ABSTRACT

Background: Carotid artery disease is a major cause of ischemic stroke, directly related to the severity of stenosis and presence of symptoms. Carotid artery stenting (CAS) is an endovascular, catheter-based procedure that unblocks stenoses of the carotid artery lumen to prevent a stroke.

Objective: The aim of this study was to analyse outcomes in a series of patients with carotid atherosclerosis (CA) who underwent carotid angioplasty and stenting.

Methods: This study was designed as a retrospective cross-sectional study. The report includes 95 patients with carotid atherosclerosis who were treated with carotid angioplasty and stenting. The efficacy of the procedures was estimated by Doppler ultrasound of carotid arteries and by magnetic resonance imaging (MRI) 12 months after the procedure.

Results: Observed complications after CAS included carotid artery restenosis in 8 (8.4%) participants and CVI in 9 (9.5%) participants. We concluded that the appearance of CVI depends on the presence of distal protection devices (p = 0.003). In contrast to CVI, restenosis of CA after angioplasty and stenting was not related to degree of CA stenosis (p = 0.600) nor to patient age (p = 0.264). Advanced age (p = 0.024) and calcified atherosclerotic plaques (p = 0.003) were independent predictors of CVI after the procedure.

Conclusions: Carotid stenting can be considered the method of choice for the treatment of carotid disease.

Keywords: Carotid artery stenting, angioplasty, carotid artery disease

SAŽETAK

Poreklo. Bolest karotidnih arterija je glavni uzrok ishemijskog moždanog udara, direktno je povezana sa stepenom stenoze i prisustvom simptoma. Stenting karotidne arterije je endovaskularna procedura bazirana na upotrebi katetera, kojom se ‘odblokira’ suženje da bi se sprečio udar.

Cilj. Cilj ove studije je da analizira ishod procedure karotidne angioplastike i stentinga, kojoj je podvrgnuta serija pacijenata sa aterosklerozom karotidne arterije.

Metod. Ovo je retrospektivna studija preseka koja obuhvata 95 pacijenata sa karotidnom aterosklerozom podvrgnutih procedurama karotidne angioplastike i stentinga. Efikasnost procedure je procenjena pregledom kolor Dopler ultrazvukom i magnetnom rezonancijom, nakon godinu dana.

Rezultati. Evidentirane komplikacije posle procedure su - kod 8 (8,4%) učesnika restenoza karotidne arterije a kod 9 (9,5%) pojava CVI. Zaključili smo da pojava CVI zavisí od korišćenja distalne protekcije (p = 0.003). Za razliku od CVI restenoza posle procedure nije vezana ni za stepen stenoze arterije (p = 0.600) ni za starost pacijenta (p = 0.264). Starost pacijenta (p = 0.024) i prisustvo kalcafiokaovanog ateroskleroškog plaka (p = 0.003) su nezavisni prediktori pojaće CVI nakon procedure.

Zaključak. Stenting se može smatrati metodom izbora za lečenje bolesti karotidnih arterija.

Ključne reči: stenting karotidnih arterija, angioplastika, bolest karotidnih arterija
INTRODUCTION

Carotid artery disease is a major cause of ischemic stroke, directly related to the severity of stenosis and presence of symptoms (1,2). It is estimated that carotid artery stenosis is responsible for 15% to 20% of all strokes (3). Stroke is the leading cause of functional impairment. More than 20% of surviving patients require institutional care and up to one-third have permanent disability. Even more concerning is the fact that the population is aging, and the number of patients with stroke is correspondingly increasing (1,2).

The primary mechanism of stroke in patients with carotid artery stenosis is embolism of atherosclerotic debris or thrombotic material from the plaque into the distal cerebral vasculature (4). Carotid endarterectomy (CEA) was the first intervention that, in addition to optimal medical therapy, was shown to reduce the risk of further ischaemic events (5). Carotid artery stenting (CAS) is an endovascular, catheter-based procedure, which widens the carotid artery lumen. CAS offers patients a less invasive and less traumatic approach than other procedures that have the same goal (6). Angioplasty is the technique of mechanically widening a blood vessel that has been narrowed or obstructed, typically as a result of atherosclerosis. Angioplasty and stenting are commonly used for the treatment of atherosclerotic stenosis in several arterial territories in the body. These techniques are very effective at reducing the degree of arterial narrowing. The procedures involve the crushing of atherosclerotic plaque material against the vessel wall with a high-pressure balloon and the subsequent placement of a metal mesh tube (stent) to hold this material back, preventing elastic recoil and covering any dissection caused by the angioplasty procedure (7).

Despite some controversy regarding the superiority of carotid angioplasty and stenting compared with carotid endarterectomy, the use of these procedures in clinical practice “exploded” in many parts of the world (8). Nevertheless, one of the limitations of CAS is the potential for embolic stroke caused by dislodging the atheromatous material in arterial plaques (9,10). To prevent stroke, a variety of cerebral protection devices (CPDs) have been developed in recent years. Preliminary results have shown that these devices can significantly reduce the risk of thromboembolic complications during CAS (9,10). However, concerns have been raised regarding protection devices, because their use requires further manipulation and increases the risk and costs of the procedure (11,12).

CAS is still an evolving intervention, and new techniques, such as specialised and miniaturised diagnostic and guiding catheters and guide wires, new stents and new adjunctive therapies (13), are rapidly being developed. A recent systematic review of the literature suggests that the risk of stroke or death after CAS is increased in patients with symptomatic stenosis, in elderly patients, and in patients with hypertension or a history of coronary artery disease (14).

The aim of this study was to analyse outcomes in a series of patients with carotid atherosclerosis (CA) who underwent carotid angioplasty and stenting.

MATERIALS AND METHODS

Our study was designed as a retrospective cross-sectional study. From March 2009 until March 2010, 95 patients with carotid atherosclerosis underwent carotid angioplasty and stenting at the Kragujevac Clinical Center in Kragujevac, Serbia.

Before the procedure, all patients received 450 mg of clopidogrel. During the procedure, patients were constantly monitored, and 1 mg of atropine was given (IV). After the procedure, all patients received three months of combination anti-platelet therapy consisting of 75 mg of clopidogrel per day and 100 mg of aspirin (acetylsalicylic acid) per day. Depending on blood cholesterol levels, patients received 20 mg per day of atorvastatin. To be included in the study, patients were required to have symptomatic disease (with neurological manifestations such as TIA, RIND or CVI). Patients also were also required to have either high-grade stenosis (more than 70%) or one occluded CA with at least 60% stenosis in the contralateral CA. Patients with clopidogrel resistance or with ulcerated/calcified plaques were excluded from this study.

Before the procedure, all patients underwent Doppler ultrasound of the carotid arteries, magnetic resonance imaging (MRI), digital subtraction angiography (DSA) and testing for clopidogrel resistance. Control MRI was performed within 24 hours after CA angioplasty and stenting. Follow-up consisted of control MRI and Doppler ultrasound examination of the carotid arteries one year after the procedure.

We used stents by Boston Scientific and Abbot as well as stents Protégé by AV-3 and Cordis stents. Filters used for distal embolic protection were the EZ by Boston Scientific, the Spyder AV-3 and the Angiogard by Cordis.

Characteristics of the study population are described with frequencies, means ± standard deviation, and medians. The statistical significance of differences between groups was tested by Fisher’s exact probability test (for frequencies) or by the non-parametric Mann–Whitney U test (for continuous variables). Multiple logistic regression analysis was performed to determine independent predictors of any medical complication resulting from the procedure. The differences were considered significant if the probability of the null hypothesis was less than 0.05.

RESULTS

Characteristics of the patient population with identified risk factors are listed in Table 1. As noted above, 95 participants were included in the report. Bilateral carotid artery occlusion was observed in 31% of patients, and 16% of patients underwent treatment of both CAs. The degree of carotid stenosis in this study population ranged from 72 to 95% (Graphic 1). After one year of follow-up, the major complications observed in this study were carotid artery restenosis in 8 (8.4%) participants and CVI in 9 (9.5%) participants.
In 45 patients who had atherosclerotic plaques with smooth contours (without ulcerations or calcium), carotid artery stenting was performed without the use of distal protection devices. In this subgroup, we did not observe any instances of CVI during the follow-up period. In the subgroup of 50 patients who underwent CAS with distal protection devices, 9 (18%) patients suffered CVI. Using Fisher’s exact test, we concluded that the risk of CVI was related to the use of distal protection devices (p=0.003).

In our study population, ulcerated plaques were observed in 24 (25.26%) patients. In patients with ulcerated plaques, CA restenosis at one year was observed in 3 (12.5%) patients, while in the 71 (74.74%) patients without ulcerations, CA restenosis was seen in 5 (6%) patients. This difference was not statistically significant (p = 0.412 by Fisher’s exact test).

We also tested the association of CVI (as a neurological complication) with the presence of ulcerated plaques. CVI was observed in 9 (37.5%) patients with ulcerated plaques, while in patients without ulcerated plaques, no cases of CVI were seen. This difference was statistically significant (p < 0.0005 by Fisher’s exact test).

Calcified atherosclerotic plaque was identified in 12 (12.63%) study participants. Of these participants, CA restenosis within the first year after the procedure was observed in 3 of these (25%) patients. In the 83 (87.37%) patients without calcified plaques, restenosis was observed in 5 (6%) patients. This difference was not statistically significant (p = 0.061 by Fisher’s exact test).

We also attempted to establish if patients with calcified plaques had a higher risk of CVI after CAS. In the subgroup of 12 patients with calcified plaques, 8 (66.7%) suffered CVI within one year. In the 83 patients without calcified plaques, only 1 (1.2%) patient suffered CVI. This was a statistically significant difference (p < 0.0005 by Fisher’s exact test).

The relation between CA restenosis after CAS and the degree of stenosis before the procedure was also tested. We found that restenosis of CA and degree of pre-procedural CA stenosis were not significantly related (Mann-Whitney U Test, p=0.600). Patient age was also not significantly related to the risk of CA restenosis (Mann-Whitney U Test, p=0.264).

Patients who suffered CVI had a higher degree of pre-procedural CA stenosis than patients those who did not experience this complication. The median percentage of CA stenosis in patients who suffered CVI was 90%. Patients who did not have CVI had a median CA stenosis percentage of 80%. This difference was statistically significant (Mann-Whitney U Test, p=0.001). Patients who experienced CVI also were also significantly older, with a median age of 78 years versus 71 years in patients who did not have CVI (Mann-Whitney U Test, p=0.0005).

The effect of clinical characteristics on the subsequent development of medical complications was analysed by logistic regression. Multiple logistic regression analysis was performed to determine the independent predictors of any post-procedural medical complication. RIND (OR 16.061, 95% CI 1.767-145.996, p = 0.014) and calcified plaques (OR 19.661, 95% CI 1.616 – 239.236, p=0.019) significantly increase the risk of CA restenosis after CAS. Multiple logistic regression analysis revealed that advanced age (p=0.024) and presence of calcified plaques (p=0.003) were independent predictors of the risk of developing CVI as a complication of CAS. In terms of age, the OR for advanced age was 1.696 (95% CI 1.072 - 2.685), implying that every year of increasing age increases the risk of CVI by 70%. The OR for CVI in patients with calcified plaques was 106.390 (95% CI 5.058- 2237.887), suggesting that the presence of calcified plaques increases the risk for CVI by a factor of 106.

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**Table 1.** Characteristics of the patient population with identified risk factors

<table>
<thead>
<tr>
<th>Demographic</th>
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</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>71.1 ± 4.433</td>
</tr>
<tr>
<td>Men</td>
<td>52 (54.7%)</td>
</tr>
<tr>
<td>Women</td>
<td>43 (45.3 %)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Present symptoms</th>
<th>Number / (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>92 (96.84%)</td>
</tr>
<tr>
<td>RIND</td>
<td>43 (45.26%)</td>
</tr>
<tr>
<td>CVI</td>
<td>21 (22.11%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Number / (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>69 (76.2%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>94 (98.9%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>67 (70.5%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>41 (43.2%)</td>
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</tbody>
</table>

![Graphic 1. Carotid stenosis in this study population](image)
DISCUSSION

Carotid artery balloon dilation with stenting with balloon dilation is a minimally invasive treatment for CA stenosis, possible cause of cerebrovascular insult. Several elements are required for a successful CAS procedure, including adequate equipment such as stents, a well-trained team of doctors, and good cooperation with neurologists. Neurologists should document symptoms such as transient ischemic attack and confirm the presence of stenosis using special diagnostic examinations. Studies of carotid stents began in 2001. Documented complications include stroke; the mortality rate ranges from 0% to 7.4%. This variation is likely related to differing patient ages and comorbidities in different published series (15).

In the present study, the incidence of risk factors, such as abnormal lipid profile and diabetes mellitus, was high. Coronary artery disease was also observed in most of our study patients. The treatment of patients with CA stenosis and medical comorbidities is complex and requires long-term follow-up. Stent placement and balloon angioplasty is only treatment of consequence, and the origin of atherosclerosis is complex and requires serious access.

The use of distal embolic protection devices during carotid stenting is necessary to increase the safety of this procedure by reducing the possibility of migration of particles from ruptured plaques. A recent meta-analysis by Kastrup supports the use of cerebral protection devices, showing a reduction in neurologic events from 5.5% to 1.8% with the use of cerebral protection devices (16).

Our study showed a statistically significant relationship between the presence of ulcerated plaques and the risk of cerebrovascular insult after the CAS procedure. Several reports have stressed the fact that high-risk morphology plaques have a high propensity to embolise and cause stroke (17).

Choosing the proper stent for the type of lesion being treated reduces the risk of CA restenosis. In our study, the grade of CA stenosis did not predict for the risk of restenosis, suggesting that the selection of stents and balloon angioplasty devices was adequate.

Finally, there still is a need to identify specific risk factors for the development of restenosis after CAS. Some studies have identified advanced age as a potential risk factor for the development of a restenosis; however, the definitive role of these factors still needs to be elucidated in larger trials (18).

Our study has showed that rates of restenosis after stenting were not significantly correlated to patient age. However, the risk of cerebrovascular insult after stenting was higher in older patients. Because advanced age has also been associated with a higher frequency of neurologic complications after CAS, the elderly should generally be considered as high-risk patients for CAS (19, 20).

The relatively low complication rate in our study points to good pre- and post-procedural antplatelet treatment as well as adequate drug treatment of hypercholesterolemia. It also points to the positive attitude of most of our patients related to the reduction of their risk factors.

CONCLUSIONS

Carotid stenting is the treatment of choice for carotid disease. Key factors for the success of the procedure are prompt diagnosis of the presence of atherosclerosis in the carotid arteries, adequate preparation of the patient before the procedure, proper stent selection and adequate positioning within the arteriosclerotic lesions. In addition, postprocedural support for risk factor reduction also plays a significant role in lowering the rates of restenosis and cerebrovascular complications.

REFERENCES