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Review

Revascularization Methods in Patients with Carotid Stenosis and Concomitant Coronary Heart Disease

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Abstract

A major feature of the atherosclerotic process is its systemic and progressive character. The plaque pathogenetic mechanisms, morphology, evolution, and predilection site (bifurcation zones) determine the frequent coincidence of carotid and coronary atherosclerosis in the same patient.

The present overview chronologically traces the history, effectiveness, and benefit of surgical and continuously improving interventional carotid revascularization. It thereby analyzes the indications, results, and complications based on a number of randomized clinical trials, industry-sponsored registries, and large single-center series in the last 3 decades. Carotid endarterectomy (CEA) and percutaneous carotid angioplasty (CAS) have evolved from 'dubious' procedures to a modern strategy resulting in a significantly lower incidence of stroke and death compared to medical treatment only. Although almost every second patient with carotid stenosis and indications for CAS has coronary atherosclerosis, studies on therapeutic modeling in such a combination are few, showing controversial results. Having both CHD and CS doubles the risk of myocardial infarction, stroke, HF, and death. An isolated revascularization approach compromises the results of therapeutic strategies and worsens patient survival. The high risk associated with coronary heart disease in CAS and CEA is a fact and minimization requires both an individualized and uniform stepwise revascularization strategy.

Keywords

carotid stenosis, coronary disease, carotid stenting, CAS

INTRODUCTION

Atherosclerotic cardiovascular disease (CVD) is the leading cause of morbidity, mortality, and disability worldwide. An estimated 16.7 million people die annually from CVDs, with CHD accounting for 7 million deaths and stroke – 6 million, which is 38% of the total mortality.[1] In the United States, 500,000 people suffer a stroke and 150,000 die each year, and about 2,600 die every day from CVD which means that CVD results in an average of 1 death every 34 seconds.[2] In Europe, cardiovascular disease accounts for one in every two deaths (49%), or around 4.35 million deaths.[3] These statistics are even more concerning for Bulgaria: CVD mortality is over 67%, which implies that two out of every three patients suffering from CVD die from the same cause, which is greater than all other causes combined. According to the National Center of Public Health and Analysis, about 82000 cases are registered annually at the SME, with a mortality rate of 270.1/100,000 for men and 265.1/100,000 for women.[4] The incidence increases with age, being 40.4/1000 in the population from 40 to 49 years of age and 63/1000 in the population between 65 and

75 years with a clear predominance of males. Of all cerebrovascular disease cases, about 35,000 are due to ischemic stroke, with 20% fatalities and 10% of survivors severely disabled.[5] The disease is the most common cause of epilepsy and the second most common cause of dementia and depression in adults. The annual cost of diagnosing and treating cerebrovascular illness is approaching and has already surpassed $45 billion.[6] Despite considerable advances in early diagnosis, therapy, and extensive monitoring of the atherosclerotic process, as well as a falling trend in CVD and cerebrovascular disease mortality in developed countries, increased life expectancy contributes to growing morbidity and financial expenditures.

Carotid atherosclerosis

Carotid atherosclerosis is among the leading causes of neurological morbidity and mortality. About 87% of strokes are ischemic with 30% of them being caused by carotid atherosclerosis. Depending on the size of the atherosclerotic plaque, it causes stenosis and/or thrombosis. Thromboembolism from stenosis of 50% -99% is the cause of approximately 10-15% of strokes, and the relative risk increases markedly in stenoses above 75%.[5] According to data from studies and meta-analyses, the incidence of carotid stenosis above 50% among the general population is 3.9%–4.2%, and in men over and under 70 it is 4.8% and 12.5%, respectively. In women of the same age, it is 2.2% and 6.9%, respectively, increasing tenfold over the age of 80.[7] Longitudinal studies have shown progression of high-grade >70% asymptomatic carotid stenosis to thrombosis in 29% of patients, with 60% becoming symptomatic.[5] This can be illustrated with the results of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST): in symptomatic carotid stenoses >70%, the risk of ipsilateral cerebral infarction in the next 2 years is 26% and reaches 30% for a period of 10 years.[8,9] Asymptomatic carotid stenoses >50% with or without other signs of atherosclerosis are considered equivalent to coronary heart disease.[5]

In clinical practice, the risk of complications is determined by the degree of stenosis and symptomatic status: "asymptomatic/symptomatic stenosis" (without and with complaints for the previous 6 months), clinically significant (narrowing over 50%) and "hemodynamically significant" (over 70%) in 2 projections. The latter leads to a decrease in blood pressure after the stenosis, increased risk of thrombosis, and significant cerebral ischemia, especially in the absence of intracranial blood flow.[10]

Carotid revascularization – from a 'dubious' procedure to a generally accepted modern strategy

The first successful carotid endarterectomy (CEA) was performed by De Bakey in 1953. Initial experiments with percutaneous carotid revascularization on animals date back to late 1970s, and the first clinical reports of its effectiveness date back to the early 1980s. Until the early 1970s, the methodology was considered a 'fake, even deceptive' treatment. On the other hand, the goal of interventional angioplasty is not to remove the plaque, but to stabilize it by reducing the embolic risk and increasing the caliber of the ICA. The main weakness of the methodology – distal cerebrovascular embolization has been largely overcome by J. Theron (1990) with the introduction of distal protection systems. In 1994, the first data on successful carotid angioplasty with stent implantation were published.[11] Targeted trials began in the end of the twentieth century, not only demonstrating the applicability and effectiveness of carotid angioplasty but also stimulating the improvement of the methodology itself. The two main innovations tested – devices for distal embolization protection (EPD) and self-expandable carotid stents make carotid stenting a modern alternative to CEA.

Studies in symptomatic carotid stenosis

Initially, randomized clinical trials (RCTs) compared the results of CEA with drug therapy. The main advantages of CEA over drug treatment were proven by the iconic RCTs of 1991 and 1998: NASCET, ECST, Veterans Affairs Cooperative Study (VACS) and some meta-analyses.[12] The analysis of data on symptomatic patients proves superiority of revascularization over drug therapy in stenoses >70% and absence of benefit in stenoses <50%. In the medical treatment arm, there was higher incidence of late strokes especially at age >75 years, symptoms in the last 14 days, in men, hemispheric manifestations, concomitant diseases, eccentric or increasing stenosis, contralateral occlusion, tandem intracranial stenosis and intracranial insufficiency. A relationship was established between the degree of stenosis, the time of CEA, and the reduction of the absolute risk of stroke (ARR)[13] (**Table** 1).

Table 1. Carotid stenosis, revascularization and reduction of the risk of stroke (NASCET and ECST meta-analysis)

Degree of stenosis	CEA until day 14	CEA between 2 and 4 weeks	CEA between 4 and 12 weeks	CEA after 12 weeks
50-60%	14.8%	3.3%	2.5%	CEA does not prevent stroke
70-99%	23%	15.9%	7.9%	7.4%

* In females, the benefit of CEA is evident only up to the 4th week.

The early risk of stroke in patients with ISA 50%–99% stenosis varies: 5%–8% in the first 48 hours, 17% until 72 hours, 8%–22% on day 7, and 11%–25% on day 14.[13] According to the UK National Audit, in 23,235 patients with CEA and a similar German study, the incidence of

death/stroke up to 48 hours was only 3.7%, and after 48 hours it was ≤2.3%.[14] However, opposite results were published for 2596 patients in the Swedish Registry: in CEA performed within 48 hours, 11.5% of patients died or had a stroke; however, the procedural risk was as low as 5% after 48 hours.[15] The numerous RCTs on a huge cohort of patients followed for a period of 5 to 10 years lead to the conclusion that CEA is a safe procedure with reliable benefits if performed in the first 7 days after TIA/stroke.

Studies in asymptomatic carotid stenosis

According to the Asymptomatic Carotid Surgery Trial (ACST) and the Asymptomatic Carotid Atherosclerosis Trial (ACAS), the incidence of fatal/disabling stroke in patients with asymptomatic >60% carotid stenosis was 6.1% in the drug arm, compared to 3.5% in CEA (p=0.004), respectively 5.1% vs. 11.0% (p=0.0001) at the 5 year mark, with the 10-year risk of any stroke being 13.4% vs. 17.9% (p=0.009). There was no significant relationship between the degree of stenosis, contralateral occlusion, and the risk of subsequent stroke in men.[16] Another fact emerges in a meta-analysis of 41 studies: the incidence of ipsilateral stroke with 50%–69% and 70%–99% stenosis was similar – 1.9/100 person/year and 2.1/100 person/year, as before 2000 it was 2.3/100, and in the period from 2000 to 2010, the same equaled 1.0/100 (p<001). It is important to note that in the asymptomatic population, the early risk associated with revascularization persists for up to 2 years after CEA, while in the drug arm, the risk of stroke is constant. These data not only demonstrate the advantage of CEA over drug therapy, but also highlight the need for elective CEA in asymptomatic stenoses above 70% with increased risk or for rapid carotid revascularization after the index event[17] **(Table 2)**.

Table 2. Criteria for increased risk of stroke in patients with asymptomatic carotid stenosis and drug treatment

Clinical criteria	Contralateral stroke/TIA
Imaging	Ipsilateral asymptomatic stroke
Ultrasound imaging	Stenosis progression >20% Spontaneous embolization in transcranial Doppler studies Lower cerebrovascular reserve Large plaque >40 mm^2 Increase in the size of the hypoechogenic zone
MRA	Plaque hemorrhage Lipid rich necrotic core

A significant disadvantage of the studies is the systematic exclusion of patients with concomitant diseases, anatomical deviations, and increased surgical risk. This makes comparison between the results of the individual RCTs difficult. For example, in a CEA registry of more than 3000 patients, it was found that 7.4% of patients with concomitant diseases (severe coronary heart disease, COPD and CKD) were more likely to suffer a stroke, MI or die compared to a risk of 2.9% for similar events in the non-comorbid group.[18]

Percutaneous carotid angioplasty

Given the outcomes of CEA, percutaneous carotid angioplasty/carotid artery stenting (CAS) with its most modern technical capabilities – EPD and self-expandable carotid stents was rapidly put to practice. When it comes to choosing the best option for carotid revascularization, RCTs have been comparing CAS to CEA for almost 30 years. The main differences result from the frequency of periprocedural complications, while early and late adverse events (stroke, heart attack, death) are not taken into consideration. Initially and almost as a rule, significant superiority of CEA was reported, especially when the procedure in the endovascular arm was balloon angioplasty. Protection systems and self-expandable carotid stents were not yet available, and the incidence of restenosis was significant. One such example is the CAVATAS study, now only of historical value, which became the prerequisite for the authorization of the first self-expandable carotid stent Precise/Cordis by the FDA.

CAS in patients at high surgical risk

The indications for CAS and CEA overlap significantly: symptomatic patients with carotid stenosis ≥50%, asymptomatic patients with stenosis of 70%–80% and, above all, comorbidities or anatomical features of the carotid artery. In contrast to the CEA, CAS results in high-risk patients were reported by single-center series, national registries, and only one randomized clinical trial. In the largest of these, EXACT (N=2145) and CAPTURE 2 (N=4175), an independent neurological assessment at day 30 reported mortality of 0.9% in both studies and 3.6% and 2.[19] The incidence of stroke from a number of CAS registries with distal protection ranged from 3.4% to 6.9%. Data from the other 2 registries in patients at high surgical risk and carotid stenting with proximal protection was below the limit of 3% (MO.MA): the incidence of stroke on day 30 was 2.5% and 2.3%, respectively.[20] It is assumed that this favorable trend is to a large degree due to greater experience in interventions. SAPPHIRE is the only multicenter RCT comparing CAS and CEA in patients with high surgical risk and an important inclusion criterion: an accessible target lesion for both an interventional and surgical approach **(Table 3)**. High surgical risk is defined as clinically significant heart disease, severe lung disease, ICA contralateral occlusion or laryngeal nerve palsy, previous radical surgery or radiotherapy in the neck, restenosis after CEA, and age above 80 years.

SAPPHIRE data provide the strongest support for the role of CAS with distal protection in high-risk patients. Compared to CEA, the total registered events – death, stroke, ipsilar stroke, MI are rare, comparable and with-

Table 3. Comparative data from the SAPPHIRE study

Events	CAS (%)			CEA (%)		
	Day 30	1 year	3 years	Day 30	1 year	3 years
Death	0.6	7.4	18.6	2.0	21.0	21.0
Stroke	3.1	6.2	9.0	3.3	9.0	9.0
MI	1.9	3.0	5.4	6.6	5.4	5.4
Death/Stroke/MI + ipsilateral stroke	4.4	12.2	24.6	9.9	26.9	26.9

out a significant difference at 30 days, at 1 and 3 years. In the CAS arm, MI was significantly less common at similar stroke rates at day 30 and year 3, the same goes for the need for revascularization of the target lesion (0.7% vs. 4.6%; p=0.04), and cranial nerve palsy. (0% vs. 5.3%; p=0.003).

CAS in patients at standard risk

CAS is still being studied in patients at standard risk with quite conflicting results. The results of 5 RCTs (CAS vs. CEA) with over 8000 patients with standard/low risk – ICSS (1500), EVA-3S (900), SPACE (1900), CREST (2500), and ACT I (1540) do not show advantage of CAS over CEA: at day 30, the incidence of stroke and death was 9.6% vs. 3.9% in EVA-3S and 6.9% vs. 6.3% in SPACE, respectively **(Table 4)**.[21]

Subsequent analyses lead to unexpected conclusions due to a number of neglected factors in the study design: suboptimal experience or lack of previous experience of CAS operators (an operator with only 5 previous CAS procedures participated in the EVA-3S study, in ICSS the minimum requirements for operational experience was 50 interventions, only 10 of which had to be in the carotid region), optional use of distal protection devices (used in only 27% of procedures in SPACE), predilation was used only in 17%, and in 15% no dual antiplatelet therapy was prescribed. These significant gaps in the protocols, and especially the lack of sufficient experience, turned out to be the 'Trojan horse' leading to unsatisfactory results in the CAS arms. The reports that there are more new ischemic lesions particularly serious in some centers using EPD are disturbing. This automatically raises the question of 'real harm' from the use of EPDs, due to the likely serious shortage of experience in their application. In the largest trial – CREST including 2,500 symptomatic and asymptomatic patients, evidence of the qualification of CAS operators was introduced as a mandatory requirement for the first time.[22] There was even a training phase in the design, after which an independent audit allowed inclusion in the research team. As a result, every fourth or 116 out of 427 CAS operators were not approved to participate in CREST. In the RCT ACT-1 (2005-2013) including 1453 patients with asymptomatic stenosis and standard procedure risk, the use of EPD was mandatory. The results of ACT-1 reduced the reliability of the data indicating superiority of CEA over CAS, namely: death/stroke – 2.9% vs. 1.7%, death/major stroke – 0.6% vs. 0.6%, death/stroke/heart attack – 3.3% vs. 2.6%.[23] The data from CREST (2000 – 2008) are interesting not because they are similar results up to 30 days, but because they led to the formation of two periods with different results: early – with a frequency of clinical events in the CAS arm of 5.7% and late in which they drop to 1.1%? The only explanation is the improving technique of the research team. In a similar aspect, CREST restores trust in CAS as a real alternative to CEA in patients at standard risk.

Data from 15 registries (1,429,860 SERs and 163,904 CAS procedures in standard-risk patients) also show 'strange variations' in the incidence of stroke/death in CAS – from 0.79% to 4.16%, as in some registries it reaches 10.9%[24] **(Table 5)**.

Other publications note additional findings: while some national registries report a hospital incidence of death/stroke below the allowable 3%, others report more than 5%, and still others show 4 multiple variations in the same hospital, but with operators of different specialties, with little experience and lack of established therapeutic ap-

Table 4. CAS vs. CEA – comparative data

RCT	Stroke %		p	MI %		p	Death %		p
	CAS	CEA		CAS	CEA		CAS	CEA	
CREST									
– total	4.1	2.3	0.01	1.1	2.3	0.03	0.7	0.3	NS
– symptomatic	5.5	3.2	0.04	1.0	2.3	0.08	3	-	NS
– asymptomatic	2.5	1.4	NS	1.2	2.2	NS	0	0	NS
ICSS	7.0	3.3	<0.01	0.4	0.5	NS	1.3	0.5	0.07
EVA-3S	8.8	2.7	<0.01	0.4	0.8	NS	0.8	1.2	NS
SPACE	7.5	6.2	NS	-	-	-	0.7	0.9	NS

Table 5. CAS vs. CEA – comparative data (1998–2012) on 1,756,445 patients by Dua A et al.[25]

Complication	CEA asymptomatic patients	CEA symptomatic patients	CAS asymptomatic patients	CAS symptomatic patients
Number of patients	1583614	162362	7317	3149
Stroke	1.3%	2.7%	1.6%	3.4%
MI	1.5%	1.8%	2.3%	2.3%
Bleeding	2.7%	2.7%	3.4%	3.7%
Death	0.2%	0.3%	0.1%	0.4%
No complications	94.3%	92.5%	93.6%	93.6%

proach.[26] Apparently, poor endovascular experience is a factor compromising the results in a number of RCTs. This necessitates the adoption of indicators for individual assessment based on the CHOICE registry[27]: 1. Baseline volume of CAS procedures; 2. Time from the first CAS to each subsequent; 3. Time from release to retraction of the distal protection device; 4. Volume of CAS procedures in the respective institution; 5. Specialty (cardiology, vascular surgery vs. radiology/neurology).

Technical aspects of CAS

There are criteria for increased difficulty in performing CAS: type III aortic arch, atheroma of the aortic arch, atherosclerotic damage to the external carotid artery, extremely angulated distal part of the ICA, and stenosis of a long section. Distal protection devices are constantly evolving: from the first balloon catheter (circa 1998) to the EPD with continuous antegrade blood flow and embolization protection devices. Although there are no comparative studies between them, some data from CREST and ACT-1[22] show that, in general, the use of EPD by a trained team leads to a reduced incidence of death/stroke (2.1% vs. 4.9%). The current consensus level of recommendation (ESC) for the use of EPD is IIa C.[28]

The era of the traditional comparison of results between CEA and CAS is over. In a recent meta-analysis (2017), Sardar et al. summarized data from 5 RCTs with 6526 patients and a mean follow-up of 63 months: CAS was associated with an increased risk of any type of stroke/death by day 30, especially in patients over 70 years of age, and with reduced risk of periprocedural MI, damage to the cranial nerve, cervical hematoma, and the combined outcome of death, MI, stroke. After day 30 and during long-term follow-up, the two methods show no statistical difference in the rate of complications. CAS has an advantage over CEA in the presence of 'hostile neck' (previous radiation therapy, restenosis), contralateral paralysis of the recurrent laryngeal nerve, difficult surgical access (very high carotid stenosis, proximal stenosis of the common carotid artery), with increased risk of perioperative MI, and last but not least, with the opportunity of immediate interventional treatment in case of intraprocedural neurological deficit.[29] Thirty years of research with comparable results have not only led to consensus-based rigorous indications for both procedures and operational protocols, but have also called into question the need to compare CEA and CAS in modern times. CAS has become a viable alternative with an ever-increasing relative share, especially after the CREST trial. Another significant conclusion drawn from all studies and meta-analyses is that the long-term results of carotid revascularization are compromised not by neurological complications but by existing coronary heart disease, other cardiac pathology, and patient comorbidity.

Carotid and coronary heart disease

The main feature of the atherosclerotic process is its systemic and progressive nature. The same pathogenetic mechanisms, the morphology of the plaque, its evolution, and the predilection bifurcation zones determine the frequent combination of carotid and coronary atherosclerosis. Affected patients are at twice the risk of cardiovascular accidents, MI, stroke, and cardiac death. The combination compromises the results of therapeutic strategies, worsens the prognosis and survival. Simultaneous involvement of the carotid and coronary arteries in the atherosclerotic process has not been the subject of RCTs and data vary widely in literature. According to Kallikazaros et al. the incidence of carotid >50% stenosis increases from 5% in one-vessel coronary disease to 40% in the presence of left main stenosis.[30] Concomitant coronary heart disease is found in 66% to 77% of patients with CAS, and in 37% of patients with CEA, with MI being the most common cause of death after CEA.[31] According to Hofman et al., the incidence of major coronary artery stenosis or previous cardiac bypass surgery is 77.1% among patients with indications for CAS.[31] Every second patient (49.1%) with CAS in the report of Enomoto et al. suffers CAD as well.[32] The majority of these patients are indicated or have undergone PCI or CABG. The varying incidence of carotid atherosclerosis in patients with known coronary heart disease is due to the studied population; on the other hand, patients with asymptomatic carotid stenosis have a higher risk of MI than of stroke. According to a representational study of the Bulgarian population, the incidence of CABG in patients with carotid stenosis revascularized by CAS and CEA is 85.5% and 75.5%, respectively.[33] A meta-analysis of 11391 pa-

tients with asymptomatic carotid stenosis >50% turned out of great significance: 63% of late deaths were related to cardiac events, with a mean cardiac-related mortality rate of 2.9% per year; the risk of cardiovascular death (2.29% vs. 1.52%, p=0.002) as well as of death/MI/stroke (6.03% vs. 4.29%, p<0.0001) was significantly higher compared to patients without carotid stenosis. The 5-year total mortality was 23.6% in carotid atherosclerosis, which is three times higher than the mortality in the general population for the same age and sex. In 62.9% mortality is due to MI or HF, due to underlying coronary heart disease.[34] Carotid stenosis in itself is a predictor of the need for CABG. In the first years after a stroke, the most common vascular event is a new stroke. At year 5, however, cardiac deaths were twice as common as recurrent stroke.[35] This cohort of patients was followed for cardiovascular events, depending on the presence or absence of CABG: the 2-year Kaplan-Meier prognosis for vascular events was 3.4% in patients without coronary heart disease, 16.2% in asymptomatic coronary stenosis >50%, and 24.1% in patients with pre-existing coronary heart disease. In a long-term follow-up in a retrospective study (2002–2014) of 194 patients with carotid stenting and coronary angiography, the incidence of cardiac death was 12.9% and that of neurological death was 5.7%.[36] In the SAPPHIRE study, the incidence of cardiac death at year 3 was 9.0% versus 1.8% for neurological death. The CREST results in both arms (CAS and CEA) documented 11.3% prevalence of cardiovascular mortality at year 4.[21] The conclusion is self-evident: cardiovascular risk in patients with carotid stenosis is extremely high due to doubled incidence of CABG than in the general population of stroke patients.[32]

Diagnosis of concomitant coronary artery and carotid disease

The indications for coronary angiography prior to revascularization in asymptomatic carotid stenosis are controversial. In symptomatic and significant carotid stenosis after a recent stroke/TIA, a non-invasive test for coronary artery disease is recommended according to the AHA. As already indicated by RCTs, the risk of MI (p<0.0001) or subsequent cardiac death when there is only an increase in the level of cardiac biomarkers during CEA (p=0.005) is significantly higher.[37] The high periprocedural risk of MI during CEA leads to the idea of preoperative coronary angiography for selection of high risk patients, who are to undergo coronary revascularization before carotid intervention. The analysis of RCT by Illuminati et al. in patients with CEA without a history of coronary heart disease is indicative in this respect.[38] Patients were randomized into 2 groups – with and without coronary angiography prior to surgery. In 39% of patients, coronary angiography revealed clinically significant coronary artery disease that required PCI prior to CEA. No peri- and post-operative MI was observed in this group compared to 2.9% of MI in the other arm (p=0.01); at year 6, the incidence of MI was significantly lower (1.4% vs. 15.7%; p<0.01) and overall survival was significantly higher (95% vs. 90%; p<0.01). PCI delayed CEA by an average of only 4 days (1 to 8 days), but there was no record of neurological events (all patients were on dual antiplatelet therapy). According to the same authors, preliminary coronary angiography is the only independent variable that not only predicts the occurrence of postoperative coronary ischemia, but also reduces 4 times the probability of cardiac ischemia after CEA. In patients with symptomatic or asymptomatic carotid disease, the presence of CABG increases the risk of vascular cardiocerebral complications during long-term follow-up. Preliminary coronary angiography in such patients is an official Class IIb recommendation.

Complex revascularization in patients with carotid stenosis and CABG

The idea of coronary revascularization in the presence of atherosclerotic changes in other vascular areas subject to surgery has a long history. Forty years ago, Hertzer et al.[39] were the first to demonstrate the benefit of coronary revascularization prior to major vascular surgery in a population of patients with a high incidence of coronary artery disease: 60% had one or more coronary arteries with >70% stenosis and 18% suffered severe three-vessel disease. Such complex behavior raises serious questions about the risk-benefit ratio and has many opponents. Despite reasonable remarks on patient selection in 2 studies CARP (Coronary Artery Revascularization Prophylaxis) and DECREASE-V (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study Group)[40], no reliable perioperative and long-term benefit of pre-surgical coronary revascularization was demonstrated. In contrast, in the DECREASE-V, a group of 49 patients showed disturbing perioperative and 1-year mortality from 11% to 22%, which has had a serious negative impact worldwide. In 2009, in a prospective study, Monaco et al. refuted the negative trend and demonstrated that routine preoperative coronary angiography and subsequent selective PCI provide better long-term and event-free survival for patients in need of vascular surgery. As already mentioned, and in contrast to the above data, the results of all RCTs and meta-analyses show unanimity: CABG and cardiac pathology compromise early and long-term outcomes in patients with CEA/CAS indications, which requires one-step or gradual complex revascularization. Optimal revascularization behavior in patients with significant carotid and coronary disease is still controversial due to the lack of RCTs. Four possible interventional strategies are applied – simultaneous or stepwise CABG and CAS, CABG and CEA, PCI and CEA, and PCI and CAS. However, the results are very different: the risk of stroke in synchronous CEA and CABG doubles to 3.9%, compared with 1.7% in isolated CABG.[41] In a review of 97 studies with 8972 patients treated with CEA and CABG, Naylor et al. reported the highest risk of stroke/death in simultaneous revascularization and the lowest in the step-by-step approach. In the analyzed studies, regardless of whether CEA and

CABG were performed simultaneously or one after the other, the overall incidence of stroke, death, or MI was 10.2%–1.5% on day 30.[42] In the SHARP study, with concomitant CAS and CABG, risk is much lower: by day 30, the death rate/stroke/ MI was 4%, and increased by 3% by the end of the year.[43] In a registry of 27,084 patients comparing CAS-CABG with CEA-CABG strategies, the incidence of postoperative stroke was 2.4% vs. 3.9% (p<0.001), the stroke/death ratio was respectively 6.9% vs. 8.6% (p=0.1) and hospital mortality was almost equivalent, namely 5.2% vs. 5.4%.[44] According to Randall et al. and Van Der Heyden et al., if CAS is performed before CABG, dual antiplatelet therapy will result in CABG delay of at least 4 weeks with an increased risk of MI (0-1.9%).[45] According to Versaci et al., the CAS strategy immediately before CABG yielded promising results with a low incidence of death/stroke. A hundred and thirty-two patients treated with CAS and CABG on the same day had an in-hospital stroke rate of 0.75% and a 5- and 10-year period free of neurological events of 95% and 85%, respectively.[46] An analysis of 350 patients with carotid revascularization up to 90 days before CABG showed similar results: CEA followed by CABG had the worst results of interstaged MI; after 1 year, patients treated with delayed CEA or combined CEA and cardiac surgery had a 3-fold higher incidence of all major adverse events than patients treated with CAS and cardiac surgery. In a Bulgarian cohort of 513 patients with significant carotid and coronary disease who underwent staged or single-stage surgical revascularization, 2.14% neurological complications (ipsilateral ischemic stroke) and 0.78% mortality were reported, again leading to the conclusion that there is no universal approach.[47] In recent surveys by the teams of Kumar S (2020), Manthey S (2020), and Tzoumas A (2020), the results and opinions are similar – a comprehensive revascularization strategy is required in the presence of underlying significant coronary heart disease.[48-50]

CONCLUSIONS

There are different revascularization strategies in patients with concomitant carotid and coronary disease – percutaneous, surgical, and hybrid. It is difficult to determine the 'ideal' approach by direct comparison due to different anatomical and clinical criteria. PCI has demonstrated at least equivalent results to CABG in terms of death/stroke/MI and is the primary method of revascularization in patients with unstable hemodynamics, acute coronary syndrome, multiple comorbidities, and high surgical risk. The adoption of CAS and CEA as competing strategies for carotid revascularization is counterproductive. It is much more appropriate to perceive these two strategies as complementary with strict criteria on the necessity of revascularization. The high cardiac risk in CAS and CEA and concomitant coronary disease is a fact. The same could be minimized through complex treatment. The definition of a clear, individual, and uniform revascularization strategy is possible in RCTs with improved design, including other variables with proven predictive significance for cardiovascular and cerebrovascular atherosclerotic diseases.

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Методы реваскуляризации у больных с каротидным стенозом и сопутствующей ишемической болезнью сердца

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Резюме

Важнейшей особенностью атеросклеротического процесса является его системный и прогрессирующий характер. Механизмы патогенеза бляшек, морфология, эволюция и локализация предрасположенности (зоны бифуркации) определяют частое совпадение каротидного и коронарного атеросклероза у одного и того же больного.

В настоящем обзоре в хронологическом порядке прослеживается история, эффективность и преимущества хирургической и постоянно улучшающейся интервенционной реваскуляризации сонных артерий. Таким образом, в нём анализируются показания, результаты и осложнения на основе ряда рандомизированных клинических испытаний, реестров, спонсируемых промышленностью, и крупных одноцентровых серий за последние 3 десятилетия. Каротидная эндартерэктомия (КЭА) и чрескожная каротидная ангиопластика (КАП) превратились из «сомнительных» процедур в современную стратегию, приводящую к значительно более низкой частоте инсульта и смерти по сравнению с только медикаментозным лечением. Хотя почти каждый второй пациент с каротидным стенозом и показаниями к КАП имеет коронарный атеросклероз, исследования по терапевтическому моделированию при такой комбинации немногочисленны и показывают противоречивые результаты. Наличие как ИБС, так и КС удваивает риск инфаркта миокарда, инсульта, СН и смерти. Изолированный подход к реваскуляризации ставит под угрозу результаты терапевтических стратегий и ухудшает выживаемость пациентов. Высокий риск, связанный с ишемической болезнью сердца при КАП и КЭА, является фактом, и для его минимизации требуется как индивидуализированная, так и единая стратегия поэтапной реваскуляризации.

Ключевые слова

каротидный стеноз, ишемическая болезнь сердца, каротидное стентирование, КАП