# Early and long-term outcomes of carotid endarterectomy in the very elderly: An 18-year single-center study

**Enzo Ballotta, MD,[a] Giuseppe Da Giau, MD,[a] Mario Ermani, MD,[b] Giorgio Meneghetti, MD,[b] Marina Saladini, MD,[b] Renzo Manara, MD,[b] and Claudio Baracchini, MD,[b]** *Padua, Italy*

***Objective:*** **To evaluate the perioperative (30-day) and long-term outcomes of carotid endarterectomy (CEA) in elderly patients with severe symptomatic and asymptomatic carotid disease. Although the efficacy of CEA in preventing stroke in selected patients has been clearly demonstrated, concern has been expressed about the role of CEA in people over 80 years old.**

***Methods:*** **An analysis was conducted on a prospectively compiled computerized database of all primary CEAs performed at our institution from 1990 to 2007. Descriptive demographic data, risk factors, surgical details, perioperative strokes and deaths, and other complications were recorded. All patients underwent postoperative duplex ultrasound scanning and clinical follow-up at one, six, and 12 months, and yearly thereafter. Survival analyses were performed using Kaplan-Meier life-tables. Long-term relative survival after CEA was assessed against age- and gender-matched controls.**

***Results:*** **In all, 1769 CEAs were performed in 1562 patients, 193 of them (207 CEAs; group I) were ≥ 80 years old and 1371 were younger (1562 CEAs; group II). All CEA procedures were performed with patients under deep general anesthesia with continuous perioperative EEG monitoring for selective shunting. No strokes or deaths occurred in group I, whereas there were 11 perioperative strokes and three deaths in group II (1%). A complete follow-up (median, 5.2 years) was obtained in 185 elderly patients: no late occlusions or restenoses were detected, while the seven-year freedom from stroke and death were 96.6% and 52.4%, respectively. The relative seven-year survival rate was 99.8%.**

***Conclusions:*** **CEA in elderly patients proved safe and effective, with an excellent long-term durability. The long-term relative survival after CEA in elderly patients was better than in an age-and gender-matched population, so the likelihood of living long enough to benefit from CEA is not jeopardized by being very elderly. (J Vasc Surg 2009;50:518-25.)**

The current demographic trend throughout the industrialized world is for a longer life expectancy and a consequently aging population. In Italy, an 80-year-old female now has a mean life expectancy of 9.6 years and a male 7.7 years, and an 85-year-old female has a mean life expectancy of 6.6 years and a male 5.4 years.[1] The Eurostat 2008-based national population projections (the EUROPOP 2008, convergence scenario) show that the proportion of people aged 65 or more in the total EU27 population is predicted to increase from 17.1% in 2008 to 30.0% in 2060, and the figure is expected to rise from 84.6 million in 2008 to 151.5 million in 2060. The number of people aged 80 or more is likely to almost triple, from 21.8 million in 2008 to 61.4 million in 2060,[2] with fewer and fewer young people supporting an increasing proportion of elderly people.

Since the incidence of stroke and stroke-related mortality is known to increase dramatically with advancing age,[3] even if the incidence of stroke is to remain stable, a marked increase in the number of strokes can be expected simply because of these demographic trends. As a growing proportion of the population lives longer and the incidence of cerebrovascular events is higher in the elderly, preventing stroke will be a tremendous challenge for societies and health systems.

Large randomized controlled trials (RCTs) have shown that carotid endarterectomy (CEA) is superior to medical therapy in the prevention of stroke in symptomatic patients with severe (≥70%) carotid stenosis[4,5] and, to a lesser extent, in those with asymptomatic carotid disease.[6,7] For CEA to be worthwhile, however, the long-term benefit (preventing stroke) must outweigh the perioperative risk (stroke and death). Although the perioperative stroke and mortality rates after CEA recorded in the RCTs are still considered acceptable, they are now 15-20 years old and the current literature has demonstrated that they have dropped drastically over time, while medical treatments have improved considerably since the RCTs were conducted. An aggressive stroke risk factor management and appropriate treatment of carotid lesions can therefore significantly improve not just the longevity but also the useful life expectancy of elderly people.

Despite the above-mentioned epidemiological forecasts and the effective and beneficial results of an aggressive treatment, concern remains about the role of CEA in patients over 80, based on the inherent risks of the surgical procedure and the uncertainty surrounding the long-term survival of this population after CEA, so a different proce-

From the Vascular Surgery Section, Geriatric Surgery Clinic; Department of Surgical and Gastroenterological Sciences,[a] and the Department of Neurological Sciences,[b] University of Padua, School of Medicine.

Competition of interest: none.

Reprint requests: Enzo Ballotta, MD, Vascular Surgery Section, Geriatric Surgery Clinic; Department of Surgical and Gastroenterological Sciences, University of Padua, School of Medicine, Via N. Giustiniani, 2 35128 Padova, Italy (e-mail: enzo.ballotta@unipd.it).

0741-5214/$36.00



doi:10.1016/j.jvs.2009.04.053

dure, such as carotid artery stenting (CAS), has been recommended as an alternative treatment option.[8-11] We analyzed the perioperative (30-day) stroke and death rates, the incidence of late occlusions and recurrent stenoses, and the long-term and stroke-free survival rates after CEA in patients aged 80 years or more with severe symptomatic and asymptomatic carotid disease.

## PATIENTS AND METHODS

Demographic and clinical data were prospectively entered into a computerized vascular surgery registry for all patients who underwent CEA for severe symptomatic and asymptomatic internal carotid artery (ICA) disease, according to the recommendations of the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[4] and the Asymptomatic Carotid Atherosclerosis Study (ACAS),[6] at our institution over an 18-year period (1990-2007). For the purposes of this study, the registry was queried to identify patients aged 80 or more (group I) and under 80 years old (group II) who underwent CEA. Patients scheduled for CEA with concomitant coronary artery bypass grafting, or with associated supra-aortic trunk lesions requiring concurrent surgery, and patients requiring procedures for recurrent disease were ruled out. The patients' demographic and clinical data were recorded on a standardized form, including potential risk factors for atherosclerosis, anatomical and clinical variables, details of surgery, and all complications. The diagnosis of an ICA lesion was based on preoperative digital subtraction angiography (DSA) during the earlier part of this study (used with decreasing frequency over the years), while duplex ultrasound (US) scan was the only preoperative carotid imaging study performed in most patients from mid-1998 onwards, combined in selected patients (those who either had a pseudo-occlusion on duplex US scan or a stenosis of the ICA intracranial segment detected by transcranial Doppler sonography) with magnetic resonance angiography (MRA), computed tomography angiography (CTA), or DSA. The velocity criteria, as described elsewhere,[12] not the features of the plaque, were taken into account for CEA decision. A neurological evaluation was performed in all patients by the consultant neurologist preoperatively, at the awakening from the anesthesia, at the dismissal from the hospital, and during the follow-up. All patients were on antiplatelet therapy: aspirin 100 mg daily or ticlopidine 500 mg daily and, in the recent years, clopidogrel 75 mg daily. All patients with diabetes, hyperlipidemia, and/or hypoechoic plaques were on statin therapy. Preoperative patient preparation was standardized.

All CEA procedures involved either traditional CEA with patch (n = 302; the only patch material used was polytetrafluoroethylene [PTFE, Gore-tex, WL Gore, Elkton, MD]) in the first period of the study, or eversion CEA later on (n = 1467). The technical details of both procedures have been described elsewhere.[13,14] All CEA were performed by the same surgeon with patients under deep general anesthesia and continuous perioperative electroencephalographic (EEG) monitoring for selective shunting. Shunting criteria were based exclusively on EEG changes consistent with cerebral ischemia. No completion imaging studies were performed. None of the CEA procedures considered in this series were aborted or incomplete, and none of the patients were refused CEA for technical reasons emerging during surgery.

Patients were usually monitored in the recovery room for two hours until their blood pressure and neurological status were considered acceptable, then they were transferred to a nursing unit specializing in vascular care and monitored for the next 12-24 hours after surgery. All patients with severe headache were observed for hyperperfusion syndrome, and hypertension was treated aggressively. Most patients were discharged 48-72 hours after CEA.

**Surveillance protocol.** After discharge, visiting nurses monitored the patients' blood pressure and neurological status. All surviving patients systematically underwent physical and neurological assessment by a consultant neurologist, and concomitant duplex US scan performed by two experienced technologists one, six, and 12 months, then yearly, after surgery, assessing any occlusion or recurrent carotid disease. A peak systolic velocity (PSV) of more than 140 cm/s with spectral broadening throughout systole and an increased peak diastolic velocity were consistent with a stenosis $\geq$ 50% diameter reduction and a PSV of more than 210 cm/s with an end diastolic velocity between 110 and 140 cm/s were consistent with $\geq$ 70% stenosis. Neurological events were always classified by the consultant neurologist as transient ischemic attack (TIA; ie, temporary hemispheric symptoms lasting no more than 24 hours, with complete recovery), amaurosis fugax (transient monocular visual loss), or stroke (*minor:* a clinical syndrome of rapidly developing signs or symptoms of focal loss of cerebral function of vascular origin, lasting more than 24 hours and not leading to any handicap or significant impairment in activities of daily living [modified Rankin-scale[15] (mRS) $<$ 3] or *major:* a focal neurological deficit lasting more than 30 days and inducing a change in lifestyle [mRS 3/5]). Brain imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) was performed in all patients presenting a new neurological deficit after CEA. Cardiac complications were classified by a single cardiologist and included: 1) myocardial infarction (MI) with a diagnosis based on creatinine kinase-MB levels and electrocardiogram (ECG) findings; 2) pulmonary edema confirmed by chest X-ray; 3) documented ventricular fibrillation or primary cardiac arrest; and 4) new complete heart failure (CHF), requiring a pacemaker. A postoperative ECG was routinely obtained in all patients who had a history of coronary artery disease, CHF, or arrhythmia (rhythm other than sinus) and cardiac isoenzymes were obtained in all patients who had new findings at postoperative ECG. Other complications and events observed during follow-up were recorded in accordance with the guidelines of the Ad Hoc Committee on Reporting Standards for Cerebrovascular Disease, Society for Vascular Surgery/North American Chapter of the International Society of Cardiovascular Surgery.[16]

**Table I.** Baseline characteristics

| | *Group I (n = 193)* | *Group II (n = 1371)* | *Total (n = 1564)* | *OR (95% CI)* | P *value* |
|---|---|---|---|---|---|
| CEA procedures, n (%) | 207 (11.7) | 1562 (88.3) | 1769 (100) | | |
| Mean age, yrs (range) | 84.8 (80-96) | 68.6 (31-79) | | | |
| Male, n (%) | 139 (72.0) | 963 (70.2) | 1102 (70.5) | | .612 |
| Risk factors | | | | | |
| Hypertension, n (%) | 129 (66.8) | 796 (58.0) | 925 (59.1) | 1.45 (1.06-2.00) | .020 |
| Smoking, n (%) | 143 (74.1) | 929 (67.8) | 1072 (68.5) | 0.73 (0.52-1.03) | .076 |
| Diabetes, n (%) | 47 (24.3) | 451 (32.9) | 498 (31.8) | 0.66 (0.46-0.93) | .017 |
| Hyperlipidemia, n (%) | 77 (39.9) | 621 (45.3) | 698 (44.6) | 0.80 (0.59-1.09) | .158 |
| Cardiac disease, n (%) | 96 (49.7) | 603 (44.0) | 699 (44.7) | 1.26 (0.93-1.70) | .132 |
| CKD, n (%) | 16 (8.3) | 101 (7.4) | 117 (7.5) | 1.13 (0.66-1.96) | .648 |
| Pulmonary disease, n (%) | 31 (16.0) | 213 (15.5) | 244 (15.6) | 1.04 (0.69-1.56) | .850 |
| Symptomatic, n (%) | 155 (74.9) | 971 (62.1) | 1126 (63.6) | 1.81 (1.30-2.52) | <.001 |
| TIA, n (%) | 73 (35.3) | 464 (29.7) | 537 (30.3) | 1.29 (0.95-1.75) | .102 |
| Amaurosis fugax, n (%) | 29 (14.0) | 211 (13.5) | 240 (13.6) | 1.04 (0.69-1.58) | .843 |
| Stroke, n (%) | 53 (25.6) | 296 (18.9) | 349 (19.7) | 1.47 (1.05-2.06) | .026 |
| Asymptomatic, n (%) | 52 (25.1) | 591 (37.8) | 643 (36.4) | 1.81 (1.30-2.52) | <.001 |
| Contralateral CO, n (%) | 82 (42.5) | 167 (12.2) | 249 (15.9) | 5.32 (3.84-7.38) | <.001 |
| CEA with patching, n (%) | 35 (16.9) | 267 (17.1) | 302 (17.1) | 0.98 (0.67-1.45) | .947 |
| Eversion CEA, n (%) | 172 (83.1) | 1295 (82.9) | 1467 (82.9) | 0.98 (0.67-1.45) | .947 |
| Shunting, n (%) | 63 (30.4) | 238 (15.2) | 301 (17.0) | 2.43 (1.75-3.37) | <.001 |

*CEA,* Carotid endarterectomy; *CKD,* chronic kidney disease; *CO,* contralateral carotid occlusion; *TIA,* transient ischemic attack.

The study endpoints were perioperative stroke and death, carotid restenoses or late occlusions, and long-term and stroke-free survival in groups I and II.

**Statistical analysis.** All values are expressed as mean ± SD. Continuous data were compared with the Student's $t$ test (two-tailed) and categorical variables with Pearson's $\chi^2$ test (two-tailed) or Fisher's exact test, as appropriate, calculating the odds ratio (OR) with 95% confidence intervals (CIs). Cumulative life-table analyses (Kaplan-Meier) were used to assess long-term and stroke-free survival rates. Curves were compared with the log-rank test. The relative survival is the ratio of the survival observed in patients to the expected survival of the general Italian population matched for age, gender, and calendar time.[1] Relative survival analysis was done with a SAS macro (SAS version 8.2; SAS Institute Inc, Cary, NC) based on the Hakulinen method.[17] Statistical significance was inferred for $P < .05$. Several data items were analyzed vis-à-vis surgical procedures rather than patients because each perioperative and long-term outcome was correlated with the surgical procedure, and because patients who underwent bilateral CEAs were exposed to twice the risk of stroke, death or carotid restenosis or occlusion.

## RESULTS

Overall, 1769 CEA procedures were performed in 1564 patients, 193 of them aged ≥ 80 years (group I, 12.3%), while the other 1371 (group II, 87.7%) were younger. Two-hundred and five patients underwent staged bilateral CEAs (14 in group I and 191 in group II, respectively). In group I, the number of CEAs progressively increased over time, from the initial 42 in 1990-1995 to 68 in 1996-2001 and then 97 in 2002-2007. The preoperative baseline characteristics of the two groups are summarized in the Table I. More than 70% of the patients were males, in both groups. The mean age was 84.8 years (range, 80-96 years) in the older group and 68.6 years (range, 31-79 years) in the younger group. The incidence of arterial hypertension was statistically higher in the older group (66.7% vs 58.0%, $P = .020$), while the younger patients were significantly more likely to have diabetes mellitus (32.1% vs 24.3%, $P = .017$). Although there were more smokers among the very elderly (74.1% vs 67.8%), the difference failed to reach statistical significance ($P = .076$). There was also no statistically significant difference between the two groups in terms of the incidence of hyperlipidemia or cardiac, pulmonary or chronic kidney diseases. Symptomatic lesions were more frequent in group I (74.9% vs 62.1%, $P < .001$), with a statistically higher frequency of patients with stroke ($P = .026$). The type of CEA procedure used (traditional with patching or eversion) was much the same in the two groups, but eversion CEA was performed more often than traditional CEA, both in the series as a whole ($P < .001$) and in each group (83.1% vs 16.9% in the older group, $P < .001$; and 82.9% vs 17.1% in the younger group, $P < .001$). Among the older patients, there was a significantly higher prevalence of contralateral ICA occlusion ($P < .001$) and use of intraluminal shunting ($P < .001$) (Table I).

**Perioperative mortality and stroke rates.** Overall, the perioperative mortality and stroke rates were 0.16% and 0.62% (11 of 1769), respectively, with a combined mortality and stroke rate of 0.79% (Table II). No significant differences emerged between the two groups in terms of perioperative neurological events or deaths. Perioperative death and stroke only occurred in the younger group. There were three perioperative deaths; two were due to an MI, and one to a fatal stroke. All the other strokes (six CEAs with patching and four eversion CEAs) occurred in symptomatic patients, and all but two were major strokes.

**Table II.** Perioperative (30-day) results

| | *Group I (193 pts, 207 CEAs)* | *Group II (1371 pts, 1562 CEAs)* | *OR (95% CI)* | P *value* | *Total (1564 pts, 1769 CEAs)* |
|---|---|---|---|---|---|
| Stroke, n (%) | 0 | 11 (0.70) | 0 (0.0-2.62) | .628 | 11 (0.62) |
| Major | | 9 | | | |
| Ipsilateral | | 7 | | | |
| Contralateral | | 2 | | | |
| Minor | | 2 | | | |
| Ipsilateral | | 1 | | | |
| Contralateral | | 1 | | | |
| Death, n (%) | 0 | 3 (0.19) | 0 (0.0-9.69) | .688 | 3 (0.16) |
| Stroke-related | | 1 | | | |
| Combined stroke and death, n (%) | 0 | 14 (0.89) | 0 (0.0-2.06) | .394 | 14 (0.79) |
| TIA, n (%) | 11 (5.3) | 47 (3.0) | 1.81 (0.93-3.51) | .080 | 58 (3.3) |
| Ipsilateral | 4 | 22 | | | |
| Contralateral | 7 | 25 | | | |
| Combined stroke and TIA, n (%) | 11 (5.3) | 58 (4.2) | 1.45 (0.76-2.79) | .264 | 69 (3.9) |
| Cardiac complications, n (%) | 2 (0.96) | 14 (0.89) | 1.08 (0.27-4.29) | .710 | 16 (0.90) |
| MI | 0 | 3 | | | 3 |
| Fatal | | 2 | | | |
| Non-fatal | | 1 | | | |
| CHF | 1 | 8 | | | 9 |
| Arrhythmia | 1 | 3 | | | 4 |
| Neck hematoma, n (%) | 12 (5.8) | 85 (5.4) | 1.07 (0.58-1.98) | .833 | 97 (5.5) |
| Nerve injury, n (%) | 7 (3.4) | 72 (4.6) | 0.72 (0.33-1.57) | .422 | 79 (4.5) |

*CEA,* Carotid endarterectomy; *CHF,* congestive heart failure; *MI,* myocardial infarction; *TIA,* transient ischemic attack.

In all cases, stroke occurred within the first 24 hours of surgery, while the patient was still in the recovery room: duplex US scan immediately confirmed ICA occlusion in the patched arteries, and ICA patency in the everted arteries. Four of the patched patients underwent redo-surgery consisting of thrombectomy and a new patch-plasty: only one patient had some improvement in neurological status. The other two strokes involved the hemisphere contralateral to the operated side (one of these was ipsilateral to an occluded ICA). Among the four strokes in everted patients, two were major and two minor. Both major strokes occurred in patients (one of them was shunted) with a mildly diseased contralateral ICA and produced, based on cerebral CT scans, a cortical infarction in the territory of the middle cerebral artery: since they could not possibly be due to technical errors, we assumed they were embolic (from the aortic arch or the heart). Both minor strokes were most likely hemodynamic in nature, since they were border zone infarcts, judging from the CT images: one developed in the hemisphere contralateral to the revascularized ICA and ipsilateral to an occluded ICA.

**Minor perioperative neurological events.** Fifty-eight (3.3%) perioperative TIAs were observed and more than half of them (32 of 58, 55.2%) occurred in the middle cerebral artery territory contralateral to the operated side. In all cases, duplex US scan performed immediately after the onset of neurological signs showed that the revascularized ICA was patent and cerebral CT or MR images were negative for any new ischemic events. The difference between the two groups was not statistically significant (Table II).

**Other complications.** Overall, there were 16 perioperative cardiac complications (0.9%). Only two were fatal (MI) and occurred in two symptomatic patients in group II. The incidence of cardiac complications did not differ statistically between the older and younger groups (Table II). No hyperperfusion syndrome was seen in any of the patients. Overall, there were 97 (5.5%) neck hematomas requiring surgical evacuation, with no further complications; the suture line was intact in all cases, and venous oozing from the superficial layers was the only apparent source of bleeding. No statistically significant difference emerged between the groups (Table II).

Other surgical morbidities included 79 nerve injuries (4.5%), with 66 (3.7%) involving the cranial nerves and 13 (0.7%) the cervical nerves. The hypoglossal nerve was involved 41 times, the recurrent laryngeal nerve 12 times, the superior laryngeal nerve eight times, the marginal mandibular nerve five times, the greater auricular nerve 10 times, and the transverse cervical nerve three times. All nerve dysfunctions were transient, and all but four recurrent laryngeal nerve injuries regressed completely within six months of the CEA; two patients took 12 months to recover and two did not recover until 31 and 37 months later. There was no statistically significant difference between the groups (Table II).

**Long-term results.** After excluding the three perioperative deaths, 1561 patients were alive 30 days after CEA, but 57 (3.6%) were lost to follow-up. A complete follow-up was therefore obtained in 1504 patients (1699 CEAs), 185 of them (198 CEAs) in the older group (Table III).

In group I, the median follow-up was 5.2 years (mean, 7 ± 2.5 years; range, 0.1-18 years); in group II, the median follow-up was 8.6 years (mean, 9 ± 4.5 years; range, 0.1-18 years).

Overall, 8 ICA occlusions were detected (0.4%; in six patched and two everted arteries), and they were all in

**Table III.** Long-term results

| | *Group I (185 pts, 198 CEAs)* | *Group II (1319 pts, 1501 CEAs)* | *OR (95% CIs)* | P *value* | *Total (1504 pts, 1699 CEAs)* |
|---|---|---|---|---|---|
| Stroke, n (%) | 3 (1.6) | 11 (0.8) | 1.96 (0.58-6.60) | .400* | 14 (0.8) |
| Ipsilateral | 1 | 3 | 2.38 (0.34-16.75) | .409* | 4 (0.2) |
| Contralateral | 2 | 8 | 1.79 (0.42-7.52) | .354* | 10 (0.6) |
| Death, n (%) | 31 (16.7) | 74 (5.6) | 3.38 (2.16-5.30) | <.001 | 105 (6.7) |
| Stroke-related | 0 | 2 | 0 (0.0-13.75) | .769* | 2 |
| Restenoses > 50%, n (%) | 3 (1.5) | 16 (1.1) | 1.43 (0.44-4.63) | .478* | 19 (1.1) |
| Restenoses ≥ 70%, n (%) | 0 | 9 (0.6) | 0 (0.0-3.23) | .610* | 9 (0.5) |
| ICA occlusion, n (%) | 0 | 8 (0.5) | 0 (0.0-3.64) | .607* | 8 (0.4) |
| Restenoses ≥ 70% plus occlusions, n (%) | 0 | 17 (1.1) | 0 (0.0-1.70) | .247* | 17 (1.0) |

*CEA,* Carotid endarterectomy; *ICA,* internal carotid artery.
*by Fisher exact test.

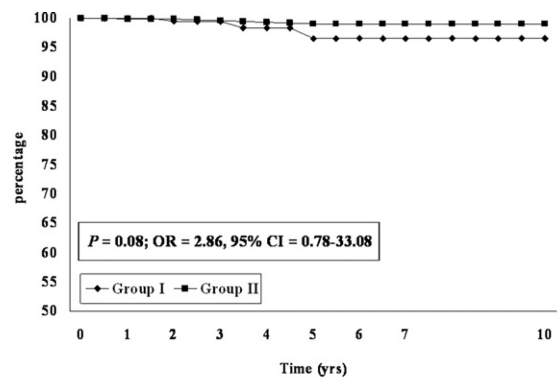
group II (Table III). All occlusions involved ICAs that were not shunted and occurred without symptoms within the first postoperative year, all in arteries patent at the first two duplex US scans.

There were 19 (1.1%) restenoses ≥ 50% altogether, three of which were detected in group I and involved ICAs that were not shunted (14 were patched), and they occurred without symptoms within 24 months of surgery. Of these 19 restenoses, 9 (0.6%, all in group II) were ≥ 70%, giving a combined occlusion/restenoses ≥ 70% rate of 1.0% (Table II). All but two remained stable at subsequent duplex US scans and were treated conservatively. In these two arteries (one patched), the restenosis ≥ 70% progressed rapidly and became severe enough (> 90%) to demand a second CEA or a CAS procedure respectively 19 and 22 months after the first revascularization.

Overall, there were 14 late strokes (0.8%), three of them in group I (1.6%): four were cardioembolic, eight lacunar (two in group I, both contralateral to the operated side) and two (one in group I, ipsilateral to the operated side, and contralateral to an ICA occlusion) were probably hemodynamic in nature, judging from the CT images.

Kaplan-Meier analysis showed that the freedom from strokes at one, three, five, and seven years was 100%, 99.4 ± 0.6%, 96.6 ± 2.4%, and 96.6 ± 2.3% in group I and 99.9 ± 0.1%, 99.6 ± 0.2% , 99.1 ± 0.3%, and 99.0 ± 0.3% in group II, (OR = 2.86; 95% CI, 0.78-33.08; $P = .088$) (Fig 1).

One hundred and five late deaths occurred in the series as a whole, two of which (both in group II) were stroke-related (a fatal stroke in a patient with an atrial fibrillation of recent onset, and another fatal stroke contralateral to the revascularized side and ipsilateral to an ICA occlusion). The cause of late death was primarily cardiac-related (n = 48) (Table IV). The observed survival at one, three, five, and seven years was 99.5 ± 0.5%, 95 ± 2%, 74.3 ± 5.4%, and 52.4 ± 9.3% in group I and 99.8 ± 0.1%, 97.5 ± 0.5%, 94 ± 0.7%, and 88.2 ± 0.9% in group II (OR = 4.30; 95% CI 8.35-34.42; $P < .001$) (Fig 2). The five- and seven-year relative survival rates of the elderly patients were 112.5% and 99.8%, respectively (Fig 3).




| | Group I | at risk | Group II | at risk |
|---|---|---|---|---|
| 1 yr | 100% | 151 | 99.9 ± 0.1% | 1227 |
| 3 yrs | 99.4 ± 0.6% | 81 | 99.6 ± 0.2% | 1003 |
| 5 yrs | 96.6 ± 2.4% | 42 | 99.1 ± 0.3% | 764 |
| 7 yrs | 96.6 ± 2.3% | 12 | 99.0 ± 0.3% | 516 |

**Fig 1.** Kaplan-Meier curves show the freedom from stroke of the two groups who underwent carotid endarterectomy.

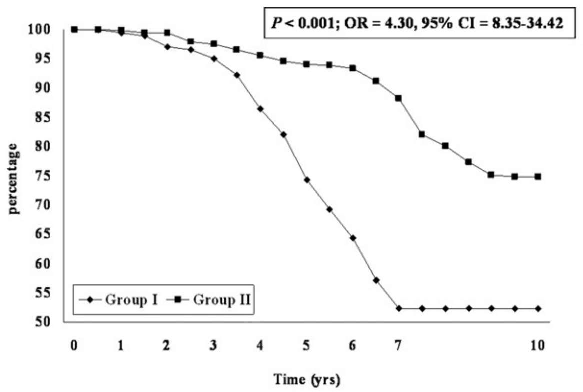
**Table IV.** Causes of late deaths

| *Cause* | *Group I, 185 pts n (%)* | *Group II, 1319 pts n (%)* | *Total, 105 deaths n (%)* |
|---|---|---|---|
| Cardiac disease | 17 (9.2) | 31 (2.3) | 48 (45.7) |
| AAA rupture | 0 | 1 (0.07) | 1 (1) |
| Stroke | 0 | 2 (0.15) | 2 (1.9) |
| Pancreatitis | 2 (1.1) | 2 (0.15) | 4 (3.8) |
| Cancer | 4 (2.2) | 19 (1.4) | 23 (21.9) |
| Renal failure | 2 (1.1) | 5 (0.38) | 7 (6.7) |
| Suicide | 0 | 1 (0.07) | 1 (1) |
| Car accident | 1 (0.5) | 6 (0.45) | 7 (6.7) |
| Trauma | 1 (0.5) | 2 (0.15) | 3 (2.9) |
| Unknown | 4 (2.2) | 5 (0.38) | 9 (8.6) |
| Total | 31 (16.7) | 74 (5.6) | 105 (100) |

*AAA,* Abdominal aortic aneurysm.

## DISCUSSION

The results of this study show that CEA is safe and effective in patients with severe symptomatic and asymp-




| | Group I | at risk | Group II | at risk |
|---|---|---|---|---|
| 1 yr | 99.5 ± 0.5% | 151 | 99.8 ± 0.1% | 1228 |
| 3 yrs | 95.0 ± 2.0% | 82 | 97.5 ± 0.5% | 1007 |
| 5 yrs | 74.3 ± 5.4% | 44 | 94.0 ± 0.7% | 769 |
| 7 yrs | 52.4 ± 9.3% | 12 | 88.2 ± 0.9% | 517 |

**Fig 2.** Kaplan-Meier curves show the long-term cumulative survival of the two groups. Standard error exceeds 10% in group I after seven years.

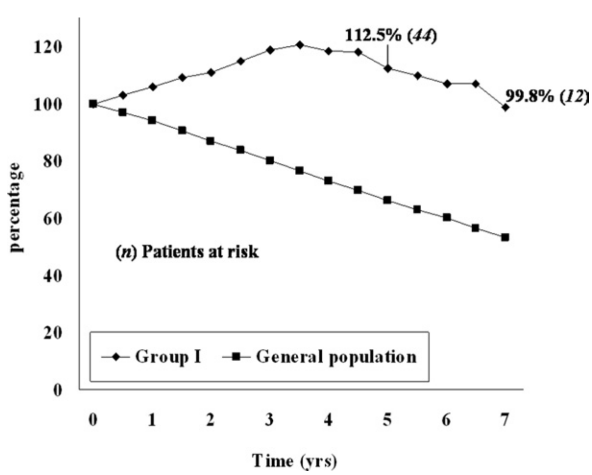



**Fig 3.** The long-term relative survival of the elderly patients who underwent carotid endarterectomy. Standard error exceeds 10% in group I after seven years. The survival of age- and gender-matched Italian population was plotted for reference.

tomatic ICA stenosis, with a combined mortality and stroke rate of less than 1%, and that CEA can be performed in patients ≥ 80 years old with perioperative stroke risk and death rates comparable with those of younger patients, as reported in many other institutional series[18-31] (Table V). Moreover, these findings correlate well with, and expand on the results of our two previous, smaller studies on early outcomes in this patient population.[32,33]

Despite evidence that the incidence of stroke increases with age, that the outcome of the best medical therapy is worse in the elderly, and that perioperative surgical treatment is safe and effective in octogenarians, many clinicians still doubt the overall benefit of CEA in such patients, given their higher risk of complications due to associated comorbidities and their limited life expectancy. This concern has significantly curtailed the referral of elderly patients for CEA, prompting many of them to accept the option of a seemingly lower-risk and less invasive treatment, such as CAS. The conviction that CAS is preferable to CEA in the very elderly appears to be based on two premises that remain to be seen (ie, that CEA is a high risk procedure and that CAS is safer than CEA). The first premise is not supported by the perioperative outcomes emerging from our own and many other institutional studies, which have failed to reveal any relationship between old age and perioperative adverse events in the performance of CEA, reporting excellent results in such patients and demonstrating that the very elderly could even benefit from CEA more than their younger counterparts.[18-31] The second premise is belied by the analysis of the periprocedural results of many observational series,[8-11] and recent data from the lead-in phase of CREST study (a 30-day death/stroke rate of 12.1%),[34] the CAPTURE 3500 study (30-day death/stroke/MI rates of 17.1% and 8% in symptomatic and asymptomatic elderly people, respectively),[35] and the CASES PMS study (a 30-day death/stroke/MI rate of 7.3%),[36] which revealed that the periprocedural risk of stroke and death increases with age, causing an unacceptable risk for the very elderly. The conclusion one may draw from all these studies is that octogenarians should be considered high-risk patients for CAS procedures and the common practice of recommending CAS for older patients is questionable and should be abandoned until the results of RCTs demonstrate that CAS under protection could give results at least no worse than CEA in this subgroup of the population.

Because the incidence of late occlusions and restenoses after CEA can be interpreted as a measure of the durability of the surgical treatment, the lack of occlusions or severe restenoses in our elderly patients over a mean follow-up of 7 ± 2.5 years, and an overall combined occlusion and severe restenosis rate of 1.0% in 1699 CEAs performed in 1504 patients consequently demonstrate that CEA is a durable procedure. Surprisingly, no occlusions stemmed from any progression of restenosis, since the endarterectomized vessel was normal on the previous duplex US scan; occlusions and restenoses developed more often in patched than in everted arteries (20/27 cases, 74%). Although recurrent carotid stenosis remains a conundrum because reports vary widely on its incidence and differ in the duration of follow-up, the criteria used to determine and define the restenosis, and the method used to close the arteriotomy, our finding is consistent with reports from other authors of a lower ICA restenosis rate after eversion than after CEA with patching or primary closure.[37]

The cumulative seven-year survival of our elderly population was 52.4%, a figure comparable with those reported by many authors.[19,21-24,26,29,30,38] However, when background all-cause mortality is taken in account, the long-term relative survival of our elderly patients after CEA was greater than in the age- and gender-matched Italian popu-

**Table V.** Reported perioperative outcomes of CEA procedures in elderly patients

| | Patients ≥ 80 yrs | | Patients < 80 yrs | |
|---|---|---|---|---|
| *Author* | *CEA, n* | *Stroke and death, n (%)* | *CEA, n* | *Stroke and death, n (%)* |
| Schultz[18] | 116 | 2 (1.7) | 105 | 3 (2.8) |
| Pinkerton and Golkar[19] | 125 | 1 (0.8) | 560 | 17 (3.0) |
| Treiman[20] | 183 | 7 (3.8) | 1487 | 59 (4.0) |
| Coyle[21] | 79 | 1 (1.3) | 992 | 42 (4.2) |
| O'Hara[22] | 182 | 6 (3.3) | 2053 | 69 (3.4) |
| Perler[23] | 1036 | 27 (2.6) | 8882 | 229 (2.6) |
| Ting[24] | 59 | 4 (6.8) | 597 | 17 (2.8) |
| Maxwell[25] | 218 | 9 (4.1) | 2180 | 93 (4.2) |
| Schneider[26] | 90 | 1 (1.1) | 492 | 10 (2.0) |
| Oszvath[27] | 125 | 1 (0.8) | 3932 | 33 (0.8) |
| Rockman[28] | 161 | 3 (1.9) | 537 | 19 (3.5) |
| Pruner[29] | 345 | 8 (2.3) | 3085 | 40 (1.3) |
| Miller[30] | 360 | 11 (3.0) | 1857 | 28 (1.5) |
| Stoner[31] | 1341 | 68 (5.0) | 12281 | 432 (3.5) |
| Present series | 207 | 0 | 1562 | 14 (0.9) |

*CEA,* Carotid endarterectomy.

lation. The finding that octogenarians CEA patients lived longer than the average ≥ 80-year-old is not new. In a population-based study on all patients who underwent CEA for a 10-year period in Western Australia, Norman et al[38] calculated a relative five-year survival of 118% (95% CIs: 102-134) in 151 patients ≥ 80 years of age, attributing this excellent survival to a careful patient selection. Similarly, Schneider et al reported that the 81% four-year survival recorded in their 90 octogenarian patients who underwent CEA was comparable with, if not better, than that of their age-matched peers. In the absence of any RCTs, it is very hard to say whether CEA increases life expectancy in elderly patients. Although the causes of four late deaths (2.2%) were undetermined, and therefore some may have been stroke-related, no late stroke-related deaths occurred in our elderly population, so CEA does not seem to afford a prolonged survival advantage. The only late ipsilateral ischemic stroke, probably due to cerebral hemodynamics, and the two other lacunar strokes, contralateral to the operated side, would support the efficacy of CEA in preventing late strokes related to carotid disease, but would suggest that CEA cannot prevent all late strokes. The seven-year rate of freedom from stroke of 96.6% nonetheless indicates that most of our octogenarians lived the rest of their lives without stroke.

This study has some limitations. Although the data were collected prospectively, the analysis was retrospective in nature. There may be a selection bias because healthier patients may have been referred for CEA, although we cannot infer this from the available data and we do not believe this is the case. The elderly patients were significantly less likely than their younger counterparts to have a history of diabetes, but it is just a reflection of the general population in that people with diabetes and carotid disease are less likely to survive into their 80s. Octogenarians had symptoms significantly more often than the younger patients, and a significantly higher incidence of prior stroke. The statistically greater presence of contralateral ICA occlusions in the very elderly might explain the significantly more frequent need for shunting, but this did not appear to negatively influence perioperative outcome. In addition, despite a high incidence of preoperative cardiac disorders (49.7%), only two patients (1%) experienced early cardiac complications, neither of which proved fatal and both were managed with ease. Finally, although this report concerns a large group of CEA procedures performed in patients ≥ 80 years of age, the size of the sample is still small, and the number of perioperative adverse events was nil, so the relative lack of power makes any definitive statistical analysis impossible.

In conclusion, CEA in patients ≥ 80 years of age is a safe and effective procedure with an excellent long-term durability. This should be the standard against which alternative treatments are judged. Although CEA cannot prevent all late strokes, most of our octogenarians lived the rest of their lives without any stroke. The long-term relative survival after CEA performed in patients ≥ 80 years of age is better than the survival of an age- and gender-matched population, so the likelihood of living long enough to benefit from a CEA is not jeopardized by the fact of being very elderly.

## AUTHOR CONTRIBUTIONS

Conception and design: EB, GDG, GM, CB
Analysis and interpretation: EB, CB
Data collection: MS, RM
Writing the article: EB, GM, CB
Critical revision of the article: EB, CB
Final approval of the article: EB, CB
Statistical analysis: ME
Obtained funding: N/A
Overall responsibility: EB, GM, CB

## REFERENCES


1. Tables of mortality. Available at: http://demo.istat.it. Accessed on January 24, 2009.
2. Giannakouris K. Eurostat. Statistics in focus. Population and social conditions. Available at: http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-SF-08-072/EN/KS-SF-08-072-EN.PDF. Accessed on February 3, 2009.
3. Jemal A, Ward E, Hao Y, Thun M. Trends in the causes of death in the United States, 1970-2002. JAMA 2005;294:1255-59.
4. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
5. European Carotid Surgery Trialists Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. Lancet 1991;337:1235-43.
6. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-8.
7. MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. Lancet 2004;363:1491-1502.
8. Roubin GS, New G, Iyer SS, Vitek JJ, Al-Mubarak N, Liu MW, et al. Immediate and late clinical outcome of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis. Circulation 2001;103:532-7.
9. Kastrup A, Groschel K, Krapf H, Brehm BR, Dichgans J, Schulz JB. Early outcome of carotid angioplasty and stenting with and without cerebral protection devices: a systematic review of the literature. Stroke 2003;34:813-9.
10. Stanziale SF, Marone LK, Boules TN, Brimmeier JA, Hill K, Makaroun MS, et al. Carotid artery stenting in octogenarians is associated with increased adverse outcomes. J Vasc Surg 2006;43:297-304.
11. Zahn R, Ischinger T, Hochadel M, Zeymer U, Schmalz W, Treese N, et al. Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte. Carotid artery stenting in octogenarians: results from the ALKK Carotid Artery Stent (CAS) Registry. Eur Heart J 2007;28:370-5.
12. Ballotta E, Da Giau G, Gruppo M, Meneghetti G, Manara R, Ermani M, et al. Diabetes and asymptomatic carotid lesion: does diabetic disease influence the outcome of carotid endarterectomy? A 10-year single center experience. Surgery 2008;143:519-25.
13. Ballotta E, Da Giau G, Saladini M, Abbruzzese E, Renon L, Toniato A. Carotid endarterectomy with patch closure vs carotid eversion endarterectomy and reimplantation. A prospective randomized study. Surgery 1999;125:271-9.
14. Ballotta E, Da Giau G. Selective shunting with eversion carotid endarterectomy. J Vasc Surg 2003;38:1045-50.
15. van Swieten JC, Kondstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604-7.
16. Baker JD, Rutherford RB, Bernstein EF, Courbier R, Ernst CB, Kempczinski RF, et al. Suggested standards for reports dealing with cerebrovascular disease. J Vasc Surg 1988;8:721-9.
17. Brenner H, Hakulinen T. On crude and age-adjusted relative survival rates. J Clin Epidemiol 2003;56:1185-91.
18. Schultz RD, Sterpetti AV, Feldhaus RJ. Carotid endarterectomy in octogenarians and nonagenarians. Surg Gynecol Obstet 1988;166:245-51.
19. Pinkerton JA, Gholkar VR. Should patient age be a consideration in carotid endarterectomy? J Vasc Surg 1990;11:650-8.
20. Treiman RL, Wagner WH, Foran RF, Cossman DV, Levin PM, Cohen JL, et al. Carotid endarterectomy in the elderly. Ann Vasc Surg 1992;6:321-24.
21. Coyle CA, Smith RB III, Salam AA, Dodson TF, Chaikof EL, Lumsden AB. Carotid endarterectomy in the octogenarian. Ann Vasc Surg 1994;8:417-20.
22. O'Hara PJ, Hertzer NR, Mascha EJ, Beven EG, Krajewski LP, Sullivan TM. Carotid endarterectomy in octogenarians: early results and late outcome. J Vasc Surg 1998;27:860-71.
23. Perler BA, Dardik A, Burleyson GP, Gordon TA, Williams GM. Influence of age and hospital volume on the results of carotid endarterectomy: a statewide analysis of 9918 cases. J Vasc Surg 1998;27:25-33.
24. Ting ACW, Taylor DC, Salvian AJ, Chen JCL, Strandberg S, Hsiang YNH. Carotid endarterectomy in octogenarians. Cardiovasc Surg 2000;8:441-5.
25. Maxwell JG, Taylor AJ, Maxwell BG, Brinker CC, Covington DL, Tinsley E Jr. Carotid endarterectomy in the community hospital in patients age 80 and older. Ann Surg 2000;231:781-8.
26. Schneider JR, Droste JS, Schindler N, Golan JF. Carotid endarterectomy in octogenarians: comparison with patient characteristics and outcomes in younger patients. J Vasc Surg 2000;31:927-35.
27. Ozsvath KJ, Darling RC, Tabatabai L, Roddy SP, Paty PS, Chang BB, et al. Carotid endarterectomy in the elderly: does gender effect outcome? Cardiovasc Surg 2002;10:534-7.
28. Rockman CB, Jacobowitz GR, Adelman MA, Lamparello PJ, Gagne PJ, Landis R, et al. The benefits of carotid endarterectomy in the octogenarian: a challenge to the results of carotid angioplasty and stenting. Ann Vasc Surg 2003;17:9-14.
29. Pruner G, Castellano R, Jannello AM, Astore D, Civilini E, Melissano G, et al. Carotid endarterectomy in the octogenarian: outcomes of 345 procedures performed from 1995-2000. Cardiovasc Surg 2003;11.105-12.
30. Miller MT, Comerota AJ, Tzilinis A, Daoud Y, Hammerling J. Carotid endarterectomy in octogenarians: does increased age indicate "high risk"? J Vasc Surg 2005;41:231-7.
31. Stoner MC, Abbott WM, Wong DR, Hua HT, LaMuraglia GM, Kwolek CJ, et al. Defining the high-risk patient for carotid endarterectomy: An analysis of the prospective National Surgical Quality Improvement Program database. J Vasc Surg 2006;43:285-95.
32. Ballotta E, Renon L, Da Giau G, Barbon B, Terranova O, Baracchini C. Octogenarians with contralateral carotid occlusion: a cohort at higher risk for carotid endarterectomy? J Vasc Surg 2004;59:1003-8.
33. Ballotta E, Da Giau G, Militello C, Barbon B, De Rossi A, Meneghetti G, et al. High-grade symptomatic and asymptomatic carotid stenosis in the very elderly: a challenge for proponents of carotid angioplasty and stenting. BMC Cardiovasc Disord 2006;6:12.
34. Hobson RW II, Howard VJ, Roubin GS, Brott TG, Ferguson RD, Popma JJ, et al. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg 2004;40:1106-11.
35. McCormick DJ, Vlad T, Fasseas P. Carotid artery stenting will replace carotid endarterectomy. Perspect Vasc Surg Endovasc Ther 2007;19:223-7.
36. Katzen BT, Criado FJ, Ramee SR, Massop DW, Hopkins LN, Donohoe D, et al.; CASES-PMS Investigators. Carotid artery stenting with emboli protection surveillance study: thirty-day results of the CASES-PMS study. Catheter Cardiovasc Interv 2007;70:316-23.
37. Cao P, De Rango P, Zannetti S. Eversion vs conventional carotid endarterectomy: a systematic review. Eur J Vasc Endovasc Surg 2002;23:195-201.
38. Normann PE, Semmens JB, Laurvick CL, Lawrence-Brown M. Long-term relative survival in elderly patients after carotid endarterectomy. A population-based study. Stroke 2003;34:e95-e98.


Submitted Mar 19, 2009; accepted Apr 20, 2009.