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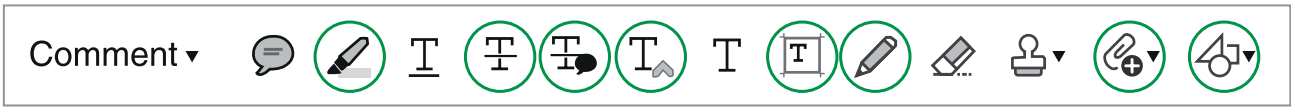

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Carotid endarterectomy in asymptomatic octogenarians: Outcomes at 30 days and 5 years

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Abstract

Background: The following study investigated the 30-day and 5-year relative survival rate and freedom from neurological events in asymptomatic carotid stenosis (ACS) octogenarians who had undergone elective carotid endarterectomy (CEA).

Methods: Between January 2008 and June 2014, a retrospective review was conducted on ACS patients who had undergone elective CEA. The patients' sample was divided into two groups: Group A (GA) included octogenarians and Group B (GB) included younger patients. The GA patients were subjected to a risk-scoring system and follow-up. The two groups were compared analysing the following primary endpoints: 30-day mortality, stroke, stroke/death and acute myocardial infarction (AMI); GA patients' survival rate and freedom from neurological events at 5 years. The 30-day secondary endpoints included carotid shunting, redo surgical, need for general anaesthesia with preserved consciousness (GAPC) conversion and length of hospital stay.

Results: We identified 620 patients with ACS, of them 144 (23.2%) belonged to the GA and 476 (76.8%) belonged to the GB. No statistical difference between the two groups was found regarding the primary and secondary endpoints. One hundred nineteen of 144 GA patients (82.6%) underwent the follow-up; the median follow-up was 78.3 months. The GA patients' 5-year survival rate was 62%, while freedom from cerebral events was 94.9%. Analysis regarding GA patients' 5-year survival rate revealed a significantly lower percentage among the patients with a severe risk score compared with those with a moderate risk score (respectively, 29.5% vs 67.7%; $p = .005$). The multivariate analysis showed that chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD) were independently associated with lower survival.

Conclusions: The 30-day outcomes of CEA in octogenarians are comparable to those in younger patients. Comprehensive life expectancy and preoperative score, rather than age alone, should be taken into account before performing CEA on octogenarian patients, considering the short- and long-term efficacy in stroke prevention.

Keywords

Carotid endarterectomy, octogenarian, asymptomatic carotid stenosis, general anaesthesia with preserved consciousness

Introduction

Annually, strokes cause 1.1 million of deaths in Europe and are thus the second most common cause of death.[1–8] Approximately, 20% to 30% of these ischaemic events are attributed to ipsilateral carotid stenosis.[4–6] In Europe, strokes cost 38 billion euros per year, representing an enormous financial burden on health systems and caregivers.[8,9] Even though the occurrence of a stroke could lead to a serious debilitation at any age, the domino effect is more important in

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AQ2

the older population; the octogenarians who have suffered a stroke have a higher mortality rate, longer hospitalization, and are less likely to be discharged to their original place of residence.[10–12] The role of carotid endarterectomy (CEA) in the stroke prevention among asymptomatic carotid stenosis (ACS) octogenarians is widely debated. It is essential to maintain their independence and quality of life; however, there is a lack of controlled data in this population, the incremental benefit of treating ACS patients is small and the life expectancy of octogenarians compared with the younger patients is limited. Furthermore, data regarding the outcomes of CEA in octogenarians are conflicting.[13,14] This study investigated 30-day and 5-year neurological results and the relative survival rate in ACS octogenarians who had undergone CEA in general anaesthesia with preserved consciousness (GAPC).

Materials and methods

After the approval of the local ethical committee, a retrospective review was conducted on patients who had undergone CEA between January 2008 and June 2014. All the patients underwent CEA with a cross-clamping at first in the internal carotid artery (ICA), subsequently in the external carotid artery (ECA) and then in the common carotid artery (CCA) under GAPC; the use of the carotid shunt was selective. The GAPC used during the intervention was described in a previous paper.[15] The inclusion criteria were absence of ischaemic events in the previous 6 months and carotid stenosis at Duplex ultrasound ≥ 70% ECST (The European Carotid Surgery Trial). Subsequently, the patients were further divided into a Group A ≥ 80 years (GA) and a Group B < 80 years (GB). The preoperative variables examined included age, gender, current smoking status, hypertension (HPT), dyslipidemia, diabetes, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), preoperative drug therapy (antiplatelet therapy (APT) and oral anticoagulant therapy (OAT)) and American Society of Anesthesiologists class (ASA).

The surgical collected data were surgical techniques (endarterectomy with Hemacarotid Patch Maquet® Dacron Patch, eversion technique, primary closure), selective intraoperative carotid shunt when needed and need for GAPC conversion to general anaesthesia during surgery. Postoperative data were admission to the intensive care unit (ICU), redo surgical procedures for neck haematoma and length of hospitalization (LOS)

The GA patients were classified as low/mild/moderate/severe risk in accordance with a risk factor score regarding remote survival, as reported by Carmo.[16] (Table 1) In the interval between April 2019 and August 2019, the GA patients were followed up with a telephone interview made by a vascular surgeon to collect data regarding mortality and ipsilateral stoke occurrence. The primary endpoints were the following: 30-day mortality, ipsilateral stroke, ipsilateral stroke/death and acute myocardial infarction (AMI); GA patients' survival rate and freedom from major neurological events at 5 years. The 30-day secondary endpoints included carotid shunting, redo surgical procedures for neck haematoma, need for GAPC conversion to general anaesthesia during surgery and LOS.

Table 1. Risk factors included in the score assigned by and stratification into four risk groups according to the total score. Risk factors included in the score assigned M. Carmo, et al.,J Vasc Surg 2018; 67:175–82).

Age, years		*Score*
< 70		0
70–80		4
> 80		8
Renal status		
Cr < 1.5 mg/dL		0
Cr ≥ 1.5 mg/dL		4
Dialysis		8
Absence of statins		1
CAD		1
DM		1
COPD		1
Score	*Group*	Risk
0–3 points	*1*	Low
4–7 points	*2*	Mild
8–11 points	*3*	Moderate
≥ 12 points	*4*	Severe

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; Cr: creatinine; DM: diabetes mellitus.

Statistical analysis

We created a database using an Excel spreadsheet. Data analysis was performed by using the commercial package IBM-SPSS v.22© and the open source statistical system Jamovi v.1.2.22, which is based on the widespread open source statistical system 'R'. Measures of central tendency, dispersion and shape were calculated for all the variables in the data set. Summaries included arithmetic mean, median, mode, 5% trimmed mean, variance, standard deviation, interquartile range, minimum, maximum, asymmetry, kurtosis and the relevant 95% confidence intervals. Normality of the data was tested by the Shapiro–Wilk test. Categorical data were reported in frequency tables and categorized on the basis of absolute frequencies, relative frequencies, cumulated frequencies and percentages. Bivariate correlations among variables, continuous or ordinal, were tested by the Pearson's correlation coefficient r and by the Spearman's correlation coefficient rho. Univariate comparisons between continuous variables were performed

using both parametric tests (Student's t-test and ANOVA) and non-parametric test (Mann–Whitney U test and Kruskal–Wallis test). Comparisons between categorical variables in contingency tables were performed using the chi-square test and Fisher's exact test. All the test results were considered statistically significant for a '*p*-value' less than 5% ($p < .05$). Mean and median time for overall survival (OS) were investigated by using the Kaplan–Meier product-limit estimator and then followed by a Cox regression analysis in order to estimate the OS association with the covariates in a multivariable framework.

Results

Eight hundred and three patients underwent CEA in the analysed period. Considering the whole patients' sample, 620 (77.2%) were ACS. Of them, 144 (23.2%) were classified into the GA and 476 (76.8%) into the GB (Figure 1). The mean age for the GA was 82.8 years (range = 80–93), while the mean age for the GB was 70.5 years (range = 44–79). A statistically significant difference (GA vs GB) was found regarding the following preoperative variables: current smoking status (8% vs 22%; $p = .001$) and dyslipidemia (54% vs 70%; $p = 0.001$) (Table 2). The surgical data were not statistically different between the two groups (Table 2). Overall, mortality rate occurred in one patient (0.1%), ipsilateral stroke occurred in 10 patients (1.6%) and ipsilateral stroke/death in 11 patients (1.7%). There was no statistically significant difference in the following primary endpoints at 30 days (GA vs GB): mortality rate, 0 (0.0%) vs 1 (0.2%) ($p = 1.0$); ipsilateral stroke occurrence, 3 (2%) vs 7 (1.5%) ($p = .705$); ipsilateral stroke/death, 3 (2%) vs 8 (1.7%) ($p = .723$); and AMI, 1 (0.7%) vs 3 (0.6%) ($p = 1.0$), (Table 3). One hundred nineteen out of 144 GA patients (82.6%) underwent the follow-up; median follow-up was 78.3 months (range = 1–135 months). On the basis of the survival risk factor score, out of the 119 aforementioned patients 102 (85.7%) had a moderate risk, while 17 (14.3%) showed a severe risk. The 5-year estimated survival and freedom from neurological events for GA was, respectively, 62.2% and 94.9%. Considering the risk score stratification, the global survival was 67.6% for patients at moderate risk and 29.5% for patients at high risk, with statistical significant difference between the two groups ($p.005$). The Kaplan–Meier analysis showed a median survival time of 51 months for patients with a severe risk vs 90 months for the patients with a moderate risk ($p = .031$) (Figure 2). The Kaplan–Meier survival analysis for COPD showed a median survival rate of 51 months for the patients with COPD and 94 months for the patients without COPD ($p = .013$) (Figure 3). In the multivariate analysis (Cox regression), significant risk factors were found in relation to COPD (HR = 1.888, 95% CI [1.055–3.380] $p = .03$) and CKD (HR = 1.986, 95% CI [1.009–3.909] $p = .04$)

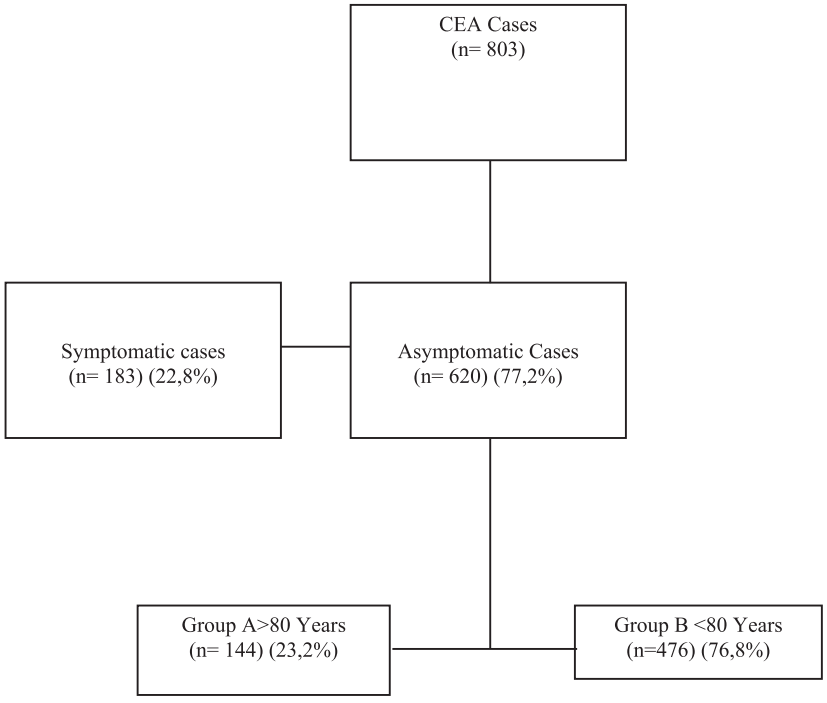

Figure 1. Inclusion and exclusion criteria for asymptomatic carotid stenosis cases who underwent carotid endarterectomy (CEA) with subsequent sub stratification into Group A ≥ 80 years and Group B < 80 years.

Table 2. Preoperative variables and surgical techniques for Group A and Group B.

Preoperative variable	Group A (n = 144)	Group B (n = 476)	p-value
Gender			
Men	92 (64)	303 (64)	.959
Women	52 (36)	173 (64)	
Current smokers	11 (8)	107 (22)	< .001
HPT	125 (87)	417 (88)	.800
Dyslipidemia	78 (54)	337 (70)	< .001
Diabetes	34 (24)	146 (31)	.102
CAD	22 (15)	101 (21)	.117
COPD	24 (17)	91 (19)	.507
CKD	19 (13)	40 (8)	.086
APT	134 (93)	446 (94)	.784
OAT	7 (5)	29 (6)	.580
ASA classification			.151
ASA 1	0 (0.0)	2 (0.4)	
ASA 2	31 (22)	146 (30.6)	
ASA 3	111 (77)	323 (68)	
ASA 4	2 (1.3)	5 (1.0)	
Surgical techniques			
Dacron patch (hemacarotid patch, Maquet®)	86 (60)	313 (66)	.185
Eversion	56 (39)	160 (34)	.244
Primary closure	2 (1.4)	3 (0.6)	.372
ICU	0 (0)	4 (0.8)	.270

Data are presented as n (%). Comparisons between the groups were performed using the Pearson's chi-square test.
HPT: hypertension; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; APT: antiplatelet therapy; OAT: oral anticoagulant therapy; ASA: American Society of Anaesthesiologists. ICU: intensive care unit.

Table 3. Primary and secondary outcomes after 30 days for Group A and Group B.

Primary outcome (30 days)	Group A (n = 144)	Group B (n = 476)	p-value
Death	0 (0.0)	1 (0.2)	1.000
Stroke	3 (2.0)	7 (1.5)	.705
Stroke/Death	3 (2.0)	8 (1.7)	.723
AMI	1 (0.7)	3 (0.6)	1.000
Secondary outcomes (30 days)			
Carotid shunting	14 (9.7)	24 (5.0)	.073
Reintervention for haematoma	1 (0.7)	2 (0.4)	.548
Conversion GAPC to general	2 (1.4)	0 (0.0)	.054
LOS: mean	3.4 (1.3)	3.3 (1.7)	.454

Data are presented as n (%) or mean ± stand deviation (SD).
AMI: acute myocardial infarction, GAPC: general anaesthesia with preserved consciousness; LOS: length of hospitalization.
p-values for categorical data were obtained by the Fisher's exact test, while the p-value for LOS was obtained by the unequal variance Student's t-test.

(Table 4). However, no significant difference was found in terms of the 30-day secondary endpoints. A shunt was performed in 14 patients of the GA (9.7%), a percentage slightly higher in comparison with 24 patients of the GB (5.0%) (p = .073); redo surgery for neck haematoma was performed in one patient of the GA vs two patients of the GB (respectively, 0.7% vs 0.4%; p = .548); need for GAPC conversion to general anaesthesia during surgery resulted in two patients of the GA vs 0 of the GB (respectively, 1.4% vs 0%; p = .054) and LOS average was set at 3.4 days (1.3) for the GA vs 3.3 days (1.7) for the GB (p = .454) (Table 3).

Discussion

Studies from Medicare and multi-institutional and state-wide databases have reached varying conclusions about the

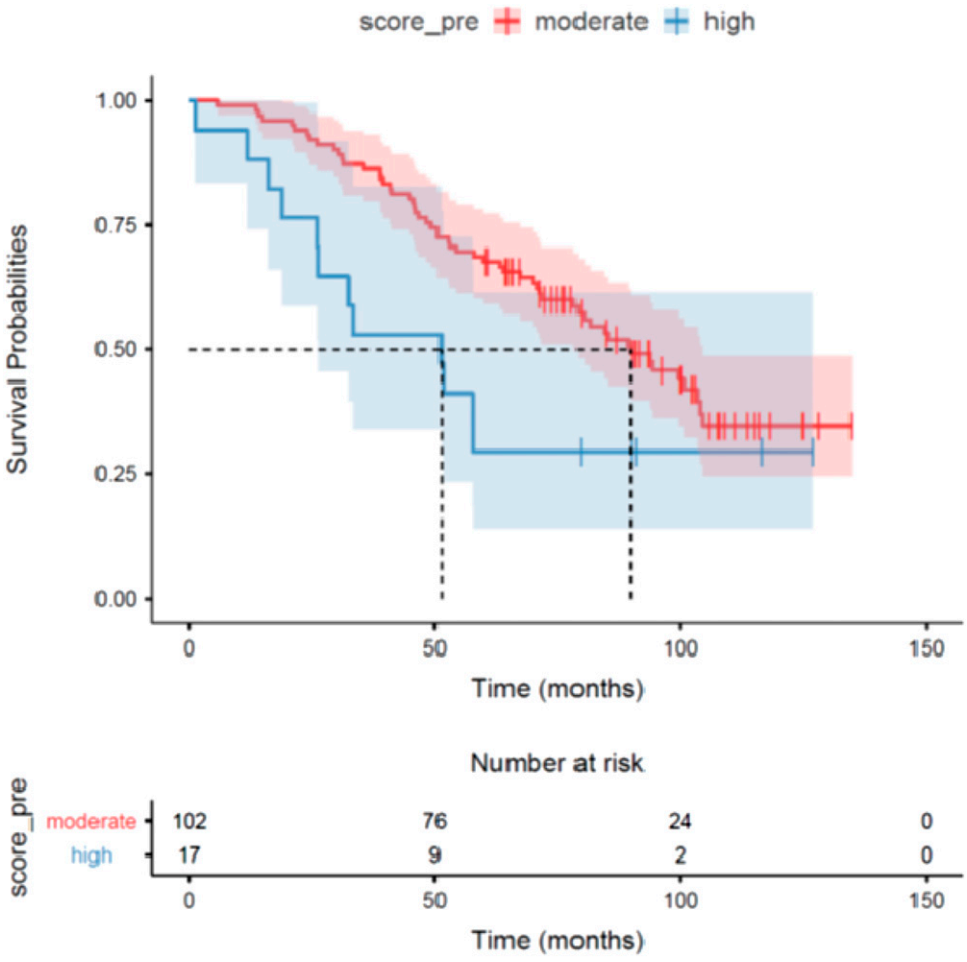

Figure 2. Kaplan–Meier survival analysis for patients with high risk factors versus patients with moderate risk factors in octogenarians post-CEA. *p*-value = .031.

benefits of CEA in octogenarians.[17–19] Some studies[20,21] have set among the Medicare population, a marked increase in mortality in older patients with mortality rate peaks in the > 80-year-old group. Similarly, De Rango et al.[22] reported that the group of > 80-year-old patients received no significant benefit from fatal stroke prevention in comparison with age-matched general populations that did not undergo surgery. Nevertheless, several single-centre studies have also found low stroke (0–2%) and mortality rates (0–1%) among the old patients.[23–26] Moreover, several other studies have underlined no difference regarding the perioperative stroke and death rate between the octogenarians with ACS and the younger patients.[27–30] Our study confirmed that there is no statistically significant difference between the octogenarians and the younger patients regarding the following 30-day parameters: the mortality rate (*p*.1.0), the ipsilateral stroke rate (*p*.7) and the ipsilateral stroke/death rate (*p*.7).

In our experience, no statistically significant difference between the two groups was found regarding the use of the shunt (*p*.073). Even though between the two groups, the reoperation and the admission to ICU score were not statistically different, LOS was slightly higher in the GA in comparison with the GB (3.4 vs 3.3; *p*..4). Likewise Pasin et al.[31] showed that length of hospital stay was longer in older patients even though reoperation and admission to ICU were not statistically different. These results can be explained by the greater and evidently unwarranted caution with which the older patient is monitored rather than the occurrence of complications during the postoperative period.

The GAPC with remifentanil infusion for CEA was first described in 2001[32] and has been reported in literature as an effective anaesthetic technique for CEA, combining the advantages of general anaesthesia and local anaesthesia.[33] The rate of conversion to general anaesthesia is 0.5–1.1%.[15,34–38]

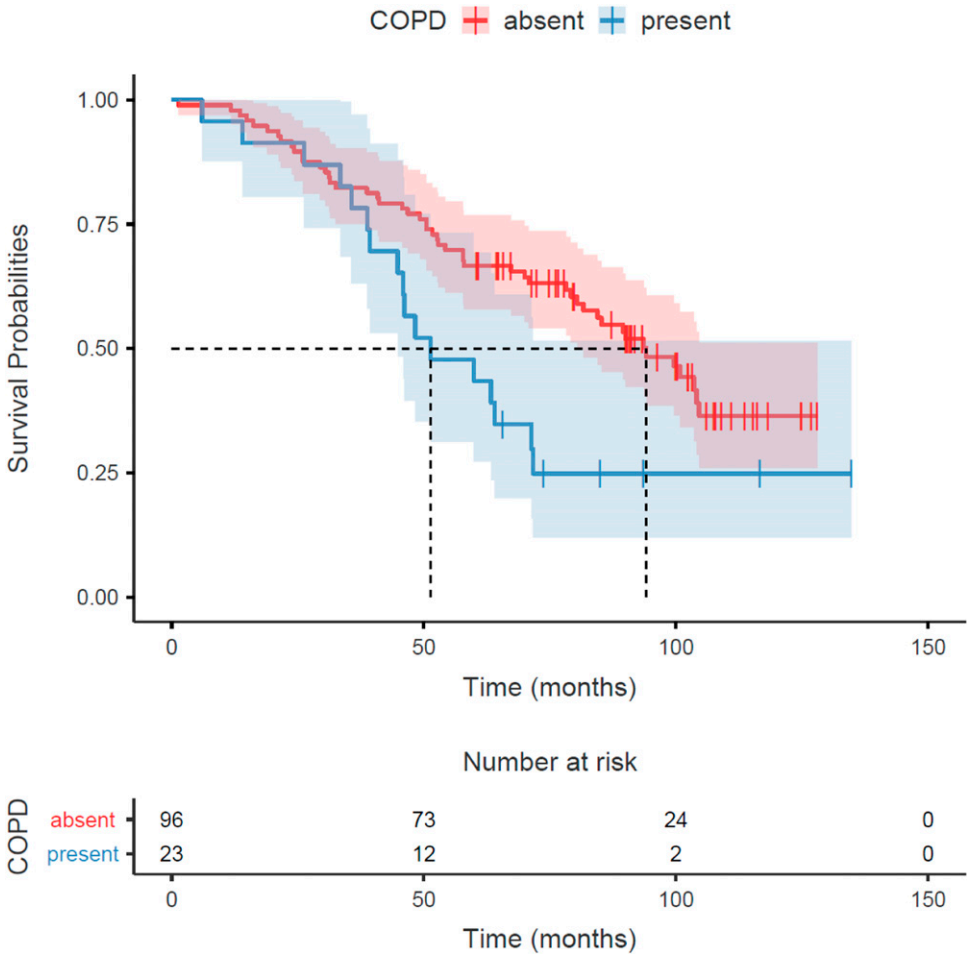

Figure 3. Kaplan–Meier survival analysis for COPD versus non-COPD octogenarians post-CEA. *p*-value = .013.

Table 4 Multivariable Cox regression analysis for various risk factors.

Predictor	HR [95% CI]	*p*-value
Gender (men)	1.356 [0.777–2.368]	.284
Curren smokers	0.865 [0.328–2.281]	.769
HPT	1.108 [0.530–2.317]	.785
Dyslipidemia	0.651 [0.387–1.094]	.105
Diabetes	1.448 [0.829–2.530]	.193
CAD	1.198 [0.643–2.233]	.569
COPD	1.888 [1.055–3.380]	.032
CKD	1.986 [1.009–3.909]	.047

HPT: hypertension; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; HR: hazard ratio, CI: confidence interval.

In our experience, the conversion was performed on two patients of the GA group (1.4%). These patients presented severe agitation and seizure during the neurological tolerance test, and a carotid shunt was employed in all cases without complications. The rate of conversion to general anaesthesia was not significantly higher compared to the GB's (*p*.054).

The presumed life expectancy in octogenarian patients may limit the efficacy of prophylactic surgery. Generally accepted guidelines currently recommend considering the CEA only with a life expectancy of at least 3–5 years, stroke and mortality risk < 3%.[39,40] Otherwise, best medical treatment (BMT) is recommended; this treatment consists in lifestyle changes as well as a triple therapy with anti-lipid, antihypertensive and antiplatelet drugs.[41,42] However, in the studies that considered the BMT, the stroke rate per year varied from 0.34% to 5.4%[43]; this variability makes the results difficult to interpret. Beside, a recent analysis by Rothenberg et al.[44] assessed the Risk Analysis Index (RAI) for measuring frailty in a population of 42,869 patients who underwent CEA (25,673 of them asymptomatic) and its influence on the long-term postoperative stroke risk and

survival rate. In the asymptomatic patients' group, the analysis revealed that the occurrence of a high RAI score was significant regarding the long-term survival rate but it did not impact the long-term postoperative stroke risk rate. A study by Ballotta et al.[45] compared octogenarian patients treated using CEA and BMT with octogenarian patients who were not treated by using the CEA but the BMT alone: the rate of freedom from cerebral ischaemic events at 5 years showed a significant higher benefit among patients who had undergone CEA as compared with those who did not (98% vs 84% p.04). This study[45] suggested that the CEA is a safe, effective and durable procedure in octogenarian patients; thus, the CEA in addition to the BMT is still preferable to the BMT alone when preventing a stroke among the elderly, however, without extending patient's life expectancy. Likewise, our experience showed a 5-year rate of freedom from cerebral ischaemia (94%) without a significant improvement of the patients' life expectancy (62%). In agreement with Ballotta et al.,[45] our experience showed that patients with COPD and CKD have a lower survival rate at 5 years. In a paper published by Carmo at al,[16] the survival risk factor score underlined that the patients with a severe risk presented a low survival rate at 5 years (54.2%). Likewise, our experience showed a low survival rate at 5 years among these patients (29.5%). Considering the risk factor score, thus, could be useful to delineate the patients who may gain the most durable outcomes.

Limits of the study

This study has some limitations due to the retrospective analysis, the small sample and absence of the control group

Conclusion

The 30-day outcomes of CEA under GAPC in octogenarian patients are comparable to those of the younger population. We believe that among older patients, the GAPC is a safe and efficient technique. Comprehensive life expectancy and preoperative score, rather than age alone, should be taken into account before performing CEA, considering the short- and long-term efficacy in stroke prevention. Future studies may help delineate the candidates among CEA octogenarians who may gain the most durable outcomes.

Declaration of conflicting interests

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