Carotid surgery today: an update after 14,000 carotid endarterectomy procedures

Karotidna hirurgija danas: novine nakon 14 000 karotidnih endarterektomija

Djordje Radak*,†‡, Nenad Ilijevski*†, Nenad Djukić*

*Vascular Surgery Clinic, “Dedinje” Cardiovascular Institute, Belgrade, Serbia; †Faculty of Medicine, University of Belgrade, Belgrade, Serbia; ‡Serbian Academy of Sciences and Arts, Belgrade, Serbia

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Introduction

Atherosclerotic lesions of the extracranial part of carotid arteries are one of the most common causes of stroke. The relationship between carotid artery occlusive disease and neurologic function has been recognized for more than 2000 years. According to Rufus of Ephesus (about 100 AD), the term carotid was derived from the Greek word καρός (ka-ros), meaning “to stun, to fall into deep sleep”. The reason for naming the artery was that compressing it causes the loss of consciousness – “deep sleep” 1.

Hippocrates “apoplexy” in 400 BC was the first written trace of human attempt to portray conditions that we know today as transient ischemic attack (TIA) or reversible ischemic neurologic deficit 1. Awareness of carotid arteries disease and surgical attempts to repair them led to the first successful carotid endarterectomy (CEA), performed by Michael DeBakey in 1953 2.

Since then, carotid surgery has developed a lot, so today we have various techniques to detect and treat diseased carotid arteries 1.

Diagnostic improvement

Preoperative imaging plays irreplaceable role in successful treatment of not just carotid arteries, but any organ, as well.

Carotid duplex scan (CDS) represents the first line in the diagnostics of carotid disease. This technology, which combines the acquisition of anatomic and blood flow information, was developed in the 1970s 3. Commercial duplex scanners became available by the 1980s, and the clinical use of CDS rapidly expanded in the past twenty years 4. Modern CDS systems provided high-resolution B-mode ultrasound imaging of tissue and vessel anatomy, including 3D vessel reconstruction and evaluation of atherosclerotic plaque morphology, with detailed assessment of blood flow characteristics 5.

CDS is noninvasive and cost-effective and thus suitable for serial examination because it also reveals natural history of disease, including progression, regression, and response to intervention. In many patients, duplex testing can establish the definitive diagnosis the basis on which CEA or angioplasty can be performed 4. However, the reliability of CDS depends on the expertise of the examiner and the interpreting physician.

When introduced in 1971, computed tomography (CT) scan brought a great improvement in the diagnostics 5. Technological development led to the invention of 4-slice in 1998 and 16-slice multidetector CT (MDCT) scanner in 2002 5, 6. Later, the 256-slice MDCT provided ability to generate “real time” 3D images (Figure 1), for about the same amount of radiation as previous MDCT scanners 5. Also, increasing use of MDCT angiography provided better visualization of the cerebral arteries, leading to an unexpected more frequent detection of unruptured intracranial aneurysms (UIAs) 5.
Early death rates following conventional and eversion carotid endarterectomy

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<thead>
<tr>
<th>The author and the year</th>
<th>Patients (n)</th>
<th>Early death (%)</th>
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<tr>
<td></td>
<td>CCEA</td>
<td>ECEA</td>
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<td>353</td>
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<td>Cao et al. 1998</td>
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<td>Shah et al. 1998</td>
<td>410</td>
<td>1,575</td>
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<tr>
<td>Ballotta et al. 1999</td>
<td>167</td>
<td>169</td>
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<td>Peiper et al. 1999</td>
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<td>475</td>
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<td>Radak et al. 2000</td>
<td>682</td>
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<td>Katras et al. 2001</td>
<td>204</td>
<td>118</td>
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<td>Littooy et al. 2004</td>
<td>125</td>
<td>64</td>
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<td>Markovic et al. 2006</td>
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<td>101</td>
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CCEA – conventional carotid endarterectomy; ECEA – eversion carotid endarterectomy.

Eversion carotid endarterectomy

Although first described by DeBakey in 1959, the modern technique of eversion CEA (ECEA) was introduced in the early 1970s. However, its use became more popular about twenty years later. At the end of the 20th and the beginning of the 21st century, surgeons worldwide began to report better outcomes following ECEA compared to the conventional technique (Table 1).

The majority of studies showed lower incidence of early postoperative death and neurological complications (seven days after surgery) in group treated with eversion technique. Also, incidence of late restenosis (follow-up period 36.4 ± 15.8 months) was much lower in patients treated with ECEA versus conventional CEA (Table 2).

In addition, Gao et al. documented surprisingly lower incidence of postoperative microembolic events in ECEA, compared to the standard endarterectomy.

One of the world’s largest single-center series of ECEA, by Radak et al., compared outcomes in patients operated on between 1991 and 1997 with those operated on in 1998-2004 period of time. The total mortality and morbidity rates and early postoperative complications were lower in the latter group. The clamping time was shorter, as well as was duration of hospital stay. At follow-up, rate of restenosis > 50% did not differ between the groups, but the incidence of < 50% restenosis was higher in the earlier group.

Improved surgical skills, shorter clamping time and better medication therapy led to preferable outcomes in patients operated on between 1998 and 2004.

As a technique, ECEA offers lower restenosis rates and...
Table 2

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<tr>
<th>Author and year</th>
<th>Patients (n)</th>
<th>Late restenosis (%)</th>
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<tr>
<td>Marković et al. 2006</td>
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CCEA – conventional carotid endarterectomy; ECEA – eversion carotid endarterectomy.

Table 3

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<tr>
<th>Trial and year</th>
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<th>Primary endpoint</th>
<th>Follow-up period</th>
<th>Results (%)</th>
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<td>SAPHIRE 39, 40</td>
<td>334</td>
<td>30-day stroke, MI, death + 1-y ipsilateral stroke, death</td>
<td>1-y</td>
<td>12.2</td>
</tr>
<tr>
<td>2004, 2008</td>
<td></td>
<td>30-day stroke, death</td>
<td>30-day</td>
<td>9.6</td>
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<td>EVA-3S 41, 42</td>
<td>527</td>
<td>4-y ipsilateral stroke + death</td>
<td>4-y</td>
<td>11.1</td>
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<tr>
<td>2006, 2008</td>
<td></td>
<td>30-day ipsilateral stroke, death</td>
<td>30-day</td>
<td>6.9</td>
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<tr>
<td>SPACE 43, 44</td>
<td>1,196</td>
<td>2-y ipsilateral stroke + death</td>
<td>2-y</td>
<td>9.5</td>
</tr>
<tr>
<td>2006, 2008</td>
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<td>120-day stroke, MI, death</td>
<td>120-day</td>
<td>8.5</td>
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<tr>
<td>ICSS 46</td>
<td>1,713</td>
<td>4-y ipsilateral stroke</td>
<td>4-y</td>
<td>7.2</td>
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<td>2010</td>
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<td>30-day stroke, MI, death</td>
<td>30-day</td>
<td>5.2</td>
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<tr>
<td>CREST 47</td>
<td>2,502</td>
<td>4-y ipsilateral stroke</td>
<td>4-y</td>
<td>7.2</td>
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CREST – carotid revascularization endarterectomy vs stenting trial; EVA-3S – endarterectomy vs angioplasty in patients with symptomatic severe carotid stenosis; ICSS – international carotid stenting study; MI – myocardial infarction, n – number of patients; SAPHIRE – stenting and angioplasty with protection in patients at high risk for endarterectomy; SPACE – stent-protected angioplasty vs carotid endarterectomy; y – year.

greater technical ease of performance 16, 25. Also, ECEA has been identified as an independent factor contributing to a better outcome following surgery. 29.

Still, there are certain relative contraindications to ECEA: restenosis after previous CEA, carotid stenosis due to radiation, ipsilateral surgical intervention in the past and lesions above second cervical vertebra 24, 30−33. Therefore, alternative techniques have evolved.

Carotid artery stenting

The endovascular era began, by seeking less invasive alternative to open surgery. First successful results of percutaneous transluminal angioplasty (PTA) of carotid arteries were reported by Matthias 34 in 1977 and Kerber et al. 35 in 1980. Balloon-expandable stents were first deployed in 1989, with improving of stent material and technique over years 36.

Despite the early enthusiasm, the high likelihood of embolic stroke during carotid artery stenting (CAS) remained a major concern. The development of embolic protection devices (EPDs) in the 1990s has lowered the incidence of microembolization and consequent neurologic deficit 24, 36−38.

From the beginning of the modern endovascular period, the procedure has been largely scrutinized. Four main innovations led to dissemination of CAS technique after 2000: routine use of stenting; routine use of EPDs; introduction of new stent materials for carotid endovascular procedures and new antiplatelet drugs 36.

However, the question of CAS as an “equivalent” therapeutic option to CEA still remained. Five large randomized clinical trials were conducted seeking for answers to this dilemma (Table 3).

Except stent protected angioplasty vs carotid endarterectomy (SPACE) and international carotid stenting study (ICSS) (27% and 72%, respectively), in other trials EPDs were used in > 90% of cases. Asymptomatic patients were enrolled in carotid revascularization endarterectomy vs stenting trial (CREST) and stenting and angioplasty with protection in patients at high risk for endarterectomy (SAPPHIRE) trial.

The results implied to a higher perioperative stroke risk with CAS compared with CEA when it is performed in unselected patients with symptomatic or asymptomatic carotid stenosis. The association between older age and increased risk of adverse events after CAS, was reported in CREST, ICSS and SPACE trial 43−47. The low absolute risk of recurrent stroke in CREST suggests that both CAS and CEA are clinically durable 47.
The risk of periprocedural myocardial infarction after CAS was reported with rates half as those of CEA: 1.1% vs 2.3% in CREST, 0.4% vs 0.6% in ICSS and 0.4% vs 0.8% in endarterectomy vs angioplasty in patients with symptomatic carotid stenosis (EVA-3S) trial 41,46,47. CAS should not be considered as an therapeutic option in patients with severe peripheral artery stenosis, aortic arch anomalies, carotid artery kinking/coiling and aneurysm, pre-occlusive lesions of the internal carotid artery (ICA); carotid stenosis longer than 2 cm, calcified, ulcerated or highly vulnerable carotid plaque and chronic renal insufficiency 42. In such cases, open surgery remains the gold standard. Currently, data suggest that with a careful patient and operator selection and improved technology, CAS may be considered as an alternative to CEA 56, 59-64.

Hybrid procedures

Significant atherosclerotic lesions involving carotid bifurcation and the proximal ipsilateral common carotid artery (CCA) or the innominate artery (IA) are uncommon, with the reported incidence of approximately 4.8% 48. However, their treatment remains a great challenge. Standard CEA exposure does not allow repair of the proximal IA or CCA; it could be approached through a median sternotomy, occasionally requiring cardiopulmonary bypass 49. On the other side, the access to skull base-level ICA mandates mandibular subluxation 50. These procedures are associated with a prolonged operative time, increased blood loss and increased morbidity/mortality incidence 51.

In 1996, Diethrich et al. 52 described a new, hybrid technique for simultaneous treatment of carotid bifurcation and proximal lesions. This procedure consisted of surgical exposure of carotid bifurcation, retrograde stenting of the proximal CCA or IA lesions, followed by CEA.

A meta-analysis by Sfyroeras et al. 53 reported a 30-day periprocedural stroke and mortality rates of 1.5% and 0.7%, respectively. During follow-up, the incidence of restenosis in patients treated with stenting was 3.7% vs 14% in patients that received simple balloon angioplasty, further signaling that proximal lesions should be solved with stent implantation. In order to assure better outcomes in patients that did not receive antplatelet therapy, an increased dose of clopidogrel (450 mg) should be delivered immediately before the intervention 54. Comparing mortality rates of hybrid procedures and open surgical approach (0.7% vs 0.5%-18.7%), stands clear that the hybrid technique made significant breakthrough in treatment of simultaneous lesions 55.

The results of hybrid procedures label that CEA and CAS should not be considered as competitive, but complementary techniques.

Local anesthesia

CEA can be performed using general anesthesia (GA) and/or local anesthesia (LA). LA comprises deep and superficial cervical block. Cervical block anesthesia (CBA) has evolved over the last 15 years with new techniques, novel methods of locating the cervical plexus and new drugs 55-57. Using CBA, neurological function is easily assessed during carotid crossclamping, with predictable haemodynamic control. In patients with significant cardiopulmonary comorbidities or in which GA is contraindicated, LA represents a safe and effective option. Disadvantages of LA include risk of seizure or allergic reaction, discomfort for some patients and anxiety for the operating surgeon 58.

The general anaesthesia vs local anesthesia for carotid surgery (GALA) trial was designed to compare outcomes in patients operated on under GA or LA. The results showed no significant difference in the incidence of stroke, myocardial infarction or death at a 30-day follow up. Adverse cardiovascular events were reported in 4.8% of patients who underwent CEA under GA and 4.5% of patients who underwent CEA under LA. Also, there was no difference in hospital length of stay between the groups 59.

Since the GALA trial, several other studies have also reported subtle differences between GA and LA 55. Referring to the results of these reports, we can say that the efficacy of vascular team looking after the patient is more important than the choice of anesthetic technique itself. Since no data showed predominance of GA or LA, selection of suitable anesthetic method remains to be discussed between the patient, his surgeon and anesthesiologist.

Best medical treatment

The invention of new, potent drugs, led to an idea of creating a novel therapeutic modality for carotid arteries disease, named the best medical treatment (BMT).

One of the most significant improvements has been the aggressive use of antiplatelet therapy, and early studies reported up to 25% reduction in overall stroke rates among patients undergoing CEA 59.

When clopidogrel bisulfate was approved by the Food and Drug Administration (FDA) in 1998 60, a new chapter in antiplatelet therapy has been opened. Addition of a single 75 mg dose of clopidogrel to a regular 75 mg dose of acetylsalicylic acid (ASA), administered the night before CEA, was associated with a significant reduction in postoperative neurological events, without any increase in hemorrhagic complications 61. A study of Sharpe et al. 62 showed a lower incidence of postoperative microembolisation in patients receiving dual therapy, compared to patients receiving only ASA. Also, the need of adjuvant dextran therapy was reduced.

The utility of dual antiplatelet therapy use after CAS has been observed in the management of atherothrombosis with clopidogrel in high risk patients (MATCH) with recent transient ischemic attack or ischemic stroke and the clopidogrel for high atherothrombotic risk and ischemic stabilisation, management and avoidance (CHARISMA) trials 63-65. The benefit of combination therapy was found to be significant in patients with symptomatic carotid disease; conversely, the related risk of bleeding obviated the benefits of treatment in patients with low risk of postprocedural neurologic complications 64,65. A recent study showed that the use of ASA and clopidogrel 4–6 weeks after CAS is suffici-

ent to decrease the risk of ischemic stroke, composite vascular events or death.\(^6^6\).

Apart from antiplatelet agents, lipid lowering drugs have significant role in prevention of major cardiovascular events. Since lovastatin had been commercialized in September 1987, 6 statins, including 2 semi-synthetic statins (simvastatin, pravastatin) and 4 synthetic statins (fluvastatin, atorvastatin, rosuvastatin, pitavastatin) have been introduced\(^6^7\)–\(^6^9\). Statins have both lipid-lowering and anti-inflammatory effects, and have been shown to reduce risk of neurologic events in symptomatic patients and in patients after CEA or CAS\(^7^0\)–\(^7^2\). Furthermore, it appears that the stroke prevention benefits of statins are related to their pleiotropic effects rather than their cholesterol lowering effects\(^5^8\).

Numerous trials and meta-analyses since the mid-1990s, revealed a strong correlation of statin use and reduced stroke risk\(^5^8\),\(^7^3\)–\(^7^5\). In a recent series of 1,566 patients who underwent CEA, at a 30-day follow-up, statins were found to be associated with a reduced incidence of death (0.3% vs 2.1%), stroke (1.2% vs 4.5%) and TIA (1.5% vs 3.6%). A fivefold lower risk of death and a threefold lower risk of stroke was found in statin users group\(^7^6\). In a single-center experience, the incidence of cardiovascular events after CAS was 4% in statin users group\(^7^6\). In a single-center experience, the incidence of cardiovascular events after CAS was 4% in statin users group\(^7^6\). Another large series showed 1.5% vs 4% 30-day stroke/death rates for users and non-users\(^7^7\). In addition, according to multi-center experience, dual antiplatelet therapy and statins with angiotensin-converting enzyme (ACE) inhibitor or beta blocker after CEA or CAS, resulted in a lower incidence of restenosis and adverse postoperative effects (Table 4)\(^1^2\),\(^3^6\),\(^5^8\),\(^7^6\),\(^7^8\).

Recently, there has been an increasing argument to favor BMT as stand-alone treatment in all neurologically asymptomatic individuals, regardless of the degree of carotid stenosis\(^7^8\). This argument deserved serious critical analysis, because the majority of carotid interventions currently performed are in asymptomatic patients. In an effort to address the question of BMT in patients with confirmed carotid disease, Abbott et al.\(^7^9\) performed meta-analyses of 11 trials that included 3724 patients with \(\geq 50\) carotid stenosis. Comparing their results with the results from endarterectomy for asymptomatic carotid artery stenosis (ACAS) trial, they determined that the contemporary risk of ipsilateral stroke and/or TIA did not differ, and possibly were better than the results reported for ACAS in 1995.

The latest data, which provides the most contemporary comparison of BMT alone to BMT plus CEA or CAS, indicate that CEA followed by medical therapy represents the best modality in reduction of cardiovascular events.

### Table 4

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Antiplatelet therapy</td>
<td>Single or dual therapy</td>
<td>Reduces both stroke rate and overall MACEs</td>
</tr>
<tr>
<td>Antihypertensive therapy</td>
<td>Decrease BP by 10 mm Hg systolic/5 mm Hg diastolic or to 120/80 mm Hg. Treat all patients regardless of baseline BP.</td>
<td>Reduces stroke recurrence and restenosis rates</td>
</tr>
<tr>
<td>Lipid lowering therapy</td>
<td>Reduce LDL by 50% or &lt; 70 mg/dL. Treat hyperlipidemia and normolipemic patients with history of stroke.</td>
<td>May be beneficial if applied prior to CEA/CAS</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Total abstinence</td>
<td>Reduces stroke and MACEs rates</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Avoid excessive consumption</td>
<td>Reduces overall MACEs rates</td>
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BP – blood pressure; CAS – carotid artery stenting; CEA – carotid endarterectomy; LDL – low density lipoprotein.

### Conclusion

Overviewing the last 20 years, we stepped forward in understanding, diagnosing and treating carotid arteries disease. More sophisticated preoperative imaging, improved surgical skills, development of new stent materials and techniques and new medication therapy led to better outcome following carotid arteries treatment. Yet, there is a long way to go in order to reduce incidence of peri- and postoperative adverse effects, especially in high risk patients and the elderly population. The saga continues...

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