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Review Article

Management of significant atherosclerotic carotid artery disease: review of literature

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ABSTRACT

Stroke is the third leading cause of death and disability in the world. Carotid artery stenosis due to atherosclerosis accounts for 20 to 30% of all strokes. The patients can be asymptomatic or present with a transient ischemic attack or stroke. Diagnosis is based primarily on imaging modalities like carotid Doppler, CT (Computed tomography) angiogram, MR (Magnetic resonance) angiogram or DSA (Digital subtraction angiogram). Treatment options include optimal medical therapy, carotid endarterectomy-touted as the gold standard for treating significant carotid stenosis; and carotid artery stenting, whose safety and efficacy have undergone significant improvements due to technological advances in the field. We presented a review of the literature outlining the various aspects of atherosclerotic carotid stenosis and the findings of several randomized controlled trials conducted to settle the debate between endarterectomy and stenting for carotid stenosis.

Keywords: Atherosclerosis, Carotid artery disease, Carotid endarterectomy, Carotid artery stenting, Randomised controlled trials

INTRODUCTION

Stroke is the third leading cause of death and disability in the world.[1] Extracranial carotid artery disease accounts for 20-30% of all strokes.[2] Intracranial carotid disease accounts for 5-10% of strokes.[3] Carotid artery stenosis is due to atherosclerosis. As atherosclerosis progresses, the atherosclerotic plaques may rupture, resulting in the formation of thrombus and arterial occlusion or dislodgement of materials from the plaques, which block the smaller branches of the carotid artery.

Carotid stenosis (CS) can be an incidental finding, or can manifest as Transient ischemic attack (TIA), or ischemic stroke. Approximately 5-10% of the population, 65 years or older have asymptomatic stenosis of 50%, or higher.[4,5] This is most eminent in patients with an abdominal aortic aneurysm (12%) and peripheral arterial disease (15%).[6] The risk of stroke rises with the degree of stenosis.[7] In asymptomatic disease, the incidence of stroke is less than 1% for ≤80% stenosis, but rises to 4.8% per year for CS greater than 90%.[6] CS greater than 50% is considered significant.

EPIDEMIOLOGY

Atherosclerosis of the carotid artery mainly occurs at the carotid bifurcation. The Internal carotid artery (ICA) ostium is primarily affected. The intracranial internal carotid artery and its branches are less affected by atherosclerosis. Prevalence is high in individuals with risk factors for acute stroke (60%) and cardiac disease (18%).[8]

The prevalence of asymptomatic moderate (50-69%) CS in the general population varies between 0.2% in men aged <50 years to 7.5% in men aged ≥80 years.[7] In women, the prevalence varies from 0 to 5%. Weerd et al

noticed that the prevalence of asymptomatic severe (≥70%) CS fluctuates from 0.1% in men <50 years to 3.1% in men aged ≥80 years.[7] In women, this prevalence ranged from 0 to 0.9%. They concluded that the prevalence of asymptomatic severe CS varies between 0-3.1%. Around 15-33% of the patients with extracranial CS can also have intracranial CS.[9,10]

Reports indicate that asymptomatic CS is high in patients with peripheral arterial disease.[11-13] Mathiesen et al noticed that the frequency of CS was greater in males than in females (3.8 vs 2.7%).[14] CS was associated with peripheral arterial diseases, cerebrovascular disease and Coronary artery disease (CAD). Additionally, with each 10% escalation in the extent of CS, the risk of cerebrovascular events rises by 26%. Prevalence of CS is high in peripheral vascular disease. The association of CS with CAD rises with the number of the affected coronary arteries.[15-17]

PATHOGENESIS OF CAROTID STENOSIS

Development of atherosclerosis causes progressive thickening of the arterial wall and narrowing of the carotid lumen, leading to CS. Carotid plaques consist of a fibrous cap covering a lipid core with inflammatory infiltrates.[18] A typical structure consists: (a) fibrous cap contains smooth muscle cells, few leukocytes, connective tissue (proteoglycans, collagen fibrils, elastin), and a basement membrane; (b) a cellular area composed of a mixture of T lymphocytes, macrophages and smooth muscle; (c) deep necrotic core containing cholesterol crystals, lipids, cellular debris and calcium deposits; and (d) a plaque can be stable and asymptomatic, be a source of embolisation. Calcification of plaque is a marker of plaque stability.[19] Asymptomatic plaques are less inflamed and more calcified than symptomatic plaques.[20] Rupture-prone carotid plaques are labelled vulnerable or unstable, characterised by thin cap with a large lipid core, active inflammation, superficial platelet aggregation fissures with endothelial denudation.[21] They are more prone for thromboembolic events.[22]

Vessel geometry and fluid dynamics play an important role in atherosclerosis.[23,24] Hemodynamic forces play a role in the localisation of intimal thickening. In both *in vitro* and *in vivo* studies, low-shear conditions and disturbed flow produce endothelial dysfunction.[23-25]

MECHANISM OF ATHEROSCLEROSIS

Reactive oxygen species (ROS) increase the expression of cell adhesion molecules. Monocyte adherence to endothelial cells is mediated through adhesion molecules. Low-density lipoprotein cholesterol (LDL-C) is mildly oxidised to Minimally modified LDL (MM-LDL), which stimulates endothelial and smooth muscle cells to produce Chemoattractant protein-1 (MCP-1).[26] MM-LDL is further oxidised to fully Oxidised LDL (OX-LDL).[27] MCP-1 and OX-LDL accelerate the migration of monocytes to the subendothelial area.[28-30] OX-LDL is a ligand for the scavenger receptor expressed in monocyte differentiated into tissue macrophage.[31,32] This monocyte/macrophage differentiation is facilitated by the release of Monocyte colony-stimulating factor (MCSF) from endothelial cells under the influence of mmHg-LDL.[26] The differentiated macrophage develops receptors for OX-LDL, which receptors take up to produce foam cells. Foam cells also generate ROS.[33]

Macrophages generate a host of growth-regulating molecules and cytokines that affect neighbouring cells. Gene expression and transcription in the smooth muscle cells could result in smooth muscle cellular proliferation and migration, synthesis of connective tissue and its matrix, migration of monocytes and formation of foam cells that results in the development and progression of atherosclerosis.[18]

CLINICAL FEATURES

Headache, loss of balance or dizziness, weakness in one or more limbs, loss of vision (in one or both eyes), sudden weakness or numbness in the face or limbs (often on just one side of the body), aphasia or carotid bruit.

Carotid disease is culpable for roughly 50% of all TIAs.[34] Risk of stroke after TIAs is as much as 20% within the first month.[2] If untreated, TIAs can result in stroke within two years. The risk of stroke is high for 10 to 15 years after TIAs.[35]

RISK FACTORS

Similar to those for CAD and other peripheral vascular diseases risk factors are- (a) hypertension; (b) dyslipidemia; (c) diabetes; (d) cigarette smoking; (e) obesity; (f) age; (g) elevated levels of serum C-reactive proteins.

IMAGING MODALITIES

Carotid duplex ultrasound (CDUS) is the initial diagnostic imaging of choice for evaluating the severity of stenosis in symptomatic and asymptomatic patients and also to screen asymptomatic populations at high risk.[36]

Recent advances in Contrast enhanced ultrasound (CEUS) using microbubbles as an intravenous contrast allows improved flow visualization free of artefacts, accurate grading of stenosis, identifying plaque ulcerations, differentiating occlusion from highly stenotic plaques, identify carotid dissection, identifying and grading intraplaque neovascularization and reducing the need for nephrotoxic contrast agents.[37]

When CDUS is non-diagnostic or suggests moderate stenosis (50% to 69%) in asymptomatic patients, Magnetic resonance angiography (MRA), Computed tomography angiography (CTA) or Digital subtraction angiography (DSA) is required before any intervention

begins. Catheter angiography, MRA, or CTA is indicated in addition to CDUS, when evaluating the vessels proximal or distal to the cervical carotid arteries. MRA is inferior CTA in delineating calcium. However, intraplaque hemorrhage, which is a very strong predictor for the risk of stroke is better visualised with MRA. DSA is a gold standard test and is indicated to resolve conflicting results. It is typically reserved for inconclusive evidence of stenosis on less invasive studies or when carotid stenting is planned.[36,38]

MEDICAL TREATMENT

The treatment of CS is directed toward the risk factors. The treatment of asymptomatic patients with CS includes lifestyle changes and the use of pharmacological agents. Optimal medical therapy is indicated for neurologically symptomatic patients with stenosis <50% or asymptomatic patients with stenosis <60% diameter reduction (grade 1, Level of evidence B).[36]

Lifestyle changes

It includes: (a) abstinence from smoking and the use of tobacco products; (b) use of foods low in saturated fats, cholesterol, and sodium; (c) control of body weight; (d) daily physical exercise; (e) reduction of dietary calories intake; and (f) limitation of alcohol use.

Pharmacological agents

Asymptomatic patients with low-grade CAS (less than 50%) should receive intensive medical treatment.

Lipid-lowering agents

To reduce the serum LDL-C to <100 mg/dl. In diabetics and CAD patients, it should be reduced to <70 mg/dl. Statins have pleiotropic effects and positively affect all the stages of atherosclerotic development.[39]

Anti-hypertensive therapy

The blood pressure should be reduced below 140/90 mmHg.[40] Pharmacologic treatment should be initiated in the general population when blood pressure is above 150/90 mmHg in adults 60 years and older or above 140/90 mmHg in adults younger than 60 years. In patients with diabetes and hypertension, treatment should be initiated when blood pressure is above 140/90 mmHg, regardless of age.

Initial antihypertensive treatment should include an angiotensin-converting enzyme inhibitor, angiotensin receptor blockers, thiazide diuretic or calcium channel blocker in the general non-black population or a calcium channel blocker or thiazide diuretic in the general black population. If the target blood pressure is not attained within one month of initiating therapy, the initial dose of the drug should be increased, or a second drug can be added.

Anti-diabetic drugs

The following anti-diabetic agents can be used depending upon the stages and type of diabetes: metformin, sulfonylureas, prandin, pioglitazone, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists and insulin.[18]

CRP lowering drugs

Celecoxib, clopidogrel, statins, carvedilol, antioxidants (α-tocopherol, vitamin C), rosiglitazone, quinapril, ramipril, candesartan, valsartan, calcium channel blockers, and a combination of hydrochlorothiazide and amlodipine.[41]

Antiplatelet therapy

Antiplatelet therapy with aspirin, clopidogrel, or ticlopidine should be instituted in patients with CS.[18]

Antioxidant therapy

The antioxidant therapy in CS has yielded variable results. Azen et al showed that vitamin E supplementation (≥100 IU/d) appears to be effective in slowing the progression of common carotid artery wall Intima-media thickness (IMT) in subjects not receiving lipid-lowering agents.[42] Vitamin C did not affect the IMT. Kritchevsky et al concluded that antioxidant protection carotid atherosclerosis is limited, especially if >55 years of age.[43] Devaraj et al demonstrated that a high dose of RRR-α-tocopherol had no appreciable impact on the carotid IMT.[44] However, biomarkers of oxidative stress were significantly reduced. Karppi et al observed an inverse association between carotid IMT and carotenoids.[45]

Gale et al noticed that antioxidants inhibited the progression of CS.[46] In another study, bilateral CDUS revealed regression of CS in 7 and progression in 2 of the 25 tocotrienol (antioxidant) group of patients. In the control group, 10 of 25 patients showed progression with no reported regression.[47]

It is important to note that statins have antioxidant activity and slow the progression of CS.[48] The variable data could be due to the small doses used. Also, the ineffectiveness of vitamin E in slowing the progression of CS could be due to the conversion of α-tocopherol to α-tocopheroxyl radical, which is prooxidant.[49,50] Vitamin C rapidly reduces α-tocopheroxyl radical to α-tocopherol.[51] Considering this, vitamin E should be combined with vitamin C to have maximum effect.

CAROTID ENDARTERECTOMY

Carotid endarterectomy (CEA) is an open surgical procedure to remove plaque in the common carotid and internal carotid arteries and improve blood flow.

Indications

Indications are as follows: (a) CS ≥50% and history of TIA or ipsilateral stroke; and (b) asymptomatic patients with 70% or more narrowing.[52]

In a CEA was performed ≤2 weeks of symptoms, the number needed to treat to preventing one stroke is five. If it is more than two weeks from the symptom onset, the number needed to treat increases to 125.

Contraindications

It involves- (a) symptomatic patients unfit for an open surgical procedure; and (b) relative contraindications include patients with multiple comorbidities, tracheostomy, prior neck radiation or dissection, large stroke area (risk of cerebral oedema), contralateral carotid occlusion, hemodynamic instability and contralateral laryngeal palsy.

It is important to note that symptomatic women may have increased postoperative complications after CEA compared to men. The outcomes are similar among the sexes in asymptomatic patients.[53]

Preparation

Unless contraindicated, a patient undergoing carotid endarterectomy should be on antiplatelets prior to surgery. Local or general anaesthesia may be used. The patient should be sterilised at the earlobe, neck and jaw.

Technique

Classical/conventional method: The Internal carotid artery (ICA) is clamped proximally and distally to the plaque, temporarily stopping blood flow. The surgeon will open along the long axis of the ICA to locate the ends of the plaque. The clamps are released one by one, and a flexible bypass stent is placed to temporarily shunt the blood around the endarterectomy site while the block is removed.

The artery is then mended with a patch that will widen the vessel lumen, and the bypass stent is removed. Different patch materials are available, including autologous vein, bovine patch, or synthetics (Dacron). After the vessel is repaired, adequate blood flow is confirmed with CDUS or angiography.

Eversion method

The ICA is transected at its origin at the carotid bifurcation. The vessel wall is everted circumferentially around the plaque, and the plaque is divided and removed.

The artery is then repaired in an end to end anastomotic fashion. The pros of the eversion method include no need for patch closure, overall shorter carotid clamping time and total operative time.

Complications

Complications depend on surgeon skill and technique, patient's risk factors, management before or after surgery.[50] Major complications are myocardial infarction, hyperperfusion syndrome, cranial nerve injury (particularly: hypoglossal, vagus, glossopharyngeal, and facial nerves), perioperative stroke, re-stenosis and mortality.

Minor complications include TIA, bleeding, infection, greater auricular nerve injury and dysphagia.

CAROTID ARTERY STENTING

Carotid artery stenting (CAS) is a formidable alternative to CEA.[54]

Indications

Indications are- (a) any patient with a significant CS is a candidate for CAS. Other indications are in patients not suitable for CEA; (b) unstable angina; (c) recent myocardial infarction; (d) left ventricular ejection fraction <30%; (e) congestive heart failure class III/IV; (f) prior irradiation of the neck; (g) contralateral carotid occlusion; and (h) previous CEA with re-stenosis.

Contraindications

It includes- (a) reaction/allergy to contrast;(b) floating thrombus in the carotid artery; (c) excessive calcification of the artery; and (d) severe tortuosity of the carotid artery.

Preparation

An informed consent should be obtained. Antiplatelets should preferrably be initiated five days before treatment. Alternatively, clopidogrel 300 mg (loading dose) should be given 5 hours prior to the intervention. Standard prophylaxis for pre-existing renal insufficiency and/or contrast allergy should be performed.

A baseline neurological examination should be performed. Site of endovascular entry (inguinal is typically preferred over radial) should be sterilised and prepared for access.

Technique

A diagnostic angiogram is performed. Oblique projections may be necessary to visualise the stenosis optimally. The right Common femoral artery (CFA) is preferred for CAS. The brachial artery and the left CFA are alternative sites for access.

The tip of the exchange length guide-wire is placed in the external carotid artery or distal common carotid artery. Unintentional wire contact with the stenosis should be avoided. A sheath with susuitable dimensions is placed (most commonly a 90-cm 6F sheath). We at our institute prefer the 6F Shuttle (Cook Medical Inc.). Intravenous anticoagulation is requisite, and most prefer the use of unfractionated heparin. A 100 units/kg bolus is administered and the dose is titrated to reach an activated clotting time (ACT) of 250 to 300 seconds. Bivalirudin bolus of 1 mg/kg followed by an infusion of 0.2 mg/kg is an effective alternative to heparin.

Embolic protection device (EPD)

The general types of EPD is proximal flow diversion, distal occlusion balloon and distal filter device. All have advantages and disadvantages. The EPD size should be approximately 1 mm more than the ICA to provide optimal embolic protection regardless of the type. Once deployed, angiography is done to ensure adequate arterial wall apposition. A sizable drawback of the distal devices is the lack of protection during the inaugural engagement.

Additionally, in the distal occlusion type, a minority of patients may develop neurological symptoms. The advantage of the proximal devices is that the entire procedure is protected. However, venous access and a larger 9F sheath are also required. Moreover, a minority of patients with insufficient collateral circulation cannot tolerate the occlusion.

Pre-dilation

Pre-dilation of the stenosis is controversial. The postulated benefits include less traumatic stent delivery and reduced need for post-delivery dilation. The potential drawbacks include distal embolisation, plaque rupture and additional time requirements. It can be performed in cases where the stent cannot be advanced safely. 0.5 to 1 mg of atropine may be given prophylactically in case bradycardia ensues.

Stent placement

Self-expanding stents (Nitinol or Elgiloy-based) are used. The stent should be sufficiently long and the stent diameter should match that of the CCA. A second stent may need to be placed if there is incomplete coverage of the stenosis. Atropine should be given in the event of bradycardia.

Post-dilation

Post-dilation is for inadequate stent expansion. Over-dilating the stents should be avoided as they can expand spontaneously over time.[55,56] Routine post-dilation may increase undesired embolic events. A judicious use of dilation may be required for heavily calcified stenoses. Post-dilation is not preferred unless the post-stenting carotid diameter is <5 mm.

EPD removal and check angiogram

The EPD should be evaluated for trapped embolic material before recapture. If the embolic load is minimal, the EPD can be collapsed successfully. An aspiration catheter is used to clear any trapped debris if there is a significant embolic load.

A check angiogram is performed to evaluate residual stenosis, including the cervical ICA and the intracranial circulation, excluding vasospasm or dissection. It is compared with the pre-procedure angiogram. A neurological examination is conducted before access discontinuation. Haemostasis is obtained with manual compression or a closure device.

Complications

It includes (a) induction of vasospasm; (b) arterial dissection; (c) hyperperfusion syndrome; (d) distal embolization; (e) severe bradycardia; and (f) the EPD may engage with the stent margin as it is withdrawn.

SUMMARY OF RANDOMISED CONTROLLED TRIALS

Endovascular vs surgical treatment in patients with carotid stenosis in the carotid and vertebral artery transluminal angioplasty study (CAVATAS)

First reported in 2001. The 30-day death or stroke rate did not differ between the stenting and the surgery group (10% vs 9.9%). A 1-year follow-up showed a greater ipsilateral re-stenosis rate in the endovascular arm p<0.0001). However, there were no differences in the ipsilateral stroke rate between the two groups at the 3-year follow-up.[57] Long-term follow-up results were published in 2009 with a median follow-up of 5 years. Severe (≥70%) re-stenosis was three times more likely in the CAS arm than in the CEA group (p<0.0001). The 5-year re-stenosis incidence was 10.5% in the endarterectomy arm vs 30.7% in the endovascular group.[58]

Endarterectomy vs angioplasty in patients with symptomatic severe carotid stenosis (EVA-3S)

The primary endpoint was death or stroke within 30 days of intervention. The trial was prematurely stopped due to safety concerns in the CAS group. The 30-day relative rate of death or stroke was 2.5 when CAS was compared to CEA (95% CI 1.2-5.1).[59]

The rates of death and stroke were high in the group CAS at 1 year and 4 years follow-up. The stroke rate was markedly increased in patients not treated with an EPD (25% without EPD vs 7.9% with EPD; p=0.03).[60]

Stenting and angioplasty with protection in patients at high risk for endarterectomy (SAPPHIRE)

SAPPHIRE evaluated peri-procedural events in high-risk CEA and CAS patients. The absolute differences in primary endpoints were 7.9% lower with CAS than CEA (32 patients) (p=0.004 for non-inferiority). However, the results were equivalent in the symptomatic group.[61]

Stent-supported percutaneous angioplasty of the carotid artery vs endarterectomy (SPACE)

SPACE was designed to be a non-inferiority study. The primary endpoint failed to demonstrate non-inferiority of CAS to CEA.[62] The 2-year results showed no significant difference in recurrent death or stroke rates between endarterectomy and stenting groups (8.8% vs 9.5%).[63]

Carotid revascularisation endarterectomy vs stenting trial (CREST)

CREST is the largest multi-center randomised trial directly comparing CAS and CEA to date. The participating proceduralist in trial centres (whether interventionalist or surgeon) had to meet rigorous standards to participate in the trial. Both asymptomatic and symptomatic patients were included. The primary composite endpoint was defined as the rate of stroke, death, or MI at 30 days or ipsilateral stroke within four years. There is no statistically significant difference in the rate of primary endpoints between CEA (6.8%) and CAS (7.2%) (p=0.51), neither in the asymptomatic nor in the symptomatic group. However, there were significant subgroup differences in the rate of MI between CEA and CAS (2.3 and 1.1%, p=0.03) and peri-procedural stroke (2.3 and 4.1%, p=0.01). The increased stroke rate was attributed to an increased risk of adverse events in elderly patients with CAS due to more significant vessel tortuosity.[64]

Recently, the 10-year follow-up results of CREST showed no significant differences in the primary endpoint of stroke, death, or MI between the CEA group (9.9%) and the CAS group (11.8%). The 10-year follow up post-procedural stroke rates were also not significantly different between the groups (HR 0.99; 95% CI 0.64-1.52). Moreover, stratification by symptomatic status did not result in any difference between the groups.

International carotid stenting study (ICSS)

ICSS evaluated the long-term efficacy of CAS vs CEA in 1713 patients at 50 centres worldwide. The endpoints of disabling strokes or death did not differ between the two populations (HR 1.06, 95% CI 0.72-1.57, p=0.77). The stroke rates (whether disabling or non-disabling) were more with CAS than CEA (HR 1.71, 95% CI 1.28-2.30, p<0.001). Overall outcomes measured by Modified Rankin Score at one year, five years, or final follow-up did not differ between the two groups, indicating the higher stroke rate in CAS did not result in statistically significant disabling strokes.[65]

Asymptomatic carotid trial-1 (ACT-1)

ACT-1 compared CEA to CAS in asymptomatic patients with CS. The 5-year follow-up results were reported with primary composite endpoints of stroke, MI, within 30 days post-procedure or ipsilateral stroke within a year. CAS was non-inferior to CEA in regards to the primary endpoints; the rate of death or stroke within 30 days was 2.9% in the CAS cohort vs 1.7% in the CEA group. From 30 days to 5 years post-procedure, the ipsilateral stroke-free rate was 97.8% in the CAS group vs 97.3% in the CEA group, with survival rates of 87.1 and 89.4%, respectively. The cumulative 5-year rate for stroke-free survival was 93.1% in the CAS group vs 97.4% in the CEA group.[66]

Second asymptomatic carotid surgery trial (ACST-2)

Published in 2021, ACST-2 is an international multi centric randomised trial. It compared the outcomes of CEA vs CAS in asymptomatic patients with severe CS. 1% had death or disabling stroke procedurally (15 in CAS group, and 18 in CEA group) and 2% had non-disabling procedural stroke (48 in the CAS group and 29 in CEA group). The estimated 5-year non-procedural stroke were 2·5% in each group for fatal or disabling stroke, and 5·3% (CAS) versus 4.5% (CEA) for any stroke (rate ratio [RR] 1·16, 95% CI 0·86-1·57; p=0·33). Combining RRs for any non-procedural stroke in all CAS versus CEA trials, the RR was similar in symptomatic and asymptomatic patients (overall RR 1·11, 95% CI 0·91-1·32; p=0·21). Serious complications were uncommon after competent CAS and CEA, and the long-term effects of these two procedures on fatal or disabling stroke are comparable.[67]

Pros of CEA

It includes- (a) proven short-term and long-term benefits compared with medical therapy in symptomatic patients with significant stenosis; (b) long-term outcomes well characterised; (c) atherosclerotic plaque is removed from the artery and not merely 'displaced', as with CAS); (d) no retention of intravascular foreign body; and (e) avoidance of risks associated with carotid angiography.[6]

Pros of CAS

It involves: (a) less invasive; (b) potentially safer in 'sicker' patients; (c) quicker recovery; (d) lower risk of wound-related complications; (e) lower incidence of cranial nerve injury; (f) ability to treat the entire length of the carotid artery; (g) safety not impaired by 'hostile neck' (prior neck surgery or radiation); and (h) permits rapid visualisation of cerebral vessels and neurologic rescue should distal embolisation occur.[68]

CONCLUSION

Carotid artery stenosis causes a significant burden to the overall health of the patient. The disease can manifest as asymptomatic disease, TIA or ischemic stroke. Depending on the patient phenotype, the best choice for treatment includes, medical management, CEA or CAS. Intimate knowledge of the etiopathogenesis and mechanism of atherosclerosis, along with the flaws and advantages of each approach, is essential for tailoring care to the particular risk profile of a patient. Better designed prospective trials and registries are needed to further delineate the unique indications for new sophisticated management strategies.

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