</td>
<td>4 (8.7)</td>
<td>1 (8.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ulceration</td>
<td>32 (69.6)</td>
<td>6 (50)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

NS, non significant
score 3 to 2). None of the patients had CT verified brain hemorrhage.

Regarding early postoperative surgical site complications the difference was not significant between the observed groups (Table 6).

During the follow-up, stroke rate was 2.2% in crescendo TIA group and 8.3% in stroke in progression group ($P = \text{NS}$) (Table 6).

In crescendo TIA group one patient had minor stroke in the contralateral ICA region after one year and fully recovered while one patient in stroke in progression group had major stroke after 50 months. In crescendo TIA group there were no lethal outcomes during the follow up while one patient (8.3%) died in stroke in progression group due to a mentioned major stroke. Overall morbidity rate was 6.8% and mortality rate 1.7%.

Kaplan–Meier curve depicts stroke-free rate in patients with crescendo TIA of 97% and for patients in stroke in progression group of 75% (Figure 1).

Neurological mortality free rate was 100% in patients with crescendo TIA and 89% in patients with stroke in progression (Figure 2).

### Discussion

The results of our study showed that urgent CEA performed within less than six hours after acute neurological ischemic events in patients with associated high-grade carotid stenosis is justified and useful procedure for stroke prevention. All patients in crescendo TIA group and nine patients (75%) in stroke in progression group completely recovered while three patients (25%) in stroke in progression group had brain CT positive for ischemia, yet neurological outcome significantly improved.

The first experiences of urgent CEA in patients with acute neurological ischemic events were not encouraging since high postoperative risk has been described mainly
due to intracranial hemorrhage. Later studies showed better results of urgent endarterectomy, but these were small studies wherein the timing of CEA was not clearly defined and often questioned. After literature review, Mead et al. identified over 2000 patients with acute carotid surgery and reported that mortality and morbidity rate was highly variable, with decreased mortality in patients with minor neurological deficits. They also concluded that emergency preoperative brain CT was not able to exclude primary cerebral hemorrhage. Dosick et al. reported that brain CT was not essential for initial exclusion of cerebral infarction in patients with recent neurological ischemic event. Kasper et al. reported favorable outcome of urgent carotid thrombendarterectomy (CTEA) in patients with acute neurological deficit with a success rate of 79% compared with 46% in previous decade, thanks to new and improved imaging modalities that allowed better patient selection and improved outcomes.

Recent years several studies have reported satisfactory results of urgent carotid endarterectomy done in patients with acute neurological ischemic event. In all studies in a different way ‘urgent CEA’ was defined in relation to the type and timing of preoperative ischemic event and to this fact we paid special attention. Musa et al. analyzed the outcome of 27 patients in whom emergency CEA was done. Crescendo TIA term was used for repeated TIAs over four to 24 hours despite the use of aggressive anticoagulation therapy with heparin. An acute stroke was defined as a fixed neurologic deficit existing for 24 hours while stroke in evolution was defined as an acute stroke in which the patient developed an unstable neurologic status with waxing and waning of neurologic function. Urgent CEA was defined as surgery performed within 24 hours after ischemic symptoms presentation. They concluded that urgent CEA can be performed safely with postoperative stroke rate of 7% and mortality rate of 4%.

Karkos et al. analyzed 42 patients in whom urgent CEA was performed for crescendo TIA. Because no agreement has been reached on the actual definition of crescendo TIA at the time they defined crescendo TIA as >3 TIAs in the preceding seven days. Patients with less than three TIAs during the previous seven days were excluded from the study. Postoperative combined stroke/death rate was 7% and stroke/death/major cardiac event rate was 14%. They concluded that postoperative complications after urgent CEA for crescendo TIA is higher than that expected after elective surgery but still acceptable considering the natural history of patients with unstable neurologic symptoms.

Dorigo et al. reported their results of 75 patients in whom urgent CEA was done acute or recent ischemic event. Recent TIA was defined as a single episode of TIA, which occurred within 24 hours, while crescendo TIA was defined as two or more episodes within 24 hours, with complete recovery after each episode.

Stroke in evolution was defined as progression of a neurological deficit that had occurred over at least 24 hours while recent stroke was defined as a fixed neurological deficit occurring within the past five days. After detailed analysis we can see that out of 75 patients urgent CEA was done for acute ischemic events in only 30 patients, 28 patients with crescendo TIA and two patients with stroke in evolution, while in 23 patients CEA was done for recent TIA, in eight patients for recent major non-disabling stroke and in 14 patients for a recent minor stroke. 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).

To our knowledge, our study includes the largest number of patients who underwent urgent CEA for acute neurological ischemic events. Crescendo TIA was defined as two or more TIA episodes within last 24 hours while stroke in progression was defined as the gradual deterioration of neurological deficit that took place over at least six hours.

What our study differs from other studies published so far is that urgent CEA was performed within the first six hours or less after neurological ischemic event occurred. This fact could be one of the main reasons for the good results of our study. Our Institute has extensive experience in carotid surgery and all of our surgeons, both senior and junior, are experienced vascular surgeons with comprehensive training in CEA. Likewise, our surgeons are well trained to recognize and rapidly response in case of acute neurological ischemic event. Since of all our patients were admitted for elective carotid surgery, color duplex scan was already done and when acute ischemic event occurred we did additional diagnostic procedures followed by urgent surgical treatment.

Vascular surgery clinic staff training, coordination of radiological, anaesthesiological and surgical teams significantly contributed to prompt reaction in case of unexpected ischemic event that resulted in rapid diagnosis and urgent surgical treatment (within less than six hours), which according to the results of our study has a crucial significance.

We believe that the CEA can be termed ‘urgent’ only if done immediately after or during arising neurological ischemic event (within six hours or less) in order to prevent stroke, while CEAs done several days after ischemic event (TIA, stroke) can be termed as ‘early’ but not ‘urgent’.

In total of 58 patients urgent CEA was done, in 46 patients for crescendo TIA and in 12 patients for stroke in
progression. Patients with recent TIA, recent major or minor stroke were not included in our study, since we considered urgent CEA a surgery done within few hours (<6) after last ischemic event.

In crescendo TIA group all patients had excellent recovery (mRS 0 or 1), brain CT did not reveal ischemic lesions in any patient. During the follow-up, one patient – 2.2% of crescendo TIA group (1.7% overall) had minor stroke and fully recovered, there were no lethal outcomes. In stroke in progression group in nine patients (75%) we accomplished to prevent stroke and these patients had excellent recovery with mRS 0 or 1, while three patients had improved neurological status – mRS better than prior to surgery (1 patient from score 4 to 3, one patient from 4 to score 2 and in one patient from 3 to score 2). Interesting finding is that in two out of these three patients fresh thrombus was found at entire level of extracranial ICA which indicates the necessity of emergent surgical response in case of neurological deficit in progression. In all these three patients postoperative brain CT was positive for ischemia, yet this patients had improved neurological status after endarterectomy (mRS better than prior to surgery). During the follow-up one patient (8.3% for stroke in evolution group, 1.7% overall) had major stroke followed by lethal outcome. Our study showed excellent results with early mortality rate of 5.3%, yet these patients improved neurological status and soon fully recovered, and overall morbidity rate of 6.8% and overall mortality of 1.7%.

We believe that urgent surgical treatment in patients with confirmed carotid stenosis and acute neurologic ischemic symptoms is crucial for stroke prevention. When vascular surgeons face with an acute neurological event in patients who are under elective preparation for carotid arteries surgical treatment, first to be suspected is ischemic complications due to the presence of high-grade carotid stenosis. After perception of this unexpected condition additional diagnostic procedures should be done immediately (color duplex scan, TCD, brain CT and CT angiography) followed by urgent CEA if there is no contraindications. What type of reconstruction will be done should depend on the surgical practice of the institution where the procedure is done and the specificity of the localization of lesions in each individual patient. Successful results should be expected in specialized vascular clinics where these diagnostic procedures could be done very quickly, of course with available number of operating rooms.

We think that time (within less that 6 h) is the key factor in order to prevent stroke and therefore when acute neurological event is present with associated high-grade carotid stenosis vascular surgeon should not hesitate but promptly respond in the form of urgent carotid surgery after completion of all relevant diagnostic procedures.

One of the drawbacks of our study could be non-standard shunt use. Our center is high-volume center for eversion CEA (ECEA) with over 900 surgeries per year and about 10,000 ECEAs done for the last 20 years. Our surgical technique is based on fast and efficient carotid plaque removal with very short clamping time, which has been proved as good treatment option regarding very low rate of postoperative morbidity and mortality. To support our approach recently published study suggests that surgeons should stick to their routine technique during carotid surgery without or with shunt use, since selective shunt use (if not standard) could be associated with increased postoperative complications.

**Conclusion**

Based on our study results urgent CEA is a safe and effective treatment option for patients with acute neurological ischemic events and associated carotid stenosis with acceptable rate of postoperative morbidity and mortality. Precise definition of urgent CEA is necessary on which basis official guidelines might be formulated for this type of surgery.

**Conflicts of interest:** None.

**Funding:** This manuscript was partly funded by Serbian Ministry of Science and Technological Development – Project No. 41002.

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