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No Benefit from Carotid Intervention in Fatal Stroke Prevention for >80-Year-old Patients CME

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WHAT THIS PAPER ADDS

- This study questions the benefit of offering carotid interventions to octogenarians, especially in females and asymptomatic patients. There is an urgent need for high-quality studies to address this issue as evidence suggests that a relatively large number of octogenarians currently undergo prophylactic carotid interventions on the unproven assumption that they will confer significant benefit.

A R T I C L E I N F O

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A B S T R A C T

Background: Invasive management of patients ≥80 years of age with carotid stenosis may be questionable. The higher likelihood of stroke needs to be balanced with the increased perioperative risk and the reduced life expectancy of this ageing population. The purpose of this study was to evaluate the clinical relevance of carotid stenosis revascularisation in octogenarians.
Methods: All patients ≥80 years of age who received carotid revascularisation in 2001–2010 were reviewed for perioperative and 5-year outcomes. The experience was comprehensive of carotid endarterectomy (CEA) and carotid stenting (CAS) performed during the training frame when age was not a contraindication for this procedure. Mortality rates were compared to those of octogenarians of the same geographical territory according to all-cause and stroke-related mortality national statistics datasets.
Results: A total of 348 procedures performed in ≥80-year-old patients (272 males) were reviewed: 162 (46.6%) were by CAS and 169 (48.6%) were for symptomatic disease. Perioperative stroke/death rate was 5.5% and was non-significantly higher for symptomatic disease (7.1% vs. 3.9% asymptomatic; $p = 0.24$), after CAS (6.2% vs. 4.8% CEA; $p = 0.64$) and in females (6.6% vs. 5.1% males; $p = 0.57$). At median follow-up of 36.18 months, 95 deaths and 21 new ischaemic strokes (12 fatal) occurred with 5-year Kaplan–Meier freedom from stroke of 84.8% (78.7%, symptomatic vs. 90.3% asymptomatic; $p = 0.003$). According to national datasets, in 80–85-year-old resident population 5-year mortality was 29.9% (23.4% females, 40.6% males) and ischaemic stroke-related mortality was 14.9% (16.8% females, 13.0% males). Corresponding figures from treated population showed a 5-year mortality of 49.4%, higher in males (39.5% females, 52.5% males) and ischaemic stroke-related mortality of 20.2%, higher in females (40.0% females, 15.6% males). Comparing data from the study population with residents' figures, ischaemic stroke-related mortality hazard was significantly higher in the study females: odds ratio (OR) 3.2, 95% confidence interval (CI) 1.16–9.17; $p = 0.029$ (for males: OR 0.97, 95%CI 0.89–1.10; $p = 0.99$).
Conclusions: Despite perioperative stroke/death risks being lower compared with CAS, the benefit of surgical carotid revascularisation in old patients remains controversial due to limited life expectancy and high fatality of stroke in this ageing population. Invasive treatment of carotid stenosis may not be warranted in most patients ≥80 years of age with carotid stenosis, especially when female and asymptomatic.

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Age is the main non-modifiable risk factor for stroke and mortality. The occurrence of both ischaemic stroke and intracerebral haemorrhage doubles in each successive decade after the age of 55 with first-stroke rates particularly high in men 75 years of age or older.[1–5]

Age is also known to be the strongest predictor of carotid disease in both the general healthy population and patients suffering from acute ischaemic stroke.[6,7] Carotid stenosis is a major well-documented modifiable risk factor for stroke and the use of surgical therapy has been shown to be the best option to reduce the risk of carotid-related stroke and the associated fatality.[1,5] Nevertheless, management of very old patients with carotid stenosis is challenging: the higher likelihood of stroke in advanced ages (stroke incidence accounts for 13.5/1000 persons 75–85 years old and of 32.1/1000 persons in men 85 years or older)[4,5] and in the presence of carotid stenosis[7] needs to be balanced with the reduced life expectancy and the increased perioperative risk, especially mortality, if an intervention is applied to carotid disease in this ageing population.[8–10] Literature data are limited since most octogenarians have been excluded from randomised clinical trials (RCTs) on carotid treatment and much of the published data on octogenarians and carotid surgery are provided from single-centre experiences with limited numbers and conflicting results. Comparisons of outcomes with octogenarians not receiving invasive treatment are lacking and the clinical relevance of invasive treatment remains questionable since we do not know how many old patients need to be treated (NNT) to prevent one stroke event in this age group.

The aim of this study was to analyse early and long-term (5 years) outcome of patients ≥80 years of age invasively treated for carotid stenosis and to compare mortality data to octogenarians in the same geographical territory.

Methods

Study population

Consecutive patients with severe carotid stenosis entered into a prospective electronic database of extracranial carotid revascularisations from January 2001 to February 2010 were reviewed.

For the purpose of the study, all patients 80 years of age or older were selected. Thereby, the experience was comprehensive of carotid endarterectomies (CEAs) but also carotid stenting (CAS) procedures performed during the early time frame (learning curve) when the procedure was not considered contraindication as it was since 2005 also due to the diffusion of Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) lead-in data.[11,12]

Indications for CAS versus CEA with multiple specialists' advice (stroke neurologists, interventional radiologists and vascular surgeons) were discussed in meetings where details of the procedure were defined by the surgical team. Usually, patients with unfavourable aortic arch anatomy, severe peripheral vascular disease precluding femoral access, extremely tortuous carotid anatomy, allergies to aspirin, clopidogrel or contrast media and renal insufficiency were excluded from CAS. High-neck carotid bifurcation, obesity and ongoing double anti-platelet were relative contraindications for CEA. In the last few years, >80-year-old patients were excluded from CAS and the indications for asymptomatic disease decreased.

Written consent was obtained from all patients before any revascularisation.

CAS procedure

All CASs were performed with cerebral protection (distal filter and selectively proximal occlusion) under local anaesthesia following a standardised protocol in an endovascular suite. Patients received aspirin (100–325 mg once daily) and clopidogrel (75 mg once daily with 300 mg loading dose) or ticlopidine (250 mg twice daily) before the procedure. Post-procedure anti-platelet therapy included dual drug treatment (aspirin and thienopyridines) for a minimum of 1 month and continued at the discretion of the treating physician.

CEA procedure

CEA was performed under local or general anaesthesia. Patients were under anti-platelet one-drug therapy, either aspirin (100–325 mg once daily) or thienopyridine (ticlopidine 250 mg twice daily or clopidogrel 75 mg daily). Shunts were used selectively based on clamping intolerance according to transcranial Doppler changes or stump pressure measurement when under general anaesthesia. Eversion or patch and occasionally direct primary closure were used as arterial closure techniques.

Patient evaluation

Neurological symptoms were evaluated by a team of neurologists who documented the presence, the type and severity (National Institute of Health (NIH) Stroke Scale) of the event. Patients were defined as symptomatic when ipsilateral hemispheric or retinal symptoms occurred within 6 months from the procedure.

Outpatient clinical and ultrasound examinations were scheduled at regular intervals after carotid treatment (6 and 12 months and yearly thereafter).

Outcome measures

Primary end points were mortality and perioperative (30-day) stroke/death. Secondary end points included ischaemic stroke-related mortality and freedom from stroke (any perioperative and late ischaemic). Haemorrhage strokes, after perioperative period, were excluded.

Local population

Area of investigation

Mortality rates in treated octogenarians were compared to rates in octogenarians from the local population. The risk of stroke-related mortality in people with carotid stenosis is higher than in those without; however, it could be assumed that after effective intervention on carotid stenosis (CEA or CAS) this risk-excess should have decreased, approaching that of the general population.

Given a mean age of 82.3 years in the treated population, the local population for comparison included all residents of 80–85 years of age in the Umbria region. This territory, located in central Italy, has an area of 8456 km^2 (2.8% of the national territory) (Fig. 1). The resident population was 870,422 (420,933 males and 449,489 females); 59,430 (6.82%) were 80 years of age or older (20,853 males and 38,577 females), and 34,412 (3.95%) were in the 80–85-year range (12,966 males; 21,446 females). The last was the population used for control group.

Ascertainment of cases

Data on residents and mortality according to age and gender as of 31 December 2008 were obtained from the Registry of Nominative Causes of Mortality (ReNCaM) of the Epidemiology and Statistical Office of the Umbria region, Department of Hygiene, University of Perugia, Perugia, Italy. Deaths and stroke-deaths were based on the National Institute of STATistic (ISTAT) codes and displayed by age, gender and geographical territory over each 5-year period.

For this study, the local ReNCaM datasets of the last 5-year period (2004–2008) for the Umbria region were analysed,

Resident Population
Total: 870,422
Males: 420,933
Females: 449,489
INSTAT code: 10
Geographic information
Kmq: 8.456
Mountain: 29,3%
Hill: 70,7%
Lowlands 0,0%

	Resident population 80-85y	Treated population >80y (mean age 82y)
Total, N.	34,412	160
Males, N.	12,966	122
Females, N.	21,446	38
Mortality 5-year		
Total, %	29.9%(10,288/34,412)	49.4% (79/160)
Males, %	40.6%	52.5%
Females, %	23.4%	39.5%
Stroke mortality 5-year		
Total, %	14.9%(1531/10,268)	20.2% (16/79)
Males, %	13.0%	15.6%
Females, %	16.8%	40.0%

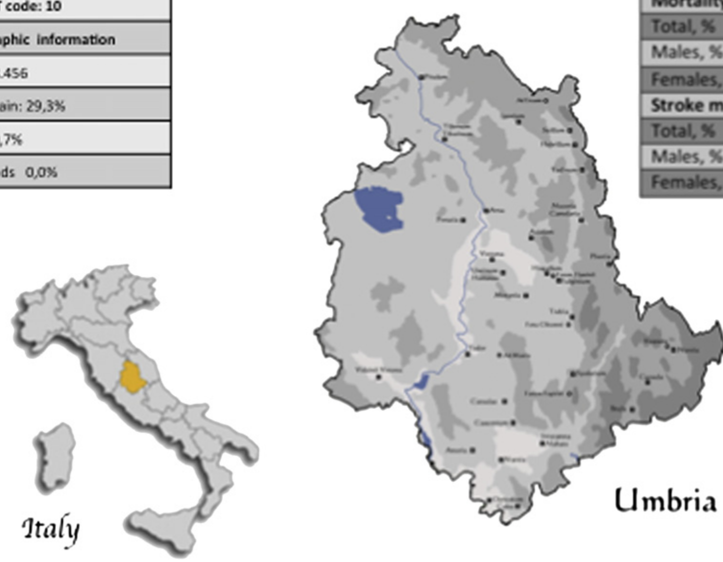


Figure 1. Diagrammatic map of the Umbria region in relation to Italy. In the right box: 5-year mortality and stroke-mortality in Umbria 80–85 y population and octogenarian study population.

selecting the codes for deaths related to 'encephalic circulation disease – occlusive cerebral vessel disease'. Deaths codified as 'cerebral haemorrhage' were excluded.

Statistical analysis

Data are shown as frequencies and percentages for categorical variables and mean (±SD) or median and interquartile range (IQR), when required, for continuous variables.

In the treated population, analyses of perioperative and late outcomes were stratified by preoperative symptoms, gender and procedure to account for evident differences in distribution of patients. Rates of end points at 5 years were estimated with the Kaplan–Meier (K–M) method to compensate for patient dropouts and the level of significance was calculated with log-rank test and its standard error (SE). Curves were displayed up to a value of SE < 0.10. To account for event rates in patients receiving bilateral procedure, at the time of the index event, only one procedure for each patient was considered and the other was censored at the same time point. This allowed to account for the double perioperative exposure included in the cumulative event rate analysis for these patients.

For comparisons between the study population and the local population of similar age in the Umbria region, absolute event rates (number of events/number of population at risk) were used in reporting mortality and stroke-related mortality to allow measurements of data in the study population comparable to those calculated by the ISTAT for the local population. Females and males were analysed separately. Data were analysed per patient (only the first intervention for patients with bilateral procedure was included).

Data were shown as odds ratio (OR) and correspondent 95% confidence interval (CI).

SPSS (PC version Statistical Package for Social Sciences, 16.00 Win package, SPSS, Inc., Chicago, IL, USA) was used for data analyses.

Table 1
Baseline characteristics in 348 CAS/CEA in >80 year old patients.

	Total		CAS		CEA		*P* value
	N 348	%	*N* 162	%	*N* 186	%	
Age, *y* (mean ± SD)	82.3 ± 2.4		82.2 ± 2.3		82.4 ± 2.5		0.44
Males	272	78.2	129	79.6	143	76.9	0.60
Females	76	21.8	33	20.4	43	23.1	0.60
Symptomatic	169	48.6	70	43.2	99	53.2	0.07
Peripheral arterial disease	72	20.7	31	19.1	41	22.0	0.60
Diabetes	51	14.7	18	11.1	33	17.7	0.10
Atrial fibrillation	23	6.6	11	6.8	12	6.5	1.00
Ischaemic heart disease	109	31.3	55	34.0	54	29.0	0.35
Hypertension	286	82.2	127	78.4	159	85.5	0.09
Hyperlipemia	95	27.3	44	27.2	51	27.4	0.96

CAS = Carotid stenting; CEA = Carotid endarterectomy; MI = Myocardial infarction.

Table 2
Medical therapy[a] in 348 CAS/CEA in >80 year old patients.

	N	%
Statin	121	34.8
Atorvastatin	46	38.3
Pravastatin	9	7.4
Fluvastatin	2	1.7
Rosuvastatin	19	15.8
Simvastatin	44	36.4
Aspirin	248	71.3
Clopidogrel	44	12.6
Ticlopidine	53	15.2
Warfarin	14	4.0
No antiplatelet/anticoagulant	32	9.2

CAS = Carotid stenting; CEA = Carotid endarterectomy.
[a] One or more.

Results

Over the study period (2001–2010) 348 carotid procedures were performed in 323 patients with ≥80 years of age (mean age 82.3 ± 2.4 years, range 80–91 years; $n = 272$ males). There were 162 (46.6%) CAS and 186 (53.4%) CEA. Indication for revascularisation was symptomatic carotid stenosis in 169 (48.6%). Demographic and baseline characteristics by procedure and medical therapy are displayed in Tables 1 and 2. Males and females shared similar characteristics with the exception of higher rate of peripheral vascular disease in women (23.9% vs. 9.2% in men; $p = 0.004$).

The 30-day (periprocedural) risk of stroke/death was 5.5% (19 of 348). Stroke risk was 4.3% ($n = 15$) and 10 (2.8%) periprocedural strokes were disabling (Rankin score ≥3).

Primary periprocedural end-point incidence was 6.6% in females versus 5.1% in males, 7.1% in symptomatic versus 3.9% in asymptomatic patients and 6.2% after CAS versus 4.8% after CEA but there were no significant differences in rates (Table 3). In symptomatic octogenarians the incidence of perioperative primary end point (stroke/death) was 10.0% after CAS and 5.1% after CEA. In asymptomatic octogenarians, the rate was 3.3% after CAS and 4.6% after CEA.

Other periprocedural complications by different subgroups are shown in Table 3. No difference resulted of statistical relevance. Four myocardial infarctions (MIs), two fatal, occurred. There were overall eight periprocedural deaths (four stroke and four cardiac related). Stroke rate was three times (6.5% vs. 2.2%) and disabling stroke two times (4.1% vs. 1.7%) higher in symptomatic patients but without statistical significance in difference rates when compared to asymptomatic. Death and cardiac complications were more similarly distributed (Table 3).

Table 3
Periprocedural (30-day) outcome by subgroup analyses in 348 CAS/CEA in >80 year old patients.

	Stroke/death	Stroke	Death	Disabling stroke[a]	MI
Overall (*N* 348)	**19 (5.5%)**	**15 (4.3%)**	**8 (2.3%)**	**10 (2.8%)**	**4 (1.2%)**
Males (*N* 272)	14 (5.12%)	11 (4.0%)	6 (2.2%)	7 (2.6%)	2 (0.7%)
Females (*N* 76)	5 (6.6%)	4 (5.3%)	2 (2.6%)	3 (3.9%)	2 (2.6%)
P value	0.57	0.75	0.68	0.69	0.2
Symptomatic (*N* 169)	12 (7.1%)	11 (6.5%)	4 (2.4%)	7 (4.1%)	–
Asymptomatic (*N* 179)	7 (3.9%)	4 (2.2%)	4 (2.2%)	3 (1.7%)	4 (2.2%)
P value	0.24	0.06	1.00	0.20	0.12
CAS (*N* 162)	10 (6.2%)	10 (6.2%)	1 (0.6%)	7 (4.3%)	1 (0.6%)
CEA (*N* 186)	9 (4.8%)	5 (2.7%)	7 (3.8%)	3 (1.6%)	3 (1.6%)
P value	0.64	0.12	0.07	0.19	0.62

CAS = Carotid stenting; CEA = Carotid endarterectomy; MI = Myocardial infarction.
[a] Rankin score ≥3.

Median follow-up was 36.18 months (IQR 20.9–50.3 months). No patient was lost. During the observation period, 87 patients died for an overall (including perioperative) of 95 deaths (18 females, 77 males). Causes of late deaths included stroke (14), cardiac events (17), cancer (18), respiratory failure (10) and miscellaneous (suicide, trauma, renal failure, etc.) reasons (13). Fifteen deaths remained undefined.

A total of 39 strokes (14 females, 25 males) occurred; 21 were ischaemic late (after the perioperative period). Sixteen strokes (12 late) were fatal and occurred in six females and 10 males. Three cerebral haemorrhages (two fatal) were additionally recorded.

The overall K–M survival rate at 5 years from all-cause mortality was 65.4% (Fig. 2a). Survival rates were not significantly higher in females (73.7% vs. 62.9% in males, $p = 0.13$) (Fig. 2b) and were similar in symptomatic and asymptomatic patients (62.6% vs. 67.8%; $p = 0.23$) (Fig. 2c). Survival rates for the CAS and CEA population are shown in Fig. 2d.

The overall K–M freedom from stroke (any perioperative and late ischaemic) at 5 years was 84.8% (Fig. 3a). Freedom from stroke tended to be higher in males (86.6% vs. 79.2% in females; $p = 0.139$) (Fig. 3b), and significantly higher in asymptomatic than in symptomatic patients (90.3% vs. 78.7%; $p = 0.003$) (Fig. 3c). There were similar stroke rates after CAS or CEA (Fig. 3d). Excluding perioperative stroke, the K–M freedom from late ischaemic strokes at 5 years was 90.8% in males versus 83.6% in females ($p = 0.122$) and significantly higher in asymptomatic (92.3% vs. 85.2% in symptomatic, $p = 0.031$) patients with an overall freedom rate of 89.1%.

Seven treated vessels developed >50% stenosis during follow-up with similar distribution by sex (four males, three females) and procedure (two after CAS and five after CEA). Only one restenosis associated with stroke.

Comparison of mortality with the local octogenarian population

For comparisons with the local population, only treated patients who had reached a 5-year follow-up or had died were analysed. There were 160 patients (38 females; 122 males). Five-year all-cause mortality rate was 49.4% ($n = 79/160$) and was higher in males ($n = 64$; 52.5%) than in females ($n = 15$; 39.5%). Five-year ischaemic stroke rate was 19.3% ($n = 31/160$); 26.3% ($n = 10$) in females and 17.2% ($n = 21$) in males. Five-year stroke-related mortality rate (rate of fatal strokes with respect to all mortality) was 20.2% ($n = 16/79$) and was particularly high in females, 40.0% ($n = 6/15$), while in males the rate was 15.6% ($n = 10/64$) (Fig. 1, right box).

According to national statistics mortality datasets, for residents 80–85 years of age at 5 years all-cause mortality rate was 29.9% (10 288/34 412) and was higher ($p < 0.0001$) in males (40.6%) than in females (23.4%). Stroke-related mortality rate was 14.9% (1531/10 268) and was higher in females than males (16.8% vs. 13.0% $p < 0.0001$) (Fig. 1, right box).

Comparing data from the study population with these figures, all-cause mortality hazard for the study population was OR 2.29,95%CI 1.68–3.12; $p = 0.0001$ and stroke-related mortality hazard was OR 1.4,95%CI 0.95–1.18; $p = 0.27$. Stroke-related mortality risk was significantly higher in the study females: OR 3.2, 95%CI 1.16–9.17; $p = 0.029$ (for males: OR 0.97, 95%CI 0.89–1.10; $p = 0.99$).

Discussion

The study failed to show any significant effect of carotid revascularisation in providing stroke fatality prevention for patients

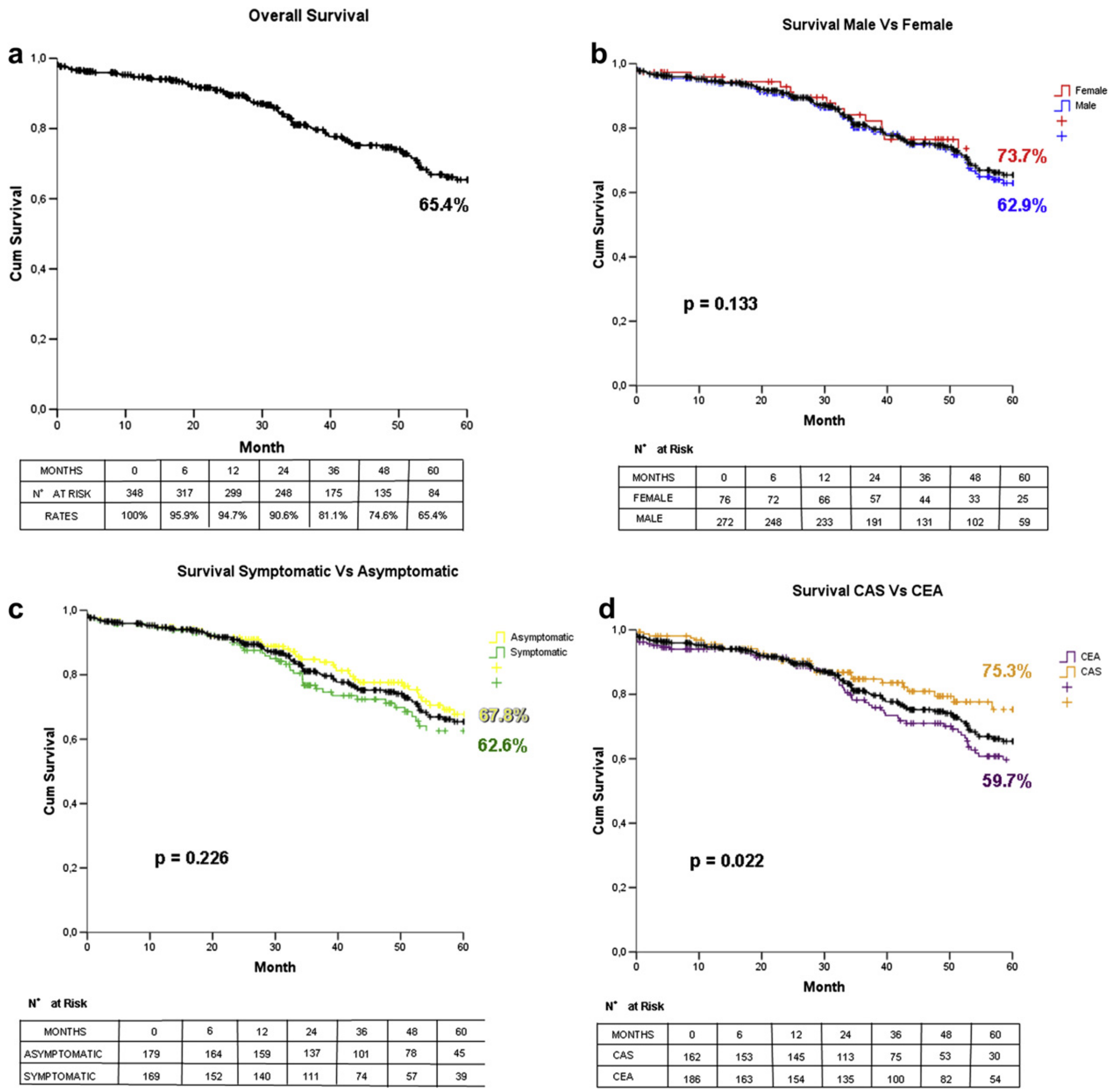
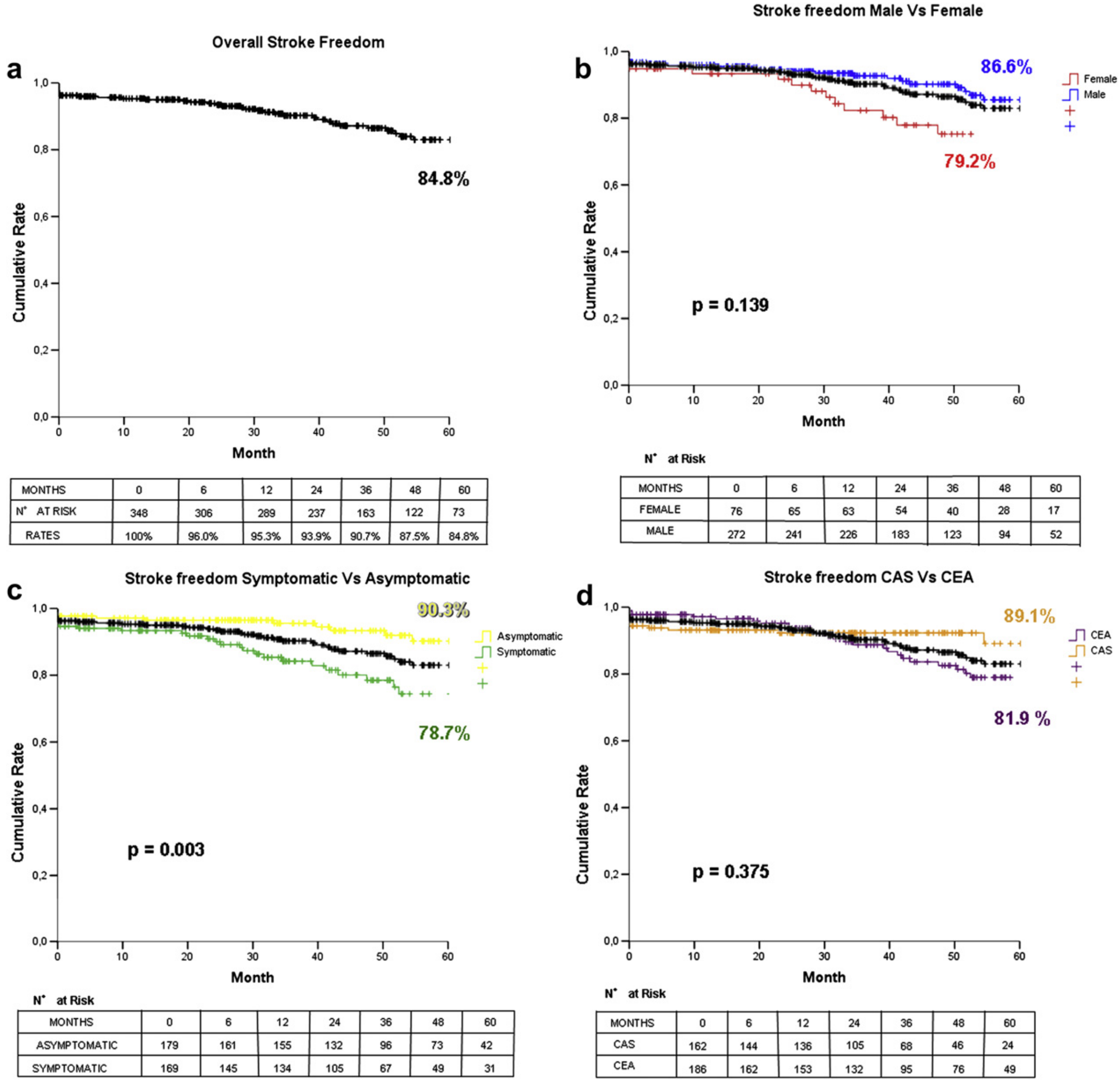


Figure 2. Kaplan–Meier survival rates from all-cause-mortality in patients ≥80 years old receiving invasive treatment. Panel a. All cases. Panel b. male versus female; log-rank test, $p = 0.133$. Panel c. symptomatic versus asymptomatic; log-rank test $p = 0.226$. Panel d. CAS versus CEA; log-rank test: $p = 0.022$. Black curve is the reference for all cases in subgroups comparison. Curves were displayed up to a value of SE < 0.10.

with ≥80 years of age compared to the age-matched general population, especially with respect to females. Lack of clinical benefit was found not only after CAS, as suggested in the literature,[12–14] but also after CEA. Many ≥80-year-old patients with carotid stenosis cannot benefit from carotid revascularisation due to limited life expectancy. In females, high ischaemic stroke fatality (40.0% at 5 years) likely occurs, while in most males there is an excess of mortality (52.5% at 5 years) mainly non-stroke-related (cancer, respiratory, etc.) preventing net benefit from carotid revascularisation. However, our findings were related to estimates of risks in the local octogenarian population and might not apply to outside settings.

This study started when there was no clear indication on the hazards from CAS in old people (2001); therefore, a number of octogenarians received this procedure during the early experience period, an indication no more in use starting from 2005.[11] A number of studies as well as our personal experience during the training CAS phase have suggested that patient's age should be considered when selecting treatment (CAS vs. CEA) for carotid stenosis.[11–14] Periprocedural risks in our CAS group was strongly negatively affected by the inclusion of patients treated during this initial time experience with CAS (learning curve period).[11]

In this study, a general population group was used to compare outcomes of the treated group of octogenarians. The latter group had undoubtedly higher stroke and stroke fatality risk due to the presence of carotid stenosis. However, outcomes between treatment and control groups were compared after an interventional treatment for carotid stenosis; should the treatment be effective, the excess of stroke exposure in the treated group should be decreased making the ischaemic stroke risk similar to that of the general population including octogenarians with and without the stenosis. Nevertheless, this comparison could not solve the main study question on the true benefit of carotid revascularisation in old people. This can be addressed only in trials, that are currently lacking, with a control group of patients >80 years with carotid stenosis receiving best medical treatment but not revascularisation.



MONTHS	0	6	12	24	36	48	60
N° AT RISK	348	306	289	237	163	122	73
RATES	100%	96.0%	95.3%	93.9%	90.7%	87.5%	84.8%

N° at Risk

MONTHS	0	6	12	24	36	48	60
FEMALE	76	65	63	54	40	28	17
MALE	272	241	226	183	123	94	52

N° at Risk

MONTHS	0	6	12	24	36	48	60
ASYMPTOMATIC	179	161	155	132	96	73	42
SYMPTOMATIC	169	145	134	105	67	49	31

N° at Risk

MONTHS	0	6	12	24	36	48	60
CAS	162	144	136	105	68	46	24
CEA	186	162	153	132	95	76	49

Figure 3. Kaplan–Meier estimates of any-stroke (including perioperative) freedom in patients ≥80 years old receiving invasive treatment. Panel a. All cases. Panel b. male versus female; log-rank test $p = 0.139$. Panel c. symptomatic versus asymptomatic; log-rank test $p = 0.003$. Panel d. CAS versus CEA: log-rank test $p = 0.375$; Black curve is the reference for all cases in subgroups comparison. Curves were displayed up to a value of SE < 0.10.

Indeed, although there is evidence supporting the safety of CEA in old age,[14–16] no study analysed long-term outcomes of old patients undergoing carotid revascularisation compared to a control group of people with carotid stenosis of the same age without revascularisation, to assess the true clinical relevance of benefit after invasive procedure. What we need to know, but we still we do not know, is the rate of stroke and stroke fatality in diseased (with carotid stenosis) but untreated old patients. Without NNT available to clearly prove the efficacy of invasive treatment versus medical therapy alone, the decision to intervene on an octogenarian with carotid stenosis is debatable and might be justified only in very selected groups with long life expectancy and higher stroke risk, which are currently unidentified. Thereby, our indications for CEA in old patients have been decreased in the last few years.

Indications for carotid intervention in elderly patients are particularly challenging for asymptomatic stenoses for which there is no clear evidence of large benefit.[17–20] Nonetheless, in the real world, carotid procedures continue to be largely applied worldwide in asymptomatic patients including octogenarians despite the lack of consistent evidence to support this practice.[1,5,18,20] Nearly half of the study population was represented by patients with asymptomatic carotid disease. Despite the risk of stroke we found at 5 years being particularly low (freedom from stroke 90.3%), the lack of consistent benefit in comparison to general old population suggested us to not have provided a true benefit in these patients. Therefore, we are decreasing application of carotid intervention, especially in asymptomatic old patients.

Old women are deemed to be at a higher perioperative risk after CEA but are more likely to experience more severe stroke and higher stroke disability.[1,4,5] In our study the stroke mortality risk was particularly evident in the women population. The higher incidence of peripheral disease observed at baseline in our women compared to men (23.9% vs. 9.2%; $p = 0.004$) could have had a role in a more aggressive generalised cardiovascular disease allowing higher stroke severity with increased fatality rate for females.

The decision to intervene in very old patients still remains unsettled and ambiguous due to the particular vulnerability of this age group. As a person ages there is an accumulation of stressors and lifetime risk factors that combine with multi-organ physiological changes and increases the risk of poor outcomes. This vulnerability, defined as 'frailty', has been suggested as a useful measure in public health planning.[21] The proportion of 'frail' older people in the population is rising in developed countries as a result of continued improvements in health care, nutrition and disease prevention.[21] Nevertheless, despite this population shift, there is evidence that today older adults are still systematically under addressed by health-care programmes. Many pharmaceutical companies and previous RCTs have preferred a healthy adult population for their trials to ensure the best possible safety and efficacy results for their product. In our study we found that common drugs for cardiovascular risk management were largely underused in older people (Table 2) receiving carotid invasive treatment (e.g., only 34.8% statin use; 9.2% no anti-platelet/anticoagulant). Medical therapy and health care should be intensified in many countries to provide the best strategy against stroke in old patients with carotid stenosis.

It could be anticipated that more in-depth and accurate patient selection, based on multi-morbidity assessment, might help to identify selected subgroups of older patients at higher stroke and lower late mortality risk who may benefit more from carotid intervention. However, at this time, the issue is unidentified and should be addressed in prospective focussed studies.

Limitations

This study compared two heterogeneous groups ≥80 years of age. Patients in the study group with carotid stenosis had a higher likelihood of cardiovascular events with respect to the general population of the same age (including people with and without carotid stenosis). However, it could be assumed that an effective carotid treatment should have decreased the stroke and stroke-mortality risk in the first group approaching levels of the population without carotid stenosis. Nevertheless, our study did not answer the main study question that can be addressed only in studies using for comparison old people with carotid stenosis not receiving invasive carotid treatment.

Second, comparisons were based on absolute rates and administrative data from local national datasets, with all the inherent restraints. The generalisation of our findings may be limited. Third, we measured mortality and stroke-related mortality but not stroke incidence (because of lack of accurate territory datasets reporting on stroke). However, stroke-fatality rate can be a measure of stroke rate and requires prevention. Fourth, the small numbers of the study population could have led to an overestimation of the true risks (especially for stroke mortality in females). Five, we included the learning curve time frame of CAS and a number of old patients received this procedure (with poorer outcomes), an indication that is no more in practice today. Finally, the study was retrospective non-randomised with all the related selection biases: we could not exclude imbalances in the treated population as those due to heterogeneity in anti-platelet therapy and type of anaesthesia and we could not provide relevant details such as the delay from symptomatic presentation and the stroke type and lateralisation.

Conclusions

The clinical benefit of carotid revascularisation in ≥80-year-old patients may be debatable not only after CAS but also after CEA. Despite perioperative risks lower than with CAS, after treatment, the mortality risk from stroke cannot be prevented in many of these patients and the life expectancy remains limited (due to high cancer/pulmonary-related mortality) to take advantages from the surgical procedure. Periprocedural hazards from CEA may be higher in females who also experience higher stroke severity and stroke fatality rates.

Today, invasive treatment of carotid stenosis for stroke prevention might not be necessary in many patients ≥80 years of age particularly when female (higher hazards from treatment) and asymptomatic (low stroke exposure without treatment).

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Conflict of Interest/Disclosures

There is no financial interest for any of the authors.

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