AUCTORES
Globalize your Research

Journal of Neuroscience and Neurological Surgery
Brandon Lucke-Wold *

Open Access

Review Article

# Update on Management of Symptomatic Carotid Stenosis

**Annu L. Kurian [1], Brandon Lucke-Wold [2*]**

[1] Florida State University College of Medicine, Tallahassee, U.S.A.

[2] Lillian S. Wells Department of Neurosurgery, University of Florida, Gainesville, U.S.A.

***Corresponding Author:** Brandon Lucke-Wold MD, PhD, MCTS, Department of Neurosurgery, University of Florida, Gainesville.

**Received date: December 28, 2022; Accepted date: January 17, 2023; Published date: January 27, 2023**

**Citation:** Annu L. Kurian, Brandon Lucke-Wold (2023). Update on Management of Symptomatic Carotid Stenosis. *J. Neuroscience and Neurological Surgery.* 13(1); DOI:**10.31579/2578-8868/255**



## Abstract

Carotid artery stenosis (CAS) is one of the leading causes of cerebral ischemia and stroke.7 When plaque builds up in the internal carotid artery, it blocks blood flow to the brain. Oftentimes, this condition only comes to light after a patient experiences a stroke or stroke-like symptoms. When this occurs, cholesterol-lowering medications and blood thinners can help to increase blood flow to the brain. However, if the plaque is so large that it severely narrows the lumen of the artery, surgery may be required to restore blood flow to the brain. Patients with severe stenosis can undergo procedures such as carotid endarterectomies (CEA), stenting, and transcarotid artery revascularization (TCAR) for this purpose. In this review, we discuss these procedures and which patients warrant which type of intervention. We look at the pathophysiology of internal carotid artery stenosis and current treatment options, while highlighting emerging treatment options. This review aims to increase understanding of the management of symptomatic carotid artery stenosis as well as provide a groundwork for more innovative treatments.

**Key words:** symptomatic carotid artery stenosis (cas); carotid endarterectomy (cea) ; carotid artery stenting ; transcarotid artery revascularization (tcar)

## Introduction

Carotid artery stenosis (CAS) is one of the leading causes of cerebral ischemia and stroke. [68] This stenosis may or may not be symptomatic. When it is symptomatic it can cause symptoms such as hemiplegia, dysphasia, amaurosis fugax, or vision loss. [7] As of now, one of the best ways to manage symptomatic carotid artery stenosis is by surgical interventions such as carotid endarterectomies (CEA) and transcarotid artery revascularization (TCAR). The other option is angioplasty with stent placement, which can manage symptoms. Lifestyle changes such as quitting smoking or medications such as statins, antiplatelet agents, and antihypertensives can also improve outcomes. [14]

### Evidence Acquisition

Epidemiology of Carotid Artery Stenosis

The prevalence of carotid artery stenosis varies with the population being studied as well as the criteria that is used. When stenosis is less than 50% as measured by carotid ultrasound, the prevalence of carotid artery stenosis was 7% in women and 9% in men. [28] Prevalence of carotid artery stenosis was evaluated to be 11% in individuals with a high risk of atherosclerosis, 18% in those with a high risk of cardiac disease, and 60% in those with a high risk of acute stroke. [69,72] When stenosis is greater than 50%, the prevalence of carotid artery stenosis is 5.9% with coronary artery diseasec [82] When stenosis is greater than 70%, the prevalence of carotid artery stenosis is 2.1% with coronary artery disease. [82] The prevalence of coronary artery disease in patients with carotid stenosis can be as high as 77%. [85] The prevalence of carotid artery stenosis is higher in men than in women, at 8.8% and 5.0% respectively. [99] Additionally, the risk of carotid artery stenosis increased with age, a higher level of low-density lipoprotein cholesterol (LDL-C), a higher systolic blood pressure (SBP), and a higher fasting blood glucose. [99] Lastly, the risk of having a cerebrovascular event increased by 26% for every 10% increase in the degree of carotid stenosis. [56] This shows that coronary artery disease is a key factor in the development of carotid artery stenosis and it plays a vital role in the treatment of it as well.

### Pathophysiology of Carotid Artery Stenosis

Carotid artery stenosis is caused by atherosclerosis, or an area of thickened plaque, on the arterial wall that causes the carotid artery to narrow over time. One of the biggest risk factors for this is hyperlipidemia. When there are increased levels of cholesterol in the plasma, there are changes in arterial endothelial permeability. [13] This leads to lipids, especially LDL-C, getting into the arterial wall. [13] Monocytes stick to the endothelial cells expressing adhesion molecules and move into the subendothelial space, where they transform into

macrophages. [13] LDL particles then become chemoattractants, leading to more cholesterol buildup. [13] This eventually leads to plaque formation, which causes the vessel to narrow.

When this process occurs in the carotid artery, it can lead to serious complications. Even shear stress or disturbed flow through the artery can prompt the aforementioned endothelial cell changes and damage. These changes can be induced by hypertension, dyslipidemia, diabetes mellitus, and cigarette smoking. [40] Smoking is a big risk factor for stenosis. [37] For those who smoke and have diabetes mellitus, the risk is even greater for developing plaques. [38] Endothelial cell dysfunction leads to inflammatory cells accumulating, smooth muscle cells proliferating, and various cytokines and chemokines to be released, boosting the plaque and leading to further vessel narrowing. [98] Plaques in the carotid artery are typically composed of a fibrous cap covering a lipid core and inflammatory cells. [98] When this plaque ruptures or a thrombus forms from this plaque, it leads to cerebral infarction. These plaques can be stable and asymptomatic or they can be unstable, leading to acute coronary syndromes. If a plaque is prone to rupturing, it is known as an unstable or vulnerable plaque. Vulnerable plaques have active inflammation, substantial accumulation of macrophages, a thin fibrous cap with a large lipid core, denudation of the endothelium with platelet aggregation, and severe stenosis.[98] Vulnerable plaques also tend to be noncalcified whereas stable plaques tend to be calcified. [76] Stable, calcified plaques are more often associated with transient ischemic attacks (TIAs) whereas unstable, non-calcified plaques are more often associated with stroke. [90]

Most patients with carotid stenosis are asymptomatic until the artery severely narrows or a clot forms. This results in a decrease or even block of blood flow to the brain, so the patient will have symptoms of a transient ischemic attack. [26] The symptoms will look like a stroke and they can include weakness or numbness on one side of the body, aphasia, facial droop, and diplopia among other vision impairments.[54] However, these symptoms will resolve within 24 hours.

Risk factors for carotid artery stenosis include older age, hypertension, and smoking. Being older can lead to increased risk for CAS, possibly due to the increasing stiffness of the walls of blood vessels. [67] High blood pressure can lead to more cholesterol deposits in the arteries, increasing the risk of plaque formation and rupture. [80] Smoking harms the endothelium of blood vessels, which makes it easier for cholesterol to deposit and form a plaque. [80] Moreover, an individual who currently smokes or used to smoke has more than a 6-fold risk of developing atherosclerotic carotid stenosis than those who do not and have not smoked. [95]

## Evidence Synthesis

Current Treatments for Symptomatic Carotid Artery Stenosis

Surgical interventions for symptomatic carotid artery stenosis are carotid endarterectomy (CEAs), carotid artery stenting, or transcarotid artery revascularization (TCAR). Carotid endarterectomy (CEA) is performed in order to decrease the risk of stroke in a patient with known cerebrovascular atherosclerotic disease. In CEAs, plaque and potential embolic material are removed from the carotid artery, which improves blood flow. [23] Afterwards, the artery is reconstructed. Carotid artery stenting involves guiding a catheter through the artery, then inserting a stent into the artery so that it keeps the artery from narrowing again. [74] Angioplasty involves inserting a catheter with an inflatable balloon through the artery and then inflating the balloon once it gets to the part of the artery that is too narrow.[18] By doing this, the atherosclerotic plaque is pushed against the wall, which improves blood flow to that area again. Carotid artery stenting and angioplasty are typically used for moderate stenosis and CEA for severe stenosis of the carotid artery. [91]

In 2014, the American Heart Association/American Stroke Association (AHA/ASA) released guidelines for the treatment of symptomatic carotid artery stenosis. [42] The recommendations read as follows: 42"For patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis as documented by noninvasive imaging, CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6% (Class I; Level of Evidence A). For patients with recent TIA or ischemic stroke and ipsilateral moderate (50%–69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging with corroboration (eg, magnetic resonance angiogram or computed tomography angiogram), CEA is recommended depending on patient-specific factors, such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6% (Class I; Level of Evidence B). When the degree of stenosis is <50%, CEA and CAS are not recommended (Class III; Level of Evidence A)." 42 See Table 1 for more details on the recommendations from the AHA/ASA.

Recommendations for Interventional Approaches for Patients with Carotid Artery Stenosis[42]

| *Risk Factor* | *Recommendations from the AHA/ASA* | *Class/Level of Evidence* |
|---|---|---|
| Patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis as documented by noninvasive imaging | CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6% | Class I; Level of Evidence A |
| Patients with recent TIA or ischemic stroke and ipsilateral moderate (50%–69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging with corroboration (eg, magnetic resonance angiogram or computed tomography angiogram) | CEA is recommended depending on patient-specific factors, such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6% | Class I; Level of Evidence B |
| The degree of stenosis is <50% | CEA and CAS are not recommended | Class III; Level of Evidence A |

| | | |
|---|---|---|
| Symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the ICA is reduced by >70% by noninvasive imaging or >50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is <6% | CAS is indicated as an alternative to CEA | Class IIa; Level of Evidence B |
| Older patients (ie, older than ≈70 years), particularly when arterial anatomy is unfavorable for endovascular intervention | CEA may be associated with improved outcome compared with CAS | Class IIa; Level of Evidence B |
| Younger patients | CAS is equivalent to CEA | Class IIa; Level of Evidence B |
| Symptomatic severe stenosis (>70%) in whom anatomic or medical conditions are present that greatly increase the risk for surgery or when other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA | CAS is reasonable | Class IIa; Level of Evidence B |
| Patients with a recent (within 6 months) TIA or ischemic stroke ipsilateral to a stenosis or occlusion of the middle cerebral or carotid artery | EC/IC bypass surgery is not recommended | Class III; Level of Evidence A |
| Patients with recurrent or progressive ischemic symptoms ipsilateral to a stenosis or occlusion of a distal (surgically inaccessible) carotid artery, or occlusion of a mid-cervical carotid artery after institution of optimal medical therapy | EC/IC bypass usefulness is considered investigational | Class IIb; Level of Evidence C |
| All patients with carotid artery stenosis and a TIA or stroke | Optimal medical therapy, which should include antiplatelet therapy, statin therapy, and risk factor modification | Class I; Level of Evidence A |

**Table I:** Recommendations for Interventional Approaches for Patients with Carotid Artery Stenosis

Moreover, 94% of guidelines for symptomatic carotid artery stenosis endorsed CEA for individuals with about 50% to 99% average-CEA-risk symptomatic carotid artery stenosis, 58% endorsed stenting, and 27% opposed stenting1,69. For individuals who are at a high risk for CEA due to comorbidities, vascular anatomy, or other reasons, 82% of guidelines endorsed stenting[1,69].

Approximately 15% of ischemic strokes are due to acute tandem occlusion in the proximal (cervical) internal carotid artery and concomitant thromboembolism involving the distal (intracranial) internal carotid artery or the ipsilateral middle cerebral artery.[70] This necessitates revascularization with balloon angioplasty and stenting followed by thromboembolectomy using an anterograde or retrograde approach. [70] Intracranial mechanical thromboembolectomy followed by angioplasty and/or stenting of the proximal occlusion, or vice versa, is often used3. Whether the extracranial or intracranial approach was done first, it was shown that there were no statistically significant differences in revascularization, intracranial hemorrhage, outcomes, or mortality within the first 90 days. [94]

This also raises the question as to whether angioplasty is enough or if stenting should be done as well. The problem here is that there is an increased risk of intracranial hemorrhage after stenting because dual antiplatelet therapy is the standard of care after the procedure. This was found to be the case as the risk of intracranial hemorrhage was higher in those after stenting versus after mechanical thromboembolectomy. [3] However, mono antiplatelet therapy was shown to increase the risk of transient ischemic attacks and strokes after stenting as compared to dual antiplatelet therapy. [10] Studies have also looked at the benefits of dual antiplatelet therapy with mono antiplatelet therapy and the results are summarized in table 2 below.

| Outcomes of Mono (MAPT) vs. Dual Antiplatelet Therapy (DAPT)[32, 39, 100] | | | |
|---|---|---|---|
| Medication | Name of Study (Year) | ICH Rate (% per week) (DAPT vs. MAPT) | Major Bleeding Rate (% per week) (DAPT vs. MAPT) |
| Aspirin + Clopidogrel[100] | Zuo et al.[100] | 0 vs. 0% | 0 vs. 0% |
| Aspirin + Cilostazol[32] | CSPS.COM[32] | 0 vs. 0% | 0 vs. 0% |
| Aspirin + Ticagrelor[39] | THALES[39] | 0.08 vs. 0.06% | 0.13 vs. 0.06% |
| ICH = intracranial hemorrhage | | | |

**Table II.** Outcomes of Mono (MAPT) vs. Dual Antiplatelet Therapy (DAPT)

Antiplatelet therapy is a balancing act because it can reduce the risk of stroke but can also increase the risk of perioperative bleeding. [64] It was also suggested that stenting should be done with angioplasty itself was not effective enough. [48] Studies have shown that there is no statistically significant difference in patients who had stenting done versus those who only had angioplasties. [94] The studies seem to suggest that stenting can be delayed until it is deemed to be necessary. In this case, if the carotid artery becomes occluded again, it may require an emergent CEA.79 According to these studies, it seems probable that the best course of action may be to perform the angioplasty, then intracranial thromboembolectomy and only stent when necessary, along with emergent CEA for extracranial occlusions.

The Society for Vascular Surgery put forth their recommendations after looking at randomized controlled trials and came up with the following guidelines: "2(1) CEA recommended over maximal medical therapy for low-risk patients; (2) is CEA recommended over transfemoral CAS for low surgical risk patients with symptomatic carotid artery stenosis of >50%; (3) the timing of carotid intervention for patients presenting with acute stroke; (4) screening for carotid artery stenosis in asymptomatic patients; and (5) the optimal sequence of intervention for patients with combined carotid and coronary artery disease." They made their recommendations based on the GRADE (grades of recommendation assessment, development, and evaluation) approach. See Table 3 for more details on the recommendations from the Society for Vascular Surgery.

| Recommendations for Interventional Approaches for Patients with Carotid Artery Stenosis[2] | | |
|---|---|---|
| *Risk Factor* | *Recommendations from the Society for Vascular Surgery* | *Level/Quality of Evidence* |
| Low surgical risk patients with asymptomatic carotid bifurcation atherosclerosis and stenosis of >70% (documented by validated duplex ultrasound or CTA/angiography) | CEA with best medical therapy instead of maximal medical therapy alone for the long-term prevention of stroke and death | Level of recommendation: grade 1 (strong); quality of evidence: B (moderate) |
| Low- and standard-risk patients with >50% symptomatic carotid artery stenosis | CEA over transfemoral carotid artery stenosis (TF-CAS) | Level of recommendation: grade 1 (strong); quality of evidence: A (high) |
| Patients with recent stable stroke (modified Rankin scale score 0-2) and >50% stenosis | Carotid revascularization to be performed as soon as the patient is neurologically stable after 48 hours but definitely before 14 days after the onset of symptoms | Level of recommendation: grade 1 (strong); quality of evidence: B (moderate) |
| Patients undergoing revascularization within the first 14 days after the onset of symptoms | CEA rather than carotid stenting | Level of recommendation: grade 1 (strong); quality of evidence: B (moderate) |

| | | |
|---|---|---|
| Patients who experienced a disabling stroke, have a modified Rankin scale score of ≥3, whose area of infarction is >30% of the ipsilateral middle cerebral artery territory, or who have altered consciousness to minimize the risk of postoperative parenchymal hemorrhage | No revascularization, regardless of the extent of stenosis. These patients can be reevaluated for revascularization later if their neurologic recovery is satisfactory. | Level of recommendation: grade 1 (strong); quality of evidence: C (low) |
| Clinically asymptomatic carotid artery stenosis in individuals without cerebrovascular symptoms or significant risk factors for carotid artery disease | No routine screening | Level of recommendation: grade 1 (strong); quality of evidence: B (moderate) |
| Asymptomatic patients who are at an increased risk of carotid stenosis | Screening for clinically asymptomatic carotid artery stenosis, especially if patients are willing to consider carotid intervention if significant stenosis is discovered | Level of recommendation: grade 2 (weak); quality of evidence: B (moderate) |
| Asymptomatic patients who are undergoing screening for carotid artery stenosis | Duplex ultrasound performed in an accredited vascular laboratory as the imaging modality of choice instead of CTA, MRA, or other imaging modalities | Level of recommendation: grade 1 (strong); quality of evidence: B (moderate) |
| Patients with symptomatic carotid stenosis of 50% to 99%, who require both CEA and CABG | CEA before, or concomitant with, CABG to potentially reduce the risk of stroke and stroke/death. The sequencing of the intervention depends on the clinical presentation and institutional experience. | Level of recommendation: grade 2 (weak); quality of evidence: C (low) |
| Patients with severe (70%-99%) bilateral asymptomatic carotid stenosis or severe asymptomatic stenosis and contralateral occlusion | CEA before, or concomitant with, CABG. | Level of recommendation: grade 2 (weak); quality of evidence: C (low) |
| Patients requiring carotid intervention, staged or synchronous with coronary intervention | Decision between CEA and CAS is determined by the timing of procedure, the need for anticoagulation or antiplatelet therapy, patient anatomy, and patient characteristics. | Level of recommendation: grade 2 (weak); quality of evidence: B (moderate) |

**Table III.** Recommendations for Interventional Approaches for Patients with Carotid Artery Stenosis

### Complications of Carotid Endarterectomy and Carotid Artery Stenting

Carotid endarterectomies are not without their risks either. Studies have shown that CEA increased the five-year risk of ischemic stroke in patients who had less than 30% stenosis of their carotid artery, had no statistically significant effect in patients with 30-49% stenosis, was beneficial in patients with 50-69% stenosis, was extremely beneficial in patients with 70-99% stenosis, and was not significantly beneficial to patients who had nearly occluded carotid arteries. [63] Both CAS and CEA are associated with high rates of failure and periprocedural stroke.51 When the carotid artery is nearly completely occluded, revascularization has not been shown to reduce the risk of stroke as compared to just medical treatment. [30] It has also been shown that long-term complications are less for CAS than for CEA. [46]

CEAs also come with operative complications to consider. [51,71] Wound bleeding after CEA was even more common than stroke or a myocardial infarction after CEA in patients in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) trial. [11] However, diagnosing patients with silent coronary ischemia and treating them with coronary revascularization after CEA has been shown to reduce the risk of cardiac death, myocardial infarction, and cardiovascular death compared to patients with CEA who only received the standard cardiac evaluation and care during a 3-year follow-up.43 Neck hematoma was also common after CEA, especially when treated with the antiplatelet clopidogrel after surgery. [9,59] Dual antiplatelet therapy was also associated with cranial nerve injury, although transient, following CEA. [19] CEA in patients with symptomatic carotid artery stenosis is also associated with cranial nerve palsy and access site hematoma with endarterectomy. [15] Stenting provides less risk of cranial nerve injury. [91] CEA can be done with either primary closure or patches.50 It was also shown that using synthetic, venous, or bovine pericardium patches did not have a significant decrease in the risk of future stroke or cranial nerve injury.88 CEA is performed to save patients with severely atherosclerotic carotid artery stenosis from stroke. [81] It was also shown that an emergent CEA had decreased rates of intracerebral hemorrhage and mortality than

stenting.[79] Moreover, using smaller incisions hidden within the neck crease during CEA has been shown to have better outcomes. [77]

Many randomized controlled trials have been done and are currently underway to compare CEA to CAS when treating carotid artery stenosis. These studies show that CAS is often associated with periprocedural stroke and CEA is often associated with myocardial infarction. [16, 46, 47] It is risky to do CAS in patients who are older than 70 years of age.25 However, some studies have shown that this extra risk is mainly attributable to an increase in minor, non-disabling strokes occurring in patients who are more than 70 years of age. [61] Studies show that discontinuing antiplatelet therapy, resistance to antiplatelet therapy, and thrombotic disorders are the main culprits for post-CAS thrombosis.60 CAS also can lead to prolonged hypotension and bradycardia, especially in patients with increased narrowing of the carotid artery. [31] However, CAS is preferred when CEA is contraindicated. For example, patients who have a "hostile neck" from previous surgery or who do not tolerate anesthesia well may opt for CAS. [20] Regardless of whether the patient underwent a CAS or CEA, no statin use was associated with a higher risk of in-hospital stroke or death and 5-year mortality as compared to those who did use a statin afterwards. [6] Outside of the periprocedural period, carotid stenting was shown to be just as effective as CEA when it came to preventing future strokes. [61] What is even more interesting is that a recent study actually found that high hospital volume and high operator volume decreased the risk of procedural death and stroke after CEA and CAS. [66]

### Restenosis

Restenosis is of the utmost importance to consider when looking at CEA versus CAS. In the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) trial, restenosis was found to have a fourfold increase in the risk of having a stroke. [45] However, when looking at patients who had CAS or CEA, they both had similar incidences of 70% or greater restenosis. [45] Studies that looked at perioperative and 1-year outcomes between patients who received either CAS or CEA also showed no significant differences. [8] It is not an exact comparison though because CEA is typically done for those who are more critically ill than those who only need CAS. It was also found that those who underwent CAS after an unsuccessful CEA, ipsilateral neck surgery, or radiation had higher rates of restenosis. [58]

### Transcarotid Artery Revascularization (TCAR)

TCAR is similar to CEA, but it can be done through a small incision at the neckline instead of a bigger incision at the neck. [49] A tube is then inserted into the carotid artery while diverting blood flow away from the brain so that plaque does not travel up to the brain while the procedure is going on. [96] Essentially, the flow reversal protects against embolism. [21, 33] This flow reversal helps make TCAR neuroprotective and unlike other stenting procedures. [84] The blood is then filtered and a stent is placed in the carotid artery to bolster its integrity and prevent future clot formation. This procedure is beneficial for those who have a higher risk of having a stroke. [92] TCAR is beneficial when stenting the cervical internal carotid artery, especially since this area tends to be stroke-prone. [65] That said, outcomes are best if flow reversal time is minimized as much as possible; studies suggest a clinical cutoff time of 10 minutes. [62] TCAR is not only less invasive, but it also can match the stroke hazard of CEA in standard risk populations. [53]

Moreover, the results of the Safety and Efficacy Study for Reverse Flow Used During Carotid Artery Stenting Procedure (ROADSTER) multicenter trial shows that the ENROUTE Transcarotid Neuroprotection System is safe and can prevent stroke during CAS, with a stroke rate of 1.4%, which is the lowest reported to date.44 Thirty days post-TCAR, no major stroke, myocardial infarction, or death occurred in a study that was done as well.5 However, more recent studies have shown that TCAR is better in the perioperative period for high-risk patients and that in the long-term, there were no significant differences in stroke or survival between groups of patients who had TCAR and CEA or TCAR and TFCAS.52 On the other hand, a study done in the United States and Europe showed that patients from ROADSTER-2 trial with risk factors such as re-stenosis or radiation injury had no perioperative myocardial infarction or stroke and that in the year following surgery, there was a low stroke and death rate. [41] TCAR is a safe and effective way to approach carotid artery stenosis. [17]

Another study also found no significant association between intolerance to flow reversal and comorbidities including "diabetes mellitus, hypertension, hyperlipidemia, congestive heart failure, prior myocardial infarction or angina, pre-operative CAS-related symptoms, prior stroke, prior CAS or CEA, prior neck radiation, tandem stenosis, high cervical stenosis, or hostile neck."87 The same study found a significant association only with chronic obstructive pulmonary disease and contralateral carotid artery occlusion. This was corroborated by another study that found that TCAR in patients considered to have too hostile necks for CEA was not associated with increased intraoperative complexity or postoperative morbidity. [86] Studies have shown that TCAR led to a lower rate of stroke and death in the hospital after the procedure. [75] In addition to that, TCAR has been shown to be effective for older adults who are at a higher risk without perioperative cerebral ischemic event, MI, or death (Ghamraoui and Ricotta, 2020). The same finding held when looking at older adults 1 year after their TCAR procedure.57 Lastly, using somatosensory-evoked potential (SSEP) and electroencephalograms (EEG) during TCARs can improve clinical decision-making for thrombosis versus vasospasm after placing stents. [36] TCAR is a premier approach to carotid revascularization, especially for patients who are at a high risk for stroke, cranial nerve injury, or cardiovascular events. [21, 83]

Studies looking at the differences between males and females in outcomes when looking at ipsilateral stroke, in-stent thrombosis, conversion to CEA, and death after TCAR found no statistically significant difference among them.34 However, if a patient has already experienced a TIA or stroke, it was found that CEA resulted in lower rates of stroke post-operatively when compared to TCAR. [27] However, most studies overall have shown that TCAR is a safe and effective method to revascularization, substantially due to its low rates of periprocedural stroke and cranial nerve injury. [73]

### Emerging Innovation

There are many novel ways of approaching carotid artery stenosis. A surgical technique that was recently tried was carotid endarterectomy (CEA) with auto-arterial remodeling of bifurcation of the common carotid artery (ARBCCA). The study looked at the difference between a classic CEA and ARBCCA and found that it does not have a significant difference in post-operative development of hypertension but the number of cases of restenosis greater than 50% during the 2-year follow-up was 4% for the ARBCCA group, compared to 12% cases in the classic CEA.[35]

Staged angioplasty (SAP) is a two-arm version of CAS and it has been proven to prevent hyperperfusion-induced intracerebral hemorrhage (HICH) in patients who have preocclusive stenosis (90%-99%) and poor collateral compensation.[97]

Sonolysis has also been tried to break apart thrombi during CEA and CAS and it was found that this can reduce the risk of new brain ischemic lesions.[78]

When it comes to medications, it has been shown that anticoagulative agents before surgery or while awaiting CEA can prevent cerebral ischemic events when compared to antiplatelet agents alone.[55]

Other ideas for innovative ways to manage carotid artery stenosis include enhanced embolic protection devices and dual-layered stents.[93] A clinical trial is currently looking at using the Xact Carotid Artery Stent and emboshield distal protection system with bivalirudin for anticoagulation in treating internal carotid artery stenosis.[24]

Current clinical trials are also testing the use of evolocumab on carotid artery atherosclerotic plaques to reduce LDL-cholesterol before CEA.4 Some clinical trials are also looking at abciximab to see if it can reduce the rate of recurrent ischemic strokes before and during CEA when compared with aspirin.[12]

Clinical trials are also underway to assess the effect of anti-PD-1 mAbs (PD-1 immune checkpoint blockades) on the progression of atherosclerotic carotid plaques.[89]

## Conclusions

Symptomatic carotid artery stenosis can be treated in many ways. The current literature vouches primarily for the use of CEA or TCAR for treatment, especially when the vessel has a greater degree of stenosis. TCAR and CEA have similar outcomes in terms of death or stroke 1 year after the respective procedure. [22] TCAR has a similar prognosis to CEA and can be performed without running the risk of myocardial infarction.[29] Here, we reviewed the literature on carotid artery stenosis, CAS, CEA, TCAR, as well as emerging innovation to provide support when making clinical decisions for treatment. For lesser degrees of stenosis, CAS is often performed and CEA is only done if the need arises. Most importantly, it is vital to always tailor treatment to each patient's condition and their unique needs. Further studies regarding treatment for carotid artery stenosis need to be conducted before we can definitively outline a proper path for treatment.

## References


1. Abbott, A, Paraskevas, K, Kakkos, S, Golledge, J, Eckstein, H, Diaz-Sandoval, L, et al. "Systematic Review of Guidelines for the Management of Asymptomatic and Symptomatic Carotid Stenosis." *Stroke* vol. 46,11 (2015): 3288-3301.
2. AbuRahma, Ali., Avgerinos, Efthymios D., Chang, Robert W., Darling, R. Clement, Duncan, Audra A., Forbes, Thomas L., et al. "Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease." *Journal of vascular surgery* vol. 75,1S (2022): 4S-22S.
3. Akpinar, C., Gürkas, E., and Aytac, E. "Carotid angioplasty-assisted mechanical thrombectomy without urgent stenting may be a better option in acute tandem occlusions." *Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences* vol. 23,4 (2017): 405-411.
4. Al-Omran, M. "A Study of Evolocumab on Carotid Artery Atherosclerotic Plaque Morphology Prior to Carotid Endarterectomy." *A Study of Evolocumab on Carotid Artery Atherosclerotic Plaque Morphology Prior to Carotid EndArterectomy. ClinicalTrials.gov*, 4 Sept. 2020.
5. Alpaslan, A., Wintermark, M., Pintér, L., Macdonald, S., Ruedy, R. & Kolvenbach, R. "Transcarotid Artery Revascularization With Flow Reversal." *Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists* vol. 24,2 (2017): 265-270.
6. Anjorin, A., Marcaccio, C., Rastogi, V., Patel, P., Garg, P., & Soden, P., et al. "Statin therapy is associated with improved perioperative outcomes and long-term mortality following carotid revascularization in the Vascular Quality Initiative." *Journal of vascular surgery*, S0741-5214(22)02208-X. 25 Aug. 2022.
7. Arasu, R., Arasu, A., & Muller, J. (2021). Carotid artery stenosis: An approach to its diagnosis and management. *Australian journal of general practice*, *50*(11), 821–825.
8. Arhuidese, I., Nejim, B., Chavali, S., Locham, S., Obeid, T., Hicks, C., et al. "Endarterectomy versus stenting in patients with prior ipsilateral carotid artery stenting." *Journal of vascular surgery* vol. 65,5 (2017): 1418-1428.
9. Baracchini, C., Gruppo, M., Mazzalai, F., Lorenzetti, R., Meneghetti, G., and Ballotta, E. "Predictors of neck bleeding after eversion carotid endarterectomy." *Journal of vascular surgery* vol. 54,3 (2011): 699-705.
10. Barkat, M., Hajibandeh, S., Hajibandeh, S., Torella. F., and Antoniou, G.A. "Systematic Review and Meta-analysis of Dual Versus Single Antiplatelet Therapy in Carotid Interventions." *European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery* vol. 53,1 (2017): 53-67.
11. Barnett, H., Taylor, D.W., Haynes, R.B., Sackett, D.L., Peerless, S.J., Ferguson, G.G., et al. "Beneficial Effect of Carotid Endarterectomy in Symptomatic Patients with High-Grade Carotid Stenosis." *New England Journal of Medicine*, vol. 325, no. 7, 1991, pp. 445–453.
12. Baumgartner, R. "Abciximab for Prevention of Stroke Recurrence Before Endarterectomy in Symptomatic Carotid Stenosis." *Abciximab for Prevention of Stroke Recurrence Before Endarterectomy in Symptomatic Carotid Stenosis. ClinicalTrials.gov*, 3 May 2007.
13. Bergheanu, S.C., Bodde, M.C., & Jukema, J.W. "Pathophysiology and treatment of atherosclerosis : Current view and future perspective on lipoprotein modification treatment." *Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation* vol. 25,4 (2017): 231-242.
14. Bohnstedt, B.N., Dhaemers, R., & Hsu, D. "Symptomatic carotid artery stenosis." *Seminars in neurology* vol. 33,5 (2013): 456-61.
15. Bonati, L.H., Jansen, O., de Borst, G.J, & Brown, M.M. "Management of atherosclerotic extracranial carotid artery stenosis." *The Lancet. Neurology* vol. 21,3 (2022): 273-283.
16. Brott, T.G., Hobson, R.W., Howard, G., Roubin, G.S., Clark, W.M, Brooks, W., et al. "Stenting versus endarterectomy for treatment of carotid-artery stenosis." *The New England journal of medicine* vol. 363,1 (2010): 11-23.
17. Cappellini, C., Zheng, H., Lamb, K.M., Sooppan, R., Coffey, J., & Luo, R.Q. "Outcomes of Transcarotid Artery Revascularization and Carotid Endarterectomy at a Single Institution." *Annals of vascular surgery* vol. 73 (2021): 329-335.
18. Chhabra, L., Zain, M.A., Siddiqui, W.J. Angioplasty. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
19. Chisci, E., Rehring, T.F., Pigozzi, C., Colon, S., Borgheresi, A., Tramacere, L., et al. "Cranial nerve injury is associated with dual antiplatelet therapy use and cervical hematoma after carotid endarterectomy." *Journal of vascular surgery* vol. 64,4 (2016): 985-989.e2.
20. Chou, D., Amin, Z., Gulati, S., Clark, E. C., & Starr, J. E. (2019). Outcomes After Carotid Artery Stenting in Patients With Normal Neck Anatomy and Hostile Neck Anatomy Are Comparable. *Journal of Vascular Surgery, 70*(3), e80–e81.
21. Coelho, A., Prassaparo, T., Mansilha, A., Kappelle, J., Naylor, R., & de Borst, G.J. "Critical Appraisal on the Quality of Reporting on Safety and Efficacy of Transcarotid Artery

Stenting With Flow Reversal." *Stroke* vol. 51,9 (2020): 2863-2871.

22. Columbo, J., Martinez-Camblor, P., Stone, D.H., Goodney, P.P., & O'Malley, A.J. "Procedural Safety Comparison Between Transcarotid Artery Revascularization, Carotid Endarterectomy, and Carotid Stenting: Perioperative and 1-Year Rates of Stroke or Death." *Journal of the American Heart Association* vol. 11,19 (2022): e024964.
23. DaCosta M., Tadi P., Surowiec S.M. Carotid Endarterectomy. [Updated 2022 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
24. Dave, R. "A Prospective, Non-Randomized, Evaluation of Low-Risk Patients Undergoing Carotid Stenting With ANgiomax (Bivalirudin)." *A Prospective, Non-Randomized, Evaluation of Low-Risk Patients Undergoing Carotid Stenting With ANgiomax (Bivalirudin)*. *ClinicalTrials.gov*, 31 July 2014.
25. Dharmakidari, S., Bhattacharya, P. & Chaturvedi, S. Carotid Artery Stenosis: Medical Therapy, Surgery, and Stenting. *Curr Neurol Neurosci Rep* 17, 77 (2017).
26. Eliasziw, M., Kennedy, J., Hill, M.D., Buchan, A.M., & Barnett, H. "Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease." *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* vol. 170,7 (2004): 1105-9.
27. Elmously, A., Rich, N., Lazar, A., Mehta, A., Patel, P., & Patel, V. "Outcomes of early transcarotid artery revascularization versus carotid endarterectomy after acute neurologic events." *Journal of vascular surgery* vol. 76,3 (2022): 760-768.
28. Fine-Edelstein, J.S., Wolf, P.A., O'Leary, D.H., Poehlman, H., Belanger, A.J., Kase, C.S., et al. "Precursors of extracranial carotid atherosclerosis in the Framingham Study." *Neurology* vol. 44,6 (1994): 1046-50.
29. Gao, J., Chen, Z., Kou, L., Zhang, H., & Yang, Y. "The Efficacy of Transcarotid Artery Revascularization With Flow Reversal System Compared to Carotid Endarterectomy: A Systematic Review and Meta-Analysis." *Frontiers in cardiovascular medicine* vol. 8 695295. 19 Nov. 2021.
30. Garcia-Pastor, A., Gil-Núñez, A., Ramirez-Moreno, J.M., González-Nafría, N., Tejada, J., & Moniche, F., et al. "Endarterectomy, Stenting, or Medical Treatment for Symptomatic Carotid Near-Occlusion: Results from CAOS, a Multicenter Registry Study." *AJNR. American Journal of Neuroradiology*, vol. 43,9 1304–1310. 18 Aug. 2022.
31. Gökçal, E., Niftaliyev, E., Deniz, Ç., Ergelen, M., Güzel, V., Göktekin, Ö., et al. "Prolonged hypotension after carotid artery stenting: incidence, predictors and consequences." *Acta neurochirurgica* vol. 159,11 (2017): 2081-2087.
32. Hankey, G. J. "CSPS.com Trial of Adding Cilostazol to Antiplatelet Therapy to Reduce Recurrent Stroke." *Stroke* vol. 51,2 (2020): 696-698.
33. Hu, J., Sohn, A., George, J., Malik, R., Ilonzo, N. "Transcarotid Artery Revascularization and Advances in Vascular Surgery for Carotid Artery Disease." *Surgical technology international* vol. 39 (2021): 277-282.
34. Husman, R., Tanaka, A., George, M., Cambiaghi, T., Leonard, S., Motaganahalli, R., et al. "An Analysis of Sex-Based Outcomes Following Transcarotid Artery Revascularization." *Vascular and endovascular surgery* vol. 57,1 (2023): 48-52.
35. Ignatenko, P., Novikova, O., Gostev, A., Starodubtsev, V., Zeidlits, G., Kuznetsov, K., et al. "Carotid Endarterectomy with Autoarterial Remodeling of Bifurcation of the Common Carotid Artery and Carotid Endarterectomy with Patch Closure: Comparison of Methods." *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association* vol. 28,3 (2019): 741-750.
36. Intagliata, A., Rountree, K., & Bath, J. "Thrombosis or vasospasm: The utility of intraoperative neuromonitoring during TCAR." *Vascular*, 17085381221080002. 28 Feb. 2022.
37. Ji, R., Pan, Y., Yan, H., Zhang, R., Liu, G., Wang, P., et al. "Current smoking is associated with extracranial carotid atherosclerotic stenosis but not with intracranial large artery disease." *BMC neurology* vol. 17,1 120. 26 Jun. 2017.
38. Jiang, Y., Pang, T., Shi, R., Qian, W., Yan, W., Li, Y., et al. "Effect of Smoking on Coronary Artery Plaques in Type 2 Diabetes Mellitus: Evaluation With Coronary Computed Tomography Angiography." *Frontiers in endocrinology* vol. 12 750773. 3 Nov. 2021.
39. Johnston, S. C., Amarenco, P., Denison, H., Evans, S. R., Himmelmann, A., James, S., Knutsson, M., Ladenvall, P., Molina, C. A., & Wang, Y. (2020). Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA. *New England Journal of Medicine*, *383*(3), 207–217.
40. Prasad, Kailash. "Pathophysiology and Medical Treatment of Carotid Artery Stenosis." *The International journal of angiology : official publication of the International College of Angiology, Inc* vol. 24,3 (2015): 158-72.
41. Kashyap, V., So, K., Schneider, P., Rathore, R., Pham, T., Motaganahalli, R., et al. "One-year outcomes after transcarotid artery revascularization (TCAR) in the ROADSTER 2 trial." *Journal of vascular surgery* vol. 76,2 (2022): 466-473.e1.
42. Kernan, W., Ovbiagele, B., Black, H., Bravata, D., Chimowitz, M., Ezekowitz, M., et al. "Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association." *Stroke* vol. 45,7 (2014): 2160-236.
43. Krievins, D., Zellans, E., Latkovskis, G., Babuskina, I., Kumsars, I., Jegere, S., et al. "Coronary revascularization of patients with silent coronary ischemia may reduce the risk of myocardial infarction and cardiovascular death after carotid endarterectomy." *Journal of vascular surgery* vol. 76,3 (2022): 750-759.
44. Kwolek, C., Jaff, M., Leal, J., Hopkins, L., Shah, R., Hanover, T., et al. "Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal." *Journal of vascular surgery* vol. 62,5 (2015): 1227-34.
45. Lal, B., Beach, K., Roubin, G., Lutsep, H., Moore, W., Malas, M., et al. "Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial." *The Lancet. Neurology* vol. 11,9 (2012): 755-63.
46. Lamanna, A., Maingard, J., Barras, C., Kok, H., Handelman, G., Chandra, R., et al. "Carotid artery stenting: Current state of evidence and future directions." *Acta neurologica Scandinavica* vol. 139,4 (2019): 318-333.
47. LaMuraglia, G., Brewster, D., Moncure, A., Dorer, D., Stoner, M., Trehan, S., et al. "Carotid endarterectomy at the millennium: what interventional therapy must match." *Annals of surgery* vol. 240,3 (2004): 535-44; discussion 544-6.
48. Leonardi, M., Dall'Olio, M., Raffi, L, Cenni, P., Simonetti, L., Marasco, R., et al. "Carotid Stenting without Angioplasty and without Protection: The Advantages of a Less Invasive Procedure." *Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences* vol. 14,2 (2008): 153-63.

49. Luk, Y., Chan, Y., & Cheng, S. "Transcarotid Artery Revascularization as a New Modality of Treatment for Carotid Stenosis." *Annals of vascular surgery* vol. 64 (2020): 397-404.
50. Maertens, V., Maertens, H., Kint, M., Coucke, C., Blomme, Y. "Complication Rate after Carotid Endarterectomy Comparing Patch Angioplasty and Primary Closure." *Annals of vascular surgery* vol. 30 (2016): 248-52.
51. Machin, M., Salim, S., Onida, S., Davies, A. "The less invasive paradox, why carotid artery stenting is not suitable for the high-risk patient." *Annals of translational medicine.* vol. 8,19 (2020): 1269.
52. Malas, M., Elsayed, N., Naazie, I., Dakour-Aridi, H., Yei, K., & Schermerhorn, M. "Propensity score-matched analysis of 1-year outcomes of transcarotid revascularization with dynamic flow reversal, carotid endarterectomy, and transfemoral carotid artery stenting." *Journal of vascular surgery* vol. 75,1 (2022): 213-222.e1.
53. Malas, M., Leal, J., Kashyap, V., Cambria, R., Kwolek, C., Criado, E. "Technical aspects of transcarotid artery revascularization using the ENROUTE transcarotid neuroprotection and stent system." *Journal of vascular surgery* vol. 65,3 (2017): 916-920.
54. Marsman, M., Wetterslev, J., Jahrome, A., Gluud, C., Moll, F., Keus, F., et al. "Carotid endarterectomy with patch angioplasty versus primary closure in patients with symptomatic and significant stenosis: a systematic review with meta-analyses and trial sequential analysis of randomized clinical trials." *Systematic reviews* vol. 10,1 139. 6 May. 2021.
55. Martinez-Gutierrez, J., Roy, A., D'Amato, S., Berkman, J., Montes, D., Kimball, C., et al. "Preoperative antithrombotic treatment in acutely symptomatic carotid artery stenosis." *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association* vol. 31,5 (2022): 106396.
56. Mathiesen, E.B., Joakimsen, O., & Bønaa, K.H. "Prevalence of and risk factors associated with carotid artery stenosis: the Tromsø Study." *Cerebrovascular diseases (Basel, Switzerland)* vol. 12,1 (2001): 44-51.
57. Mehta, A., Patel, P., Bajakian, D., Schutzer, R., Morrissey, N., Malas, M., et al. "Transcarotid artery revascularization versus carotid endarterectomy and transfemoral stenting in octogenarians." *Journal of vascular surgery*vol. 74,5 (2021): 1602-1608.
58. Moon, K., Albuquerque, F., Levitt, M., Ahmed, A., Yashar, M., Kalani, S., et al. "The myth of restenosis after carotid angioplasty and stenting." *Journal of neurointerventional surgery* vol. 8,10 (2016): 1006-10.
59. Morales Gisbert, S.M., Almonacil, V., García, J., Gascó, B., Palonés, F., Monzón, E. "Predictors of cervical bleeding after carotid endarterectomy." *Annals of vascular surgery* vol. 28,2 (2014): 366-74.
60. Moulakakis KG, Mylonas SN, Lazaris A, Tsivgoulis G, Kakisis J, Sfyroeras GS, et al. Acute carotid stent thrombosis: a comprehensive review. Vasc Endovasc Surg. 2016;50(7):511–21.
61. Müller, M., Lyrer, Ph., Brown, M., & Bonati, L. "Carotid artery stenting versus endarterectomy for treatment of carotid artery stenosis." *The Cochrane database of systematic reviews* vol. 2,2 CD000515. 25 Feb. 2020.
62. Naazie, I., Dodo-Williams, T., Janssen, C., Lane, J., Smeds, M., Malas, M. "Impact of Flow Reversal Duration on Neurological Outcomes of Transcarotid Artery Revascularization (TCAR)." *Annals of vascular surgery*, S0890-5096(22)00643-4. 28 Oct. 2022.
63. Orrapin, S. & Rerkasem, K. "Carotid endarterectomy for symptomatic carotid stenosis." *The Cochrane database of systematic reviews* vol. 6,6 CD001081. 7 Jun. 2017.
64. Patel, R., Marmor, R., Dakour, H., Elsayed, Ramachandran, M., Malas, M. "Dual Antiplatelet Therapy Is Associated with Increased Risk of Bleeding and Decreased Risk of Stroke Following Carotid Endarterectomy." *Annals of vascular surgery*, S0890-5096(22)00452-6. 31 Jul. 2022.
65. Piper, K., Farooq, J., Yeung, E., Flores-Milan, G., Van Loveren, H., & Lau, T. "Transcarotid artery revascularization (TCAR) stenting or angioplasty for intracranial carotid artery stenosis: Case series and novel application." *Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences*, 15910199221090724. 24 Mar. 2022.
66. Poorthuis, M., Brand, F., Halliday, A., Bulbulia, R., Bots, M., de Borst, G. High Operator and Hospital Volume Are Associated With a Decreased Risk of Death and Stroke After Carotid Revascularization: A Systematic Review and Meta-analysis. Annals of Surgery: April 2019 - Volume 269 - Issue 4 - p 631-641.
67. Prati, P., Vanuzzo, D., Casaroli, M., Di Chiara, A., De Biasi, F., Feruglio, G.A., et al. "Prevalence and determinants of carotid atherosclerosis in a general population." *Stroke* vol. 23,12 (1992): 1705-11.
68. Puccinelli, F., Roffi, M., Murith, N., & Sztajzel, R. "Prise en charge de la sténose carotidienne" [Management of carotid artery stenosis]. *Revue medicale suisse* vol. 13,560 (2017): 894-899.
69. Qureshi, A., Alexandrov, A., Tegeler, C., Hobson, R., Baker, J., Hopkins, L. "Guidelines for screening of extracranial carotid artery disease: a statement for healthcare professionals from the multidisciplinary practice guidelines committee of the American Society of Neuroimaging; cosponsored by the Society of Vascular and Interventional Neurology." *Journal of neuroimaging : official journal of the American Society of Neuroimaging* vol. 17,1 (2007): 19-47.
70. Rangel-Castilla, L., Rajah, G. B., Shakir, H. J., Shallwani, H., Gandhi, S., Davies, J. M., et al. (2017). Management of acute ischemic stroke due to tandem occlusion: Should endovascular recanalization of the extracranial or intracranial occlusive lesion be done first? *Neurosurgical Focus*, *42*(4).
71. Rerkasem, A., Orrapin, S., Howard, D., & Rerkasem, K. "Carotid endarterectomy for symptomatic carotid stenosis." *The Cochrane database of systematic reviews* vol. 9,9 CD001081. 12 Sep. 2020.
72. Rockman, C., Jacobowitz, G., Gagne, P., Adelman, M., Lamparello, P., Landis, R., et al. "Focused screening for occult carotid artery disease: patients with known heart disease are at high risk." *Journal of vascular surgery* vol. 39,1 (2004): 44-51.
73. Sagris, M., Giannopoulous, S., Giannopoulous, S., Tzoumas, A., Texakalidis, P., Charisis, N., et al. "Transcervical carotid artery revascularization: A systematic review and meta-analysis of outcomes." *Journal of vascular surgery* vol. 74,2 (2021): 657-665.e12.
74. Saleem T, Baril DT. Carotid Artery Stenting. [Updated 2022 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
75. Schermerhorn ML, Liang P, Eldrup-Jorgensen J, Cronenwett JL, Nolan BW, Kashyap VS, et al. Association of transcarotid artery revascularization vs transfemoral carotid artery stenting with stroke or death among patients with carotid artery stenosis. JAMA. 2019; 322:2313–2322.

76. Shi, X., Gao, J., Lv, Q., Cai, H., Wang, F. Ye, R., et al. "Calcification in Atherosclerotic Plaque Vulnerability: Friend or Foe?." *Frontiers in physiology* vol. 11 56. 5 Feb. 2020.
77. Sinha, S., Fok, M., Goh, A., & Gadhvi, V. "Outcomes after Transverse-Incision 'Mini' Carotid Endarterectomy and Patch-Plasty." *Vascular specialist international* vol. 35,3 (2019): 137-144.
78. Školoudík, D., Kuliha, M., Hrbáč, T., Jonszta, T., & Herzig, R. "Sonolysis in Prevention of Brain Infarction During Carotid Endarterectomy and Stenting (SONOBUSTER): a randomized, controlled trial." *European heart journal* vol. 37,40 (2016): 3096-3102.
79. Slawski, D., Jumaa, M., Salahuddin, H., Shawver, J., Junaid Humayun, M., Russell, T., et al. "Emergent carotid endarterectomy versus stenting in acute stroke patients with tandem occlusion." *Journal of vascular surgery* vol. 68,4 (2018): 1047-1053.
80. Sobieszczyk, P. & Beckman, J. "Carotid artery disease." *Circulation* vol. 114,7 (2006): e244-7.
81. Stasiowski, M. & Krawczyk, L. "SPI-Guided Analgesia during CEA under Ra - Full Text View." *SPI-Guided Analgesia During CEA Under RA - ClinicalTrials.gov*, 5 Aug. 2020.
82. Steinvil, A., Sadeh, B., Arbel, Y., Justo, D., Belei, A., Borenstein, N., et al. "Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease." *Journal of the American College of Cardiology* vol. 57,7 (2011): 779-83.
83. Stonko DP, Goldsborough E, Kibrik P, Zhang G, Holscher CM, Hicks CW. Use of Transcarotid Artery Revascularization, Transfemoral Carotid Artery Stenting, and Carotid Endarterectomy in the US From 2015 to 2019. *JAMA Netw Open.* 2022;5(9):e2231944.
84. Sujijantarat, N., Antonios, J., Koo, A., Renedo, D., Cord, B., Zetchi, A., et al. "Transcarotid artery revascularization (TCAR): a technical video." *Journal of neurointerventional surgery*vol. 14,8 (2022): 842.
85. Sulženko, J., & Pieniazek, P. (2018). The cardiovascular risk of patients with carotid artery stenosis. *Cor et Vasa*, *60*(1), e42–e48.
86. Tanaka, A., Madison, M., Motaganahalli, R., Fajardo, A., Husman, R., Keyhani, A., et al. "Transcarotid artery revascularization is safe in necks with anatomy hostile for carotid endarterectomy." *Journal of vascular surgery* vol. 76,4 (2022): 961-966.
87. Teter, K., Rockman, C., Lamparello, P., Macdonald, S., Garg, K., Barfield, M., et al. "Risk Factors for and Intraoperative Management of Intolerance to Flow Reversal in TCAR." *Annals of vascular surgery* vol. 79 (2022): 41-45.
88. Texakalidis, P., Giannopoulous, S., Charisis, N., Giannopoulous, S., Karasavvidis, T., Koullias, G., et al. "A meta-analysis of randomized trials comparing bovine pericardium and other patch materials for carotid endarterectomy." *Journal of vascular surgery* vol. 68,4 (2018): 1241-1256.e1.
89. Wang, Jianan. "A Perspective, Self-control Study on the Progression of Carotid Plaques in Anti-PD-1 mAb Treated Tumor Patients by Artery Ultrasound Follow-up." *A Perspective, Self-control Study on the Progression of Carotid Plaques in Anti-PD-1 mAb Treated Tumor Patients by Artery Ultrasound Follow-up. ClinicalTrials.gov*, 17 Nov. 2021.
90. Wang, X., Chen, X., Chen, Z., & Zhang, M. "Arterial Calcification and Its Association With Stroke: Implication of Risk, Prognosis, Treatment Response, and Prevention." *Frontiers in cellular neuroscience* vol. 16 845215. 11 May. 2022.
91. Wangqin, R., Krafft, P.R., Piper, K. Kumar, J., Xu, K., Mokin, M., et al. Management of De Novo Carotid Stenosis and Postintervention Restenosis—Carotid Endarterectomy Versus Carotid Artery Stenting—a Review of Literature. *Transl. Stroke Res.* 10, 460–474 (2019).
92. Welz, M., Sattur, M., Richter, K., & Bendok, B. "Transcarotid Artery Revascularization With Flow Reversal: Bypassing the Arch and Limiting Distal Emboli." *Neurosurgery* vol. 81,5 (2017): N41-N42.
93. White, C., Brott, T., Gray, W., Heck, D., Jovin, T., Lyden, S., et al. "Carotid Artery Stenting: JACC State-of-the-Art Review." *Journal of the American College of Cardiology* vol. 80,2 (2022): 155-170.
94. Wilson, M., Murad, M., Krings, T., Pereira, V., O'Kelly, C., Rempel, J., et al. "Management of tandem occlusions in acute ischemic stroke - intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis." *Journal of neurointerventional surgery* vol. 10,8 (2018): 721-728.
95. Woo, S., Joh, J., Han, S., & Park, H. "Prevalence and risk factors for atherosclerotic carotid stenosis and plaque: A population-based screening study." *Medicine* vol. 96,4 (2017): e5999.
96. Wu, W.W., Liang, P., O'Donnell, T.F.X., Swerdlow, N. J., Li, C., Wyers, M.C., et al. (2019). Anatomic eligibility for transcarotid artery revascularization and transfemoral carotid artery stenting. *Journal of Vascular Surgery*, *69*(5), 1452–1460.
97. Xu, S., Sun, B., Zhang, T., Wu, P., Ji, Z., Wang, C., et al. "Staged carotid artery stenting for prevention of hyperperfusion-induced intracerebral hemorrhage in patients with very high-grade carotid stenosis and poor collateral compensation." *World neurosurgery*, S1878-8750(22)01609-6. 14 Nov. 2022.
98. Uchiyama, S., Yamazaki, M., & Iwata, M. *Brain and nerve = Shinkei kenkyu no shinpo* vol. 62,12 (2010): 1269-75.
99. Zhang, K., Lin, Q., Zhang, T., Guo, D., & Cao, L. (2020). Contemporary Prevalence and risk factors of carotid artery stenosis in asymptomatic low-income Chinese individuals: a population-based study. *Postgraduate Medicine*, *132*(7), 650–656.
100. Zuo, F., Liu, H., Wu, H., Su, N., Liu, J., & Dong, A. "The effectiveness and safety of dual antiplatelet therapy in ischemic cerebrovascular disease with intracranial and extracranial arteriostenosis in Chinese patients: A randomized and controlled trail." *Medicine* vol. 96,1 (2017): e5497.

**DOI: 10.31579/2578-8868/255**