ENDOVASCULAR REVASCULARIZATION OF CAROTID ARTERY STENOSIS

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Summary

Introduction. Endovascular revascularization is a peripheral artery disease therapy used to improve blood flow in blood vessels. The objective of this study was to analyze the types and prevalence of comorbidities in patients with indications for carotid artery revascularization, as well as early results of endovascular carotid artery revascularization in relation to periprocedural complications. Material and Methods. This retrospective study was conducted from October 2014 to October 2019 and included 96 patients. Descriptive and comparative statistical analysis was performed in all patients, male and female, and those with both symptomatic and asymptomatic carotid diseases. Results. The study included 96 patients, of whom 69.8% were male and 30.2% were female. A successful endovascular procedure was performed in 89.6% of patients, while in 10.4% of patients the procedure failed. The distribution of patients by sex, age and the duration of procedure, showed a statistically significant difference (p < 0.05) between the two groups. Conclusion. Endovascular revascularization has a high success rate in the treatment of atherosclerotic disease of the carotid arteries as well as low periprocedural morbidity and mortality. The analysis of gender-related differences, we concluded that endovascular revascularization lasts significantly longer in female patients, and that the average age is significantly higher in male patients compared to females. We also concluded that hyperlipoproteinemia is a major risk factor for carotid artery disease.

Key words: Carotid Stenosis; Stroke; Cerebral Revascularization; Endovascular Procedures; Treatment Outcome; Stents; Atherosclerosis; Minimally Invasive Surgical Procedures; Risk Factors; Comorbidity

Sažetak

Uvod. Endovaskularna revaskularizacija podrazumijeva rekonstrukciju oboljelog krvnog suda metodama koje se koriste da poboljšaju protok krv kroz krvni sud. Cilj rada bila je analiza komorbiditeta po tipu i učestalosti javljanja kod pacijenata sa indikacijom za revaskularizaciju karotidnih arterija, kao i analiza ranih rezultata endovaskularne revaskularizacije karotidnih arterija u odnosu na periproceduralne komplikacije. Materijal i metode. Retrospektivna studija između oktobra 2014. i oktobra 2019. godine obuhvata 96 pacijenata. Rađena je deskriptivna i komparativna statistika za celu populaciju između grupe muškog i ženskog pola i simptomatske i asimptomatske bolesti. Rezultati. Istraživanjem je obuhvaćeno 96 bolesnika, od kojih je 69,8% bilo muškog, dok je 30,2% bilo ženskog pola. Uspješno uvrštena endovaskularna procedura je urađena kod 89,6% bolesnika, dok kod 10,4% bolesnika procedura nije uspela. Poređenjem pacijenata po polu, starosti (p = 0.0003) i trajanja procedure (p = 0.022) pokazala se statistički značajna razlika (p < 0.05). Poređenjem dve grupe pacijenata sa simptomatskom i asimptomatskom karotidnom ateroskleroskom bolesti, hiperlipoproteinemija (p = 0.015) pokazala se takođe statistički značajna razlika (p < 0.05). Zaključak. Endovaskularnom revaskularizacijom se postiže visok uspeh lečenja aterosklerotske bolesti karotidnih arterija, prcaćenja je malim periproceduralnim morbiditetom i mortalitetom. Analizom rezultata po polu, zaključili smo da endovaskularna revaskularizacija značajno duže traje kod pacijenata ženskog pola i da je prosečna starost značajno veća kod pacijenata muškog pola u odnosu na ženski pol. Zaključili smo i da hiperlipoproteinemia ima značajnu ulogu u simptomatologiji karotidne bolesti, kao i da je hiperlipoproteinemija značajno faktor rizika za bolest karotidne arterije.

Ključne reči: karotidna stenoza; moždani udar; cerebralna revaskularizacija; endovaskularne procedure; ishod lečenja; stentovi; ateroskleroz; minimalno invazivne hirurške procedure; faktori rizika; komorbiditet

Introduction

Endovascular revascularization is a peripheral artery disease therapy that involves reconstruction of diseased blood vessels in order to improve blood flow [1]. Carotid disease commonly manifests as atherosclerotic stenosis, which can lead to ischemic stroke with a high mortality, and revascularization has shown its place in its prevention [2]. Ischemic cerebrovascular disease (ICVD) has a very high mortality rate, and the fact that it is a neurological disease with the highest degree of disability is equally serious [3]. Cerebrovascular insult (CVI) or stroke is the third...
leading cause of death in developed countries, after heart disease and malignancies [4].

Carotid revascularization for prevention of ischemic stroke can be surgical or endovascular revascularization [5]. Surgical treatment involves carotid endarterectomy (CEA), and involves direct access to a blood vessel followed by complete removal of atherosclerotic plaque [6]. Endovascular treatment involves placement of a stent in the carotid artery, carotid stenting (CAS) and it is a less invasive method compared to surgical treatment [7]. Surgical revascularization is the method of choice for the treatment of carotid artery stenosis, but in high-risk patients (several associated diseases) who are contraindicated for CEA, with stenosis of a surgically inaccessible place, restenosis after CEA, the best choice is endovascular treatment. Endovascular treatment of carotid arteries is a minimally invasive branch of vascular surgery using percutaneous transluminal angioplasty (PTA) and CAS [1]. Stents are metal cylinders of mesh structure, designed to keep the lumen of the artery open by preventing the progression of plaque into the lumen. Some of the embolic protection devices during endovascular revascularization are distal occlusion balloons and distal filters [8].

The aim of this research was to analyze risk factors and comorbidities in patients with indicated endovascular revascularization of carotid arteries, and to analyze early results of endovascular revascularization in relation to periprocedural complications.

**Material and Methods**

The retrospective study included 96 patients who were treated with endovascular revascularization at the Clinical Center of Vojvodina in the period from October 2014 to October 2019 (5 years). The data on patients were collected from medical records of the Department of Interventional Radiology, Center for Radiology, and at the Clinic of Vascular and Endovascular Surgery of the Clinical Center of Vojvodina in Novi Sad (computer database, operative protocol, accompanying clinical and radiological documentation, discharge lists). All endovascular interventions were performed in the angio-hall of the Department of Interventional Radiology, Center for Radiology, by a team of interventional radiologists, vascular surgeons and anesthesiologists. Carotid revascularizations were performed according to the guidelines of the European Society for Vascular and Endovascular Surgery [9].

In order to analyze the results of the endovascular revascularization, the following parameters were analyzed:

1. Before the treatment:
   - Gender and age of patients,
   - Associated diseases (arterial hypertension (HTA), diabetes mellitus, hyperlipoproteinemia (HLP), chronic obstructive pulmonary disease (COPD), cardiomyopathy (CMP), and other vascular and cardiac diseases, nicotine, obesity),
   - Clinical stage of extracranial cerebrovascular disease,
   - Degree of carotid artery stenosis or restenosis.
2. After the treatment:
   - Duration of the surgical procedure,
   - The amount of heparin given during the procedure,
   - Postoperative complications,
   - Procedural success rate (%).

In addition to the medical history data and clinical examination, accurate diagnosis was made by a combination of duplex ultrasound, multislice computed tomographic angiography (MSCTA) and magnetic resonance angiography (MRA). After the diagnostic algorithm and morphological assessment of suitability for endovascular treatment of the carotid artery were performed, each intervention was done under local anesthesia. The functionality of the reconstruction was determined by physical examination and duplex ultrasound. Other vascular and cardiac diseases include the following diseases: pectoral angina, valvular heart disease, valvular aortic disease, extrasystolic ventricular arrhythmia, pulmonary artery hypertension, peripheral arterial occlusive disease (PAOD), myocardial infarction and chronic renal failure. Carotid restenosis or restenosed carotid artery, involves stenosis of the artery that had already been treated with one of the surgical or endovascular methods. Each endovascular procedure was performed with distal filter protection as well as predilatation of the carotid artery wall.

Descriptive and comparative statistics were done for all the patients, with sex distribution and symptomatic and asymptomatic distribution of patients. As part of the descriptive statistics, the following parameters were used: statistical mean and median, minimum and maximum values, and standard deviation. To compare differences in the intensity of impressions between the tested groups for non-parametric attributes, we used the Pearson χ²-test.

**Results**

The study included 96 patients, of whom 67/96 (69.8%) were male, while 29/96 (30.2%) were female. The average age of patients was 67.2 years; the oldest patient was 79 years old, and the youngest 42 years old. The most common comorbidities in the entire group of patients were: HTA in 71.87% of patients, followed by CMP in 53.12% of patients. Non-insulin-dependent diabetes mellitus (NIDDM) affected 28.2% and HLP 26.04% of all patients. The COPD was present in 15.62%, nicotine in 16.66%, insulin-dependent diabetes mellitus (IDDM) in 4.16% of patients. Only
2.08% patients were obese. Other vascular and cardiac diseases were found in 54.16% of patients. Other concomitant cardiac and vascular diseases were present in 54.2% of patients, of which PAOD was present in 16.7% and myocardial infarction in 15.6% of patients. Pectoral angina was present in 14.6% of the total number of patients, while 5.2% patients suffered from chronic renal insufficiency.

Based on the medical history data and clinical examination, 51/96 (53.1%) patients had a symptomatic carotid disease, while in the rest of 45/96 (46.9%) patients it was asymptomatic. In patients with symptomatic carotid disease, CVI occurred in 33/51 patients, transient ischemic attack (TIA) in 14/51, while reversible ischemic neurological deficit (RIND) occurred in 4/51 patients.

Treatment of restenosed artery was done in 26% of patients, while in the remaining 71/96 (74%) patients the stenosis was primary. The degree of the artery stenosis, which was determined by diagnostic methods, was divided into stenosis of less than 90% and of more than 90% of the normal lumen of the artery. Artery stenosis less than 90% was found in 71.9% of patients, while more than 90% was found in 28.1%. Contralateral significant stenosis, i.e. greater than 70% of the artery on the opposite side from the planned endovascular revascularization, was present in 17/96 (17.7%) patients. Right carotid artery stenting was indicated in 50/96 (52.1%) patients, while slightly less was indicated in the left carotid artery, in 46/96 (47.9%) patients. The endovascular procedure went smoothly in 84/96 (87.5%) patients (Graph 1), while complications occurred in 12/96 (12.5%). Transient carotid spasm occurred in 6/12 patients. In 2/12, a hematoma occurred at the access site. Transient hemodynamic instability (hypotension and bradycardia) occurred in 2/12 patients. Two out of 12 patients had moderate neurological deficits (i.e. transient loss of vision in one eye). One of 12 patients had iatrogenic rupture of the femoral and iliac arteries. Complications were present in 8/67 (11.9%) males, while in females they were present in 4/29 (13.8%) females. The average amount of heparin applied for anticoagulant action was 5800 IU (maximum amount was 10000, minimum 2500 IU).

Technically successful endovascular procedure was performed in 89.6% of patients, while in 10.4% the

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Table 1. Comparative statistics of comorbidities and other parameters with gender distribution

| Gender/Pol | Male/Muški | Female/Ženski | p |
|------------|------------|--------------|---|
| **No/Br. (Age/Starost (године))** | 67/69.164 | 29/62.448 | 0.0003 |
| **Mean/Standard deviation/Srednja/Standardna devijacija** | 7.470 | 9.276 |
| **Heparin (IU)/Heparin (ij)** | 56/5723.214 | 20/6175.000 | 0.220 |
| **Mean/Standard deviation/Srednja/Standardna devijacija** | 1310.516 | 1640.563 |
| **Duration of procedure (min)/Trajanje procedure (min.)** | 27/73.926 | 11/90.000 | 0.022 |
| **Mean/Standard deviation/Srednja/Standardna devijacija** | 19.729 | 16.125 |
| **HTA** | 47/22 | 0.746 |
| **NIDDM/IZNDM** | 25/2 | 0.173 |
| **IDDM/IZDM** | 3/1 | 0.710 |
| **HLP** | 17/8 | 0.979 |
| **Nicotinism** | 10/6 | 0.691 |
| **COPD/HOBP** | 12/3 | 0.528 |
| **CMP** | 40/11 | 0.082 |
| **Other diseases/Druge bolesti** | 38/14 | 0.590 |
| **Asympt. – Sympt. Asimp – Simptomat.** | 31/14-15 | 0.967 |
| **Left–Right side Leva – desna strana** | 32-35/14-15 | 0.860 |
| **Protection/Zaštita** | 61/26 | 0.868 |
| **Predilatation/Predilatacija** | 4/5 | 0.174 |
| **Complications/Komplikacije** | 8/4 | 0.933 |
| **Preliminary examination Preliminarni pregled** | 5/5 | 0.282 |
| **70 – 90%** | 46/23 | 0.413 |
| > 90% | 21/6 | 0.413 |

Legend/Legenda: HTA = arterial hypertension/arterijska hipertenzija; NIDDM/IZNDM = non-insulin-dependent diabetes mellitus/insulin-nezavisan dijabetes melitus; IDDM/IZDM = insulin-dependent diabetes mellitus/insulin-zavisan dijabetes melitus; HLP = hyperlipoproteinemia/hiperlipoproteinemija; Nicotinism = smoking/pušenje; COPD/HOBP = chronic obstructive pulmonary disease/hronična opstruktivna bolest pluća; CMP = cardiomyopathy/kardiomiopatija; Other diseases/Druge bolesti = other cardiac and vascular diseases/druge kardijalne i vaskularne bolesti; Asympt. Sympt. = asymptomatic-symptomatic disease/asimptomatska – simptomatska bolest; 70–90% = stenosis above 70% and below 90%; > 90% = stenosis above 90%.
procedure failed (Graph 2). In 3/10 patients the procedure failed due to unfavorable separation of internal carotid artery from common carotid artery (a sharp angle), in 2/10 patients due to carotid artery occlusion, in 1/10 due to iatrogenic artery rupture at the access site, in 2/10 due to difficult passage through aortic arch, in 1/10 due to unfavorable morphology of the brachial tree, while in 1/10 patient the procedure failed due to pseudoaneurysmatic dilatation and significant artery stenosis in the petrous region. Failed procedures were present in 5/67 (7.5%) males and in 5/29 (17.2%) female patients (Table 1).

In both male and female patients, the age (p = 0.0003) and duration of the procedure (p = 0.022) showed a statistically significant difference (p < 0.05) (Table 2).

In the groups of patients with symptomatic and asymptomatic carotid atherosclerotic disease, hyperlipoproteinemia (p = 0.015) showed a statistically significant difference (p < 0.05).

Table 2. Comparative statistics of comorbidities and other parameters in relation to symptoms of carotid disease

| Asympt./Sympt./Asimpt./Simptomat. | Asymptomatic/Asimptomatski | Symptomatic/Simptomatski | p |
|----------------------------------|----------------------------|--------------------------|---|
| Age/Starost                      | No/Br. Mean Srednja Standard deviation N Mean Srednja Standard deviation | 45 68.822 8.105 51 65.647 8.802 | 0.070 |
| Heparin                          | 33 5984.848 1481.579 43 5732.558 1355.539 | 0.442 |
| Duration/Trajanje                | 17 81.824 22.269 21 75.952 18.001 | 0.374 |
| Gender (male - female) Pol (muški - ženski) | 31-14 36-15 | 0.967 |
| HTA                              | 33 36 | 0.943 |
| NIDDM/IZNDM                      | 17 14 | 0.389 |
| IDDM/IZDM                        | 3 1 | 0.741 |
| HLP                              | 6 19 | 0.015 |
| Nicotinism                       | 6 10 | 0.583 |
| COPD/HOBP                        | 7 8 | 0.792 |
| CMP                              | 29 8 | 0.060 |
| Other diseases/Druge bolesti     | 28 24 | 0.200 |
| Left–Right side/Leva – desna strana | 20-25 26-25 | 0.664 |
| Protection/Zaštita               | 43 44 | 0.228 |
| Predilation/Predilatacija        | 4 5 | 0.844 |
| Complications/Komplikacije       | 8 4 | 0.246 |
| Preliminary examination          | 6 4 | 0.586 |
| Preliminarni pregled             | 33 36 | 0.943 |
| 70 – 90%                         | 12 15 | 0.943 |

Legend: HTA = arterial hypertension/arterijska hipertenzija; NIDDM/IZNDM = Non-insulin-dependent diabetes mellitus/insulin nezavisna dijabetes mellitus; IDDM/IZDM = insulin-dependent diabetes mellitus/insulin zavisan dijabetes mellitus; HLP = hyperlipoproteinemia/hyperlipopro- teinemija; Nicotinism = smoking/pušenje; COPD/HOBP = chronic obstructive pulmonary disease/chronična opstruktivna bolest pluća; CMP = cardiomyopathy/kardiomapijacija; Other diseases/Druge bolesti = other cardiac and vascular diseases/druge kardijalne i vaskularne bolesti; Asympt. - Sympt. = asymptomatic-symptomatic disease/asimptomatska – simptomatska bolest; 70% - 90% = stenosis above 70% and below 90%; saženje iznad 70% a ispod 90%; > 90% = stenosis above 90%; saženje iznad 90%.
Discussion

The study included 96 patients, 69.8% male and 30.2% female, which is in agreement with the available literature data [10]. The mean age of patients was 67.2 years, which is lower compared to the literature data, where the average age is 75.6 years [1].

The obtained results on the prevalence of HTA, diabetes mellitus, and CMP are in line with the global data [11], while the prevalence of HLP in our patients is significantly lower than in T. Reiff et al. where it was present in 66.6% [10].

In 53.1% of patients, carotid disease was symptomatic, which is consistent with the literature where symptomatic carotid disease was present in 52.2% [12]. Treatment of restenosed artery was present in 26.0% of patients, while in 74.0% of patients the stenosis was primary, which is not in accordance with the available literature data where treatment of restenosed artery was present only in 11% [13]. Significant carotid stenosis of the opposite side from the planned endovascular revascularization was present in 17.7% of patients, which is consistent with the literature [14].

Right carotid stenting was more often indicated (52.1%) compared to the left carotid artery, while the left side was slightly higher in the literature (50.6%) [14]. The endovascular procedure was done without complications in 87.5% of patients, while complications occurred in 12.5%, which is in line with the percentage of complications in the world literature [15]. No patients died during the stent placement, which is not in agreement with the literature data, where death occurred in 0.7% of patients [14]. Technically successful endovascular procedure was performed in 89.6% of patients, while in 10.4% the procedure failed. In the literature data, failed stent placement was reported somewhat less frequently, only in 2.1% [16].

In the groups of male and female patients, age (p = 0.0003) showed a statistically significant difference (p < 0.05). This indicates that the average age of male patients was 69.2 years, while in female patients it was 62.4 years. These data show that the female patients were treated about 7 years earlier than the male patients. However, these data were not found in the available literature.

In the groups of male and female patients, the duration of the procedure (p = 0.022) showed a statistically significant difference (p < 0.05). This indicates that the average duration of the procedure in males was 74 minutes, while in females it was 90 minutes. This information was not found in the available literature.

The comparison of two groups of patients, with symptomatic and asymptomatic carotid atherosclerotic disease, HLP (p = 0.015) showed a statistically significant difference (p < 0.05). This shows that HLP largely accounts for the symptomatology. This data has been found in the available literature [10], which proves that the reduction of HLP by using statins also reduces the consequences of carotid disease.

Conclusion

We concluded that endovascular revascularization has a high success rate in the treatment of atherosclerotic disease of the carotid arteries and it is associated with low perioperative morbidity and mortality.

The analysis of gender-related differences, we concluded that endovascular revascularization lasts significantly longer in female patients, and that the average age is significantly higher in male patients compared to females. We also concluded that hyperlipoproteinemia is a major risk factor for carotid artery disease.

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