Carotid artery stenting in octogenarians in high volume centre

Karotický stenting u osemdesiatnikov v centre s vysokým počtom výkonov

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Abstract. *Background:* There is conflicting data about the risk of stroke and death among elderly patients (pts) undergoing carotid artery stenting (CAS). Accordingly, the aim of our study was to analyze early and mid-term results of CAS performed in a high-volume centre in octogenarians when compared to the younger population.

Methods: The 53 consecutive CAS pts of ≥ 80 years of age (mean age 83±3 years, group A) and 236 consecutive CAS pts <80 years of age (mean age 67±7 years, group B) were treated in the high-volume centre with extensive CAS experience. The 30-day and 6-month follow-up data including neurological complications, myocardial infarction (MI) and all-cause mortality after CAS procedure were evaluated. 98% of procedures were performed under distal filter protection.

Results: Technical success of procedure was 99% (286 pts, 51 group A, 235 group B). There was no in-hospital mortality or 30-day MI in the overall group of pts. The 30-day and 6-month major stroke/mortality rate was 1.7% (5 pts), and 5.2% (15 pts), respectively. There was no significant difference in 30-day major stroke/mortality rate [3.9% vs 1.3%, OR 1.03 (0.97-1.09)], nor in 6-month follow-up results [7.8% vs 4.6%, OR 1.03 (0.95-1.13)] in groups A and B.

Conclusion: Carotid artery stenting performed in the high-volume centre is associated with acceptable low 30-day as well as 6-month morbidity/mortality rate regardless of age. Though there is a trend towards the higher frequency of adverse events in the elderly population, our results do not support exclusion of octogenarians from CAS in a high-volume centre. Fig. 1, Tab. 4, Ref. 18, Online full text (Free, PDF) www.cardiology.sk

Key words: carotid artery stenting – octogenarians – stroke – atherosclerosis – high-volume centre

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Abstrakt. *Úvod:* Existujú rozdielne údaje o riziku mozgovej príhody a smrti u starších pacientov (pac) absolvujúcich karotický stenting (CAS). Cieľom štúdie bolo analyzovať skoré a strednodobé výsledky CAS realizovaných v centre s vysokým počtom výkonov u pacientov vo veku ≥ 80 rokov v porovnaní s mladšou populáciou.

Metódy: Päťdesiattri nasledujúcich pacientov absolvujúcich CAS vo veku ≥ 80 rokov (vek 83 ± 3 rokov, skupina A) a 236 nasledujúcich pacientov po CAS mladších ako 80 rokov (vek 67 ± 7 rokov, skupina B) bolo liečených v centre s vysokým počtom výkonov a skúsenosťami s CAS. Hodnotený bol výskyt neurologických komplikácií, infarktu myokardu a celkovej mortality po CAS v 30-dňovom a šesťmesačnom sledovaní. Distálna emboloprotekcia bola použitá v 98 % výkonov.

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Výsledky: Technický úspech výkonu bol 99 % (286 pacientov, 51 skupina A, 235 skupina B). Nezaznamenali sme úmrtie počas hospitalizácie, alebo IM v 30-dňovom sledovaní. Výskyt mozgovej príhody/mortalita v 30-dňovom, respektíve šesťmesačnom sledovaní boli 1,7 % (5 pac) a 5,2 % (15 pac). Nebol významný rozdiel vo výskyte CMP/mortality po 30-dňoch [3,9 % vs 1,3 %, OR 1,03 (0,97 – 1,09)], podobne ako po šiestich mesiacoch v skupine A verzus B [7,8 % vs 4,6 %, OR 1,03 (0,95 – 1,13)].
Záver: Karotický stenting realizovaný v centre s vysokým počtom CAS výkonov je spojený s akceptovateľne nízkou morbiditou a mortalitou po 30-dňoch, respektíve po šiestich mesiacoch bez zreteľa na vek pacientov. Hoci existuje trend zvýšeného výskytu komplikácií u staršej populácie, naše výsledky nepodporujú vylúčenie pacientov starších ako 80 rokov z CAS indikácie v centrách so skúsenosťami s ich realizáciou. Obr. 1, Tab. 4, Lit. 18, Online full text (Free, PDF) www.cardiology.sk
Kľúčové slová: karotický stenting – osemdesiatnici – mozgová príhoda – ateroskleróza – vysoko-objemové centrá

Carotid artery stenting (CAS) has been shown as an alternative to carotid endarterectomy for the treatment of carotid stenosis, mainly in surgically high-risk patients (1-3). However, the choice of revascularization technique for elderly patients with carotid stenosis is not certain. There is conflicting data about the risk of stroke and death among elderly patients undergoing CAS. A stroke and death rate of 12% was reported in elderly patients during the lead-in phase of CREST (Carotid Revascularization Endarterectomy versus Stent) Trial (4). Also, according to the final CREST results, the selection of patients for CAS or CEA may require attention to age, with older patients having a better outcome with carotid endarterectomy (CEA) (3). On the contrary, recent studies suggest that CAS can be performed in octogenarians with low complication rates between 2% and 3% (5, 6). Importantly, the number of procedures realized by the operator and by the vascular centre was described as the key factor for CAS safety. In the Pro-CAS registry the authors have shown that operators who had performed fewer than 15 CAS procedures had a markedly higher stroke/death rate when compared with operators who had performed well beyond 15 CAS procedures (7).

Accordingly, the aim of the study was to evaluate the impact of age on the complication rate after CAS in the high-volume cardiovascular centre.

Methods

Patients

The 286 patients (age 69±9 years, mean diameter stenosis 83±9%) treated by CAS in a single centre were collected. Patients with either symptomatic ≥50% diameter stenosis, or asymptomatic ≥70% diameter stenosis according to colour-duplex ultrasound, CT angiography or digital subtraction angiography were considered as candidates for revascularization. Diameter stenosis was determined according to NASCET criteria (8). Symptomatic patients had suffered a stroke or a transient ischemic attack (TIA) within the previous 6 months.

To minimize periprocedural hemodynamic complications, the antihypertensive medication was not administered in the morning before CAS procedure if the systolic blood pressure did not exceed 180 mmHg. All patients were pretreated by aspirin and clopidogrel, and were discharged on dual antiplatelet therapy with aspirin and clopidogrel for 3 months after CAS. In patients treated with anticoagulation therapy, the combination of anticoagulation medication with clopidogrel was administered. All patients without relevant contraindication were discharged on statin therapy.

Interventional procedure

Patients underwent carotid artery stenting in the angiography interventional suite. The CAS procedure was performed according to standard centre protocol. 98% of procedures were performed under distal embolic protection device with filter. Choice of stent was at the discretion of the intervention list (tapered stents, open versus closed cell designed stents). After stent deployment, postdilatation was performed in all procedures to achieve optimal struts apposition. Digital subtraction angiography was performed before and after the procedure **(Figure)**. All CAS procedures

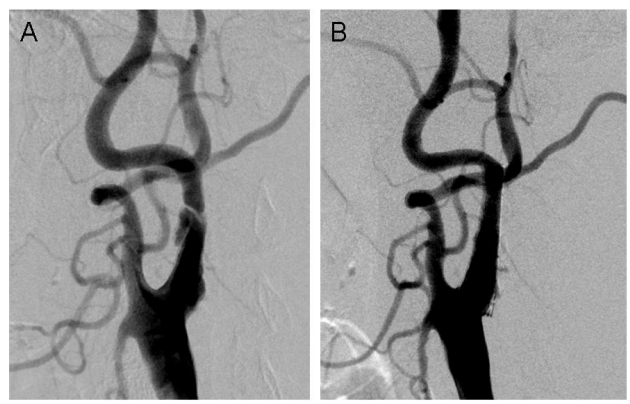

Figure Digital subtraction angiography of critical ulcerated internal carotid artery stenosis
A – before CAS, B – after CAS, CAS – carotid stenting

Table 1 Baseline characteristics

	All patients (n=286)	Group A ≥80 years (n=51)	Group B <80 years (n=235)	P Group A vs B
Age (years)	69 ± 9 (50-89)	83 ± 12 (80-89)	67± 7 (50-79)	<0.0001
Sex (males)	200 (70%)	38 (75%)	162 (69%)	0.50
Symptomatic stenosis	87 (30%)	19 (37%)	68 (29%)	0.24
Bilateral stenosis	52 (18%)	9 (18%)	43 (18%)	1.00
Diameter stenosis (%)	83±9 (55-95)	84±8	82±9	0.91
Coronary artery disease	45 (16%)	11 (22%)	34 (14%)	0.21
Arterial hypertension	260 (91%)	45 (88%)	215 (92%)	0.43
Dyslipidemia	232 (81%)	42 (82%)	190 (80%)	1.0
Diabetes mellitus	126 (44%)	25 (49%)	101 (43%)	0.44
Smoking	106 (37%)	14 (27%)	92 (39%)	0.15
BMI	29±5	26±4	32±5	0.43

BMI – body mass index

were undertaken by one of two experienced operators with more than 300 CAS procedures performed.

Follow-up

The 30-day and 6-month follow-up data including neurological complications: myocardial infarction (MI) and all-cause mortality were evaluated. All neurological evens were evaluated by an independent neurologist. Outcomes of patients ≥80 years of age (n=51, group A) and <80 years (n=235, group B) were analyzed. Major stroke was defined as a new neurological deficit persisting longer than 24 hours. Minor stroke was defined as a new neurological deficit that resolved completely within 24 hours. The primary end point was defined as combination of any 30-day death or major stroke.

Statistical analysis

Data evaluation was performed using a statistical software package SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Discrete variables are presented as counts and percentages. Continuous variables are presented as mean values ± SD. Gaussian distributions of data were tested by the Kolmogorov-Smirnov test. The frequencies of categorical variables were compared using Fisher´s exact test. Mean values for continuous parameters were compared using the Student *t* test and Mann-Whitney test, used as appropriately. For all analyses, a p value <0.05 was considered statistically significant.

Table 2 Overall group (n=286), 30-day and 6-month results after CAS

	30-day	6-month
Major stroke	4 (1.4%)	8 (2.8%)
Minor stroke	2 (0.7%)	2 (0.7%)
Mortality	1 (0.3%)	7 (2.4%)
Myocardial infarction	0	4 (1.4%)
Major stroke/mortality	5 (1.7%)	15 (5.2%)
Hyperperfusion sy.	2 (0.7%)	–
Retroperitoneal bleeding	2 (0.7%)	–
Postcathet. pseodoaneurysm	4 (1.4%)	–

CAS – carotid stenting

Results

The baseline characteristics of patients are given in **Table 1**. The technical success of procedure was 99% (286 patients). The cause of technical failure of CAS in the remaining 3 patients was unfavourable anatomy, with hostile aortic arch and extreme tortuosity of supraaortic vessels.

About 1/3 of patients had relevant central neurological symptomatology in the 6 months period before CAS procedure. In about 20% of patients the bilateral CAS was performed. There was no in-hospital mortality or 30-day MI in the overall group of patients. The 30-day and 6-month major stroke/mortality rate was 1.7% (5 patients), and 5.2% (15 patients), respectively **(Table 2)**. There was no significant difference at 30-day or at 6-month follow-up results in group A compared to group B, though there is a strong trend towards high incidence of complication in octogenarians **(Table 3)**. Despite the strong trend, there was also no significant difference in evaluated adverse events between symptomatic and asymptomatic subjects **(Table 4)**.

Discussion

The present study investigated the clinical results of carotid artery stenting carried out in the high-volume centre in

Table 3 Major stroke/mortality after CAS: <80 years patients versus octogenarians

Follow-up	Group A (≥80y) n=51	Group A (<80y) n=235	OR (95%CI)	P
30-day	3.9% (2 pts)	1.3% (3 pts)	3.16 (0.51-19.4)	0.22
6-month	7.8% (4 pts)	4.6% (11 pts)	2.2 (0.67-7.28)	0.25

CAS – carotid stenting

Table 4 Major stroke/mortality after CAS: symptomatic versus asymptomatic patients

	Symptomatic n=87	**Asymptomatic** n=199	OR (95%CI)	P
30-day	3.4% (3 pts)	1% (2 pts)	3.5 (0.58-21.4)	0.17
6-month	8% (7 pts)	4% (8 pts)	2.0 (0.75-5.35)	0.25

CAS – carotid stenting

patients ≥80 years of age. The main findings can be summarized as follows: 1) CAS realized in the high-volume centre by experienced operators is linked with acceptable 30-day as well as 6-month morbidity/mortality rate, regardless of the age of the patients; 2) despite the trend towards higher complication rate, there was no significant difference in 30-day or 6-month results of symptomatic patients undergoing carotid stenting, when compared to asymptomatic.

CAS in octogenarians

Several studies have shown increasing age as an important predictor of complications associated with CAS. The lead-in phase of The Carotid Revascularization Endarterectomy Versus Stent Trial (CREST) demonstrated that octogenarians had a markedly elevated 30-day periprocedural stroke or death rate of 12.1%, compared to 3.2% in non-octogenarians (4). Similarly, the German ALKK CAS registry has shown that in-hospital stroke or death rates increase significantly with older age (5.5% in octogenarians versus 3.2% in non-octogenarians, p=0.03) (9). Also in the CAPTURE 2 trial patients age ≥80 years have higher 30-day rates of death and stroke than younger patients, due primarily to age-related anatomic changes (4.5% versus 3.0%). However, these challenges do not rule out the CAS procedure if careful patient selection is applied. Though in the overall CAPTURE 2 trial age was a predictor of periprocedural death and stroke, it was not a predictor of periprocedural stroke outcomes within the subgroup of patients ≥80 years old. It is possible that lesion characteristics associated with aging (eg, increased tortuosity and calcification of the arch and supra-arch vessels) are of crucial importance in risk stratification of adverse outcomes (10, 11). Similarly, the Vitek group has shown that CAS can be performed safely in anatomically suitable elderly patients with low adverse event rates (30-day stroke/death rate of 3.3%), and that CAS should remain a revascularization option in appropriately selected elderly patients (6). This group has also reported that 85% of their elderly patients selected for CAS survived for 2 years and more than 75% survived for 3 years after the CAS procedure (12). In concordance, based on the recent experiences of Leipzig centre the anatomical conditions and octogenarian age were associated with an increased rate of neurologically adverse events during the CAS procedure (13). In summary, it is not clear whether the age-related results are due to age per se, or whether the effect of advanced age is confounded by other factors that might affect CAS outcomes (14). These factors include unfavourable anatomy with hostile aortic arch, calcification of the aortic arch and carotid arteries, tortuosity of supraaortic vessels, as well as more pronounced atherosclerotic disease.

Symptomatic versus asymptomatic patients

Data comparing results of CAS in symptomatic and asymptomatic patients are scarce. In the CREST Trial the rate of stroke or death among symptomatic patients after CAS was 6.0%, compared to 2.5% in the asymptomatic group. Prespecified analyses did not show a modification of the treatment effect by symptomatic status comparing the CAS and CEA procedures (p=0.84), (3). In the comparison of Colombo et al., the 30-day major adverse event rate of symptomatic patients undergoing CAS was 6.7% (11/163) versus 2.1% (7/237) in the asymptomatic group (p=0.02) (15). In our study, despite the trend towards the higher complication rate, there was no significant difference in 30-day or 6-month results of symptomatic patients compared to asymptomatic.

Importantly, the benefit of carotid revascularization in the asymptomatic elderly population remains questionable, because in asymptomatic subject the longer postoperative survival is required to achieve the benefit of procedure. Despite the uncertainties, CAS as well as CEA are increasingly performed in this patient group as a result of population ageing.

Need for embolic protection devices

The use of an embolic protection device was described as an important factor influencing the outcomes of CAS procedure. The subanalysis of the ALKK registry showed that patients treated with EPD (668 of 1483 patients) had a lower rate of ipsilateral stroke (1.7% versus 4.1%, p=0.007) and a lower rate of all non-fatal strokes and deaths (2.1% versus 4.9%, p=0.004) during hospital stay compared to patients treated without EPD (9). In our study, the distal protection filter device was used in 98% of cases with 30-day major stroke/mortality rate of 2.2%. Similarly, in the multicentre registry with the use of proximal endovascular occlusion cerebral protection device in 198 octogenerians, the overall 30-day combined stroke/death rate was 2.5% (16).

The role of the high-volume centre and the operator's experience

A major criticism of randomized clinical trials comparing CAS and CEA focused on the incomplete learning curve of interventionists, with the learning curve strongly influencing the results of CAS. The disappointing results of CAS in the EVA-3S study are frequently explained by the low experience of operators, with 85% of interventionists performing ≤50 cases in total (17). Furthermore, registries like ProCAS have revealed that experience was an independent predictor of outcome, with a significant difference in performance for those who had performed 50 cases compared to 150 cases, and between those who had performed ≤150 and those who had performed ≥150 cases (7). In the prospectively multicentre CAPTURE 2 study the most important determinant of perioperative CAS outcomes was both site and operator CAS volume. A threshold of 72 cases was found to be necessary for consistently achieving a death and stroke rate below 3% (10). In a recent observational study using administrative data on fee-for-service Medicare beneficiaries aged 65 years or older undergoing carotid stenting, 24 701 procedures were performed by 2339 operators. Among older patients undergoing carotid stenting, lower annual operator volume and early experience were associated with increased 30-day mortality (18). Importantly, in our study, all procedures were performed by two intervention lists, with experience of >300 CAS procedures, which could have had a crucial influence on overall results, especially in octogenarians.

Limitations

The relatively small number of elderly patients in the B group could be considered the limitation of the study. It is likely that, with the increase number of patients, the difference between octogenarians and the group of younger patients in the main outcome could have reached statistical significance. Similarly, the low number of primary end-points events in the follow-up period do not let us realize statistically relevant multivariate analysis of predictors linked to major adverse events after CAS procedure. Therefore, the findings of the present study need to be confirmed in larger, prospectively designed, cohorts undertaken entirely in high-volume centres.

Conclusions

Carotid artery stenting procedure realized in high-volume centres is linked with acceptable 30-day, as well as 6-month mortality/morbidity rates, regardless of the age of patients. Despite the trend of increase frequency of complications, an age over 80 years is not a contraindication for CAS procedure. Operators experiences and individual careful selection of patients are crucial for further decrease of the adverse events after CAS, especially in elderly patients.

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