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REVIEW

Screening, diagnosis and management of carotid artery stenosis: a state-of-the-art review

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Abstract

Stroke causes substantial morbidity and mortality in the United States, with nearly 800,000 cases each year. Carotid artery stenosis (CAS) accounts for 20-30% of ischemic strokes. CAS reflects systemic atherosclerosis and affects roughly 1.5% of adults worldwide aged 30-79 years (~58 million people), while moderate-to-severe asymptomatic CAS affects 4-8% of U.S. adults. Severe asymptomatic CAS (70-99% stenosis) affects 0.5% of adults aged ≥65, and meta-analyses estimate a 3.1% prevalence in the general population. Contemporary optimal medical therapy has lowered annual stroke rates in asymptomatic CAS to ~1.3% for stenosis <75% and 2-2.5% for stenosis ≥75%, with a five-year ipsilateral stroke risk of 5% in a large U.S. cohort. These findings support selective screening in high-risk groups and align with the U.S. Preventive Services Task Force recommendation against routine screening in asymptomatic adults. Symptomatic and asymptomatic CAS differ in stroke risk and treatment benefit. Symptomatic CAS carries high early recurrence risk, with stroke recurrence exceeding 18% within 30 days. The Asymptomatic Carotid Surgery Trial found that about half of ischemic strokes in patients with >60% asymptomatic CAS caused disability or death. Carotid duplex ultrasonography serves as the first-line diagnostic tool, while CT angiography and magnetic resonance angiography provide complementary imaging. Clinicians reserve digital subtraction angiography for complex cases. Luminal stenosis alone does not predict risk, as vulnerable plaque features such as intraplaque hemorrhage, ulceration, and other morphologic markers can cause events even when stenosis is <50%. Contemporary evidence establishes optimal medical therapy as foundational therapy. Revascularization remains essential for selected symptomatic patients but remains controversial in asymptomatic disease. In the North American Symptomatic Carotid Endarterectomy Trial, carotid endarterectomy reduced the five-year risk of death or stroke by 29% in patients with 50-69% stenosis and substantially lowered major stroke or death in those ≥70% stenosis. In symptomatic disease, a meta-analysis showed lower 30-day mortality with carotid endarterectomy than with stenting (1.4% *vs*. 1.9%), lower stroke rates (4.6% *vs*. 8.5%), and higher rates of myocardial infarction with endarterectomy (1.6% *vs*. 0.8%). Severe restenosis at five years also favored endarterectomy (5.8% *vs*. ≥10%). Transcarotid artery revascularization (TCAR) has produced favorable registry outcomes, with peri-procedural stroke or death rates of 1.2% for TCAR, 1.1% for carcinoembryonic antigen, and 1.8% for stenting in asymptomatic CAS. However, randomized evidence remains limited. This state-of-the-art review synthesizes contemporary evidence on screening, diagnosis, and management of CAS in asymptomatic and symptomatic populations.

Key words: ischaemic stroke; stroke prevention; carotid artery stenosis; risk stratification; screening strategies.

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Introduction

Stroke remains the fifth leading cause of death in the U.S. and the second leading cause of death worldwide.[1,2] Approximately 7 million U.S. adults have experienced a stroke, nearly 75% of whom represent first-ever events, with an estimated 795,000 strokes occurring annually in the U.S.[3-5] By 2030, an additional 3.4 million adults aged ≥18 years are projected to have suffered a stroke, representing a 20.5% increase in prevalence compared with 2012.[2] Stroke accounts for nearly 150,000 deaths each year in the U.S.; however, non-fatal stroke imposes a substantial long-term burden, including prolonged recovery, loss of independence, and the need for institutional care in approximately one in seven survivors.[5,6] The direct medical cost of stroke in the U.S. was estimated at $28 billion during 2014-2015, with total direct and indirect costs reaching $45.5 billion, and these expenditures are projected to increase by 129% by 2030.[7,8]

Ischemic cerebral infarction accounts for approximately 87% of all strokes.[9] Carotid artery stenosis (CAS) is a major contributor to ischemic stroke, transient ischemic attack (TIA), and cognitive impairment, accounting for nearly 20-30% of acute ischemic strokes and conferring an estimated 25% risk of recurrence within five years following an initial event.[10-13] CAS also serves as a marker of systemic atherosclerosis and frequently coexists with coronary and peripheral arterial disease.[14] Globally, more than 800 million individuals have carotid atherosclerotic plaque, with a pooled prevalence of carotid stenosis of 1.5% among adults aged 30-79 years, corresponding to approximately 58 million affected individuals.[15] In the U.S., ultrasound-based studies indicate that moderate-to-severe asymptomatic carotid stenosis affects 4-8% of adults and is associated with a 16% five-year risk of stroke among those with ≥60% stenosis.[16-18] Moreover, reflecting its systemic nature, CAS is associated with heightened cardiovascular risk, with up to a 22% increase in the composite risk of myocardial infarction, cardiovascular events, and coronary hospitalization among patients with asymptomatic carotid stenosis >70%, a finding consistently demonstrated in the SMART study and supported by a large meta-analysis of 19 studies.[19-21]

Concerningly, the incidence of CAS is increasing in the general population, largely driven by population aging, sedentary lifestyles, and dietary patterns characterized by high fat and salt intake.[22] Globally, the prevalence of CAS has risen by approximately 59% since 2000, a trend attributed predominantly to demographic aging.[15] The burden of disease is strongly age-dependent, with the prevalence of severe asymptomatic CAS in men increasing from 0.1% among those younger than 50 years to 3.1% among those aged ≥80 years.[23] Consistent with these observations, a pooled analysis of 59 studies from 21 countries demonstrated a 34% increase in carotid atherosclerotic plaque incidence among men and a 21% increase among women aged 55-59 years between 2000 and 2020.[24] At present, asymptomatic CAS ≥50% affects approximately 5-10% of individuals older than 65 years, with prevalence rising further to about 7.5% in men and 5% in women aged >80 years.[24-26]

Additionally, patients with symptomatic CAS carry a substantially higher absolute risk of stroke, whereas those with asymptomatic CAS have a lower but nonetheless clinically meaningful risk.[27] Data from the international REACH registry demonstrated that individuals with asymptomatic CAS experienced a one-year absolute stroke risk exceeding 3% and a relative stroke risk at least 50% higher than that of individuals without carotid stenosis.[28] Contemporary optimal medical therapy has lowered the annual stroke risk in asymptomatic CAS, which helps explain why the U.S. Preventive Services Task Force (USPSTF) recommends against population-level screening in asymptomatic adults.[29] Nevertheless, asymptomatic CAS remains clinically important, and the key unresolved issue is how best to identify the small subset of patients who may still benefit from intervention.[30,31] Importantly, the Asymptomatic Carotid Surgery Trial (ACST) demonstrated that among patients with >60% asymptomatic CAS, approximately half of ischemic strokes were disabling or fatal, underscoring the clinical relevance of effective preventive strategies in this population.[32]

Given the substantial morbidity, mortality, and economic burden associated with CAS and the related TIAs and strokes, both primary prevention in unaffected individuals and secondary prevention to reduce recurrent events are increasingly important.[6] Importantly, the prognosis and management strategies differ substantially between symptomatic and asymptomatic CAS.[33] Two major unresolved questions continue to define the field: whether population-wide screening for asymptomatic CAS improves outcomes, and whether revascularization provides net benefit over contemporary optimal medical therapy in selected asymptomatic patients. Accordingly, this state-of-the-art review synthesizes current evidence on the screening, diagnosis, and management of CAS across both symptomatic and asymptomatic populations.

Literature search

This state-of-the-art review used a structured literature search to identify contemporary evidence on the screening, diagnosis, and management of CAS. We searched PubMed/MEDLINE, Embase, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL) through March 2026. Search terms included combinations of “carotid artery stenosis,” “carotid atherosclerosis,” “asymptomatic carotid stenosis,” “symptomatic carotid stenosis,” “stroke,” “transient ischemic attack,” “screening,” “diagnosis,” “carotid duplex ultrasonography,” “computed tomography angiography,” “magnetic resonance angiography,” “digital subtraction angiography,” “plaque vulnerability,” “plaque morphology,” “carotid endarterectomy,” “carotid artery stenting,” “transcarotid artery revascularization,” “medical therapy,” and “stroke prevention.”

We prioritized high-quality evidence, including randomized controlled trials, meta-analyses, systematic reviews, prospective and retrospective cohort studies, comparative effectiveness studies, major guideline documents, and landmark investigations that informed contemporary clinical practice. We also reviewed reference lists from key articles and guideline

statements to identify additional relevant publications. We selected studies based on their relevance to the epidemiology, risk factors, screening strategies, diagnostic evaluation, medical management, revascularization approaches, and emerging concepts in CAS. Preference was given to recent studies and contemporary guideline documents, while landmark older studies were included when they provided foundational evidence that continues to influence current practice. Moreover, this article aims to provide a comprehensive state-of-the-art overview rather than a quantitative synthesis of evidence. Hence, a formal systematic review methodology was not applied.

Risk factors for carotid artery stenosis

Cigarette smoking, hypercholesterolemia, elevated systolic blood pressure, and advancing age are consistently identified as the principal risk factors driving the development and progression of CAS.[34,35] Smoking demonstrates a clear dose-response relationship, with the odds of CAS increasing by approximately 1.3-1.5 for every 10 cigarettes smoked per day.[36] Dyslipidemia further contributes to disease burden, and hypercholesterolemia remains a reversible risk factor for carotid atherosclerosis, while systolic blood pressure levels exceeding 120 mmHg confer a progressive risk increase of approximately 1.2 per 10-mmHg increment.[34,35,37] Advancing age is associated with a stepwise increase in risk, with odds rising by approximately 1.6-1.7 for every 10-year increment.[34,35] CAS is more common in men than in women, and population-based data show higher carotid plaque and stenosis prevalence in men across age groups.[15,16] Additional contributors include diabetes mellitus, chronic kidney disease, diets with high glycemic load and advanced glycation end-product formation, elevated C-reactive protein levels, and coexisting systemic atherosclerosis.[38] Reflecting this systemic association, CAS is observed in approximately 25% of individuals with peripheral arterial disease, 16% of adults older than 60 years with multiple cardiovascular risk factors, 7-31% of patients with coronary artery disease, and nearly 12% of those with aortic aneurysm (Figure 1).[38]

Symptomatic *versus* asymptomatic carotid artery stenosis

Distinguishing symptomatic from asymptomatic CAS is fundamental to accurately assessing disease progression and determining the potential benefit of invasive interventions.[39] Symptomatic CAS is defined by the occurrence of a neurological ischemic event, such as a TIA or ischemic stroke, within the preceding six months after exclusion of alternative etiologies.[40] Although symptomatic disease is commonly associated with hemodynamically significant stenosis (>50%), luminal narrowing alone does not determine stroke risk. Growing evidence indicates that plaque vulnerability plays a critical role, and ipsilateral ischemic events may arise from non-stenotic or mildly stenotic plaques (<50%) that exhibit high-risk features such as intraplaque hemorrhage, a lipid-rich necrotic core, fibrous cap rupture, plaque ulceration, or surface thrombus.[41] These features promote plaque instability and artery-to-artery embolization, which may precipitate cerebrovascular events independent of stenosis severity. Clinical manifestations commonly include sudden-onset sensory or motor deficits, dysphasia, or monocular vision loss, with visual symptoms occurring ipsilateral to the stenotic lesion and cerebral symptoms affecting the contralateral hemisphere. Many patients experience one or more TIAs prior to an initial stroke.[40] Accordingly, symptomatic plaques are increasingly characterized by both the degree of stenosis and the presence of high-risk morphological features, which identify lesions with greater embolic potential and recurrent stroke risk. Arteries remain classified as symptomatic for six months following the initial event, reflecting the period of highest risk for recurrent stroke.[42]

In contrast, asymptomatic CAS is defined as the presence of hemodynamically significant stenosis in the absence of a neurological ischemic event within the preceding six months.[40] Although many asymptomatic plaques remain clinically stable, some harbor vulnerable features similar to those observed in symptomatic disease and may confer a substantially higher stroke risk than stenosis severity alone would suggest. In routine clinical practice, CAS is often identified during evaluation for nonspecific symptoms such as dizziness, generalized weakness, syncope or near-syncope, and visual disturbances; however, these presentations do not constitute ischemic events, and patients are therefore classified as asymptomatic even in the presence of high-grade stenosis.[39] Most cases of asymptomatic CAS are detected following identification of a carotid bruit on physical examination or as incidental findings on carotid computed tomography angiography (CTA) or magnetic resonance angiography (MRA) performed for unrelated indications.[38]

Screening for carotid artery stenosis

Identification of CAS enables early intervention aimed at reducing stroke risk.[6] While screening for asymptomatic CAS remains controversial, there is broad consensus supporting screening in symptomatic individuals, given the high risk of early stroke recurrence, which exceeds 18% within 30 days.[43]

In contrast, the annual stroke risk associated with asymptomatic CAS has declined substantially with contemporary optimal medical therapy.[44] Recent studies report annual stroke rates of approximately 1.3% for stenosis <75% and 2-2.5% for stenosis ≥75%, with even lower rates under intensive medical management.[44] A large U.S. cohort study demonstrated that severe asymptomatic CAS (70-99% stenosis) is uncommon, affecting only 0.5% of individuals older than 65 years, with a five-year ipsilateral stroke risk of 5%.[45] Similarly, meta-analyses estimate the prevalence of severe asymptomatic CAS (≥70% stenosis) in the general population to be approximately 3.1%.[23,46] These findings prompted the USPSTF recommendation against routine population-level screening for asymptomatic CAS, concluding

that low prevalence, modest absolute stroke risk, and potential harms of screening outweigh anticipated benefits.[47] Additional concerns include false-positive results, downstream testing, and the small but finite risk of stroke associated with confirmatory angiography when used as a second-line investigation.[6]

One hypothetical study estimated that 4348 individuals would need to be screened to prevent a single stroke over five years.[48] Despite these concerns, some guidelines endorse selective screening in high-risk asymptomatic individuals, particularly older adults and patients with carotid bruits or multiple atherosclerotic risk factors such as hypertension, diabetes, smoking, and hypercholesterolemia.[49] Historically, carotid bruits were viewed as markers of carotid atherosclerosis; however, studies have demonstrated limited diagnostic accuracy.[34] In the North American Symptomatic Carotid Endarterectomy Trial (NASCET), ipsilateral bruit detection demonstrated a sensitivity of 63% and specificity of 61% for identifying 70-99% stenosis, findings confirmed in subsequent studies.[50,51] As a result, auscultation has

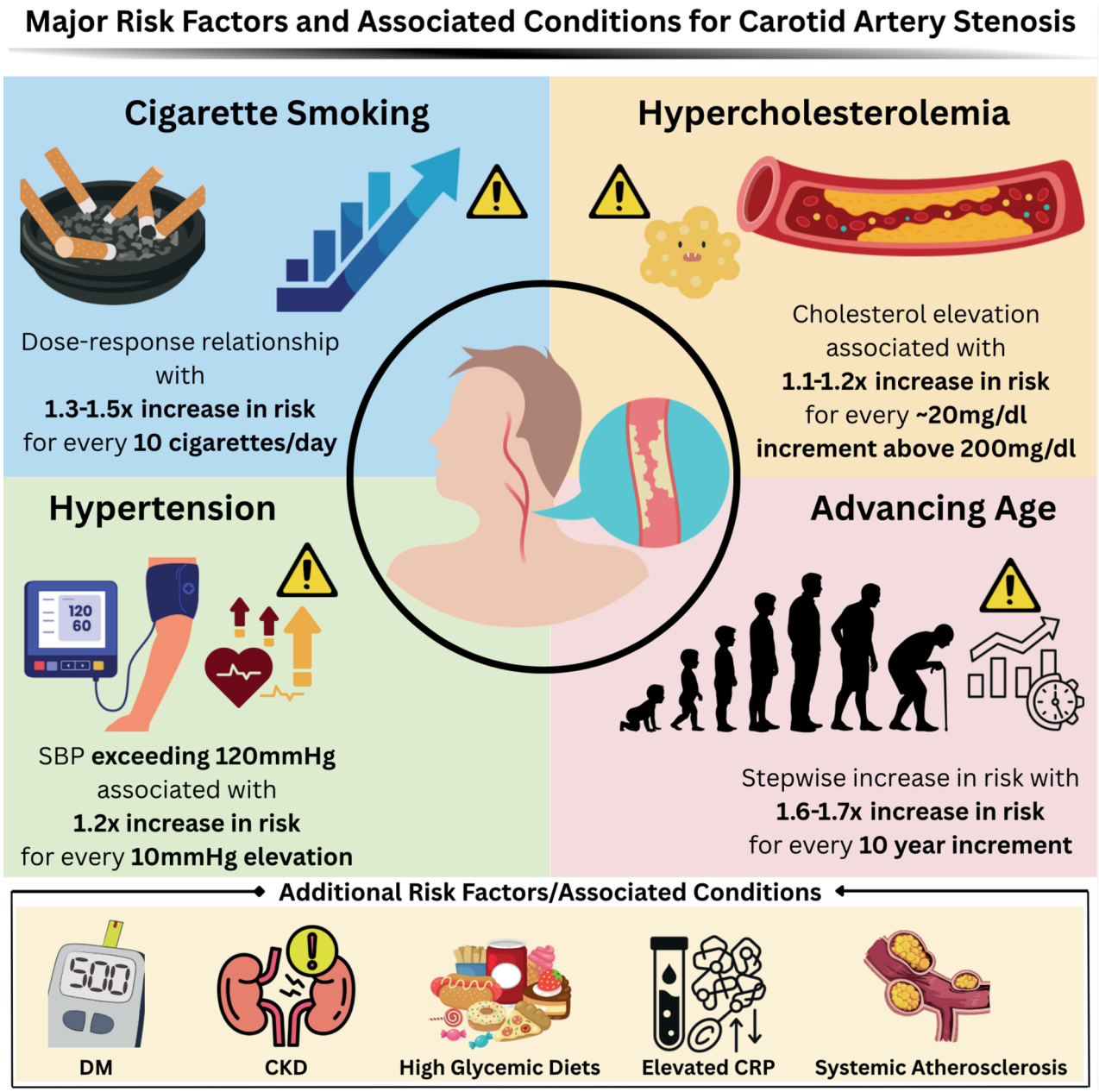

Figure 1. Risk factors and conditions associated with carotid artery stenosis.
Mg/dl, milligrams per deciliter; SBP, systolic blood pressure; mmHg, millimeters of mercury; DM, diabetes mellitus; CKD, chronic kidney disease; CRP, C-reactive protein.

largely been supplanted by carotid duplex ultrasonography as the preferred initial screening modality.[34]

Targeted screening of asymptomatic adults with elevated atherosclerotic risk, especially those with carotid bruit or established vascular risk factors, may improve the yield of screening strategies.[6] Importantly, the principal benefit of identifying asymptomatic CAS likely lies in facilitating aggressive medical therapy to reduce both cerebrovascular and overall cardiovascular risk, as optimal medical management has been estimated to be substantially more cost-effective than surgical intervention in this population.[52] However, no externally validated risk stratification tools currently exist to reliably identify asymptomatic individuals at highest risk for stroke or progression of CAS.[53] To date, no randomized controlled trials (RCTs) have evaluated screening versus no screening for CAS in the general population or demonstrated a reduction in stroke or cardiovascular outcomes attributable to screening alone.[6] Identification of severe asymptomatic CAS is constrained by its low prevalence in asymptomatic individuals and by uncertainty regarding which patients derive the incremental benefit of revascularization over contemporary medical therapy. Conversely, identification of moderate CAS or subclinical atherosclerosis broadens the target population and enables earlier intervention, most often through intensified medical management.[6] Detection of CAS has also been proposed as a motivator for lifestyle modification, although supporting evidence remains limited.[54]

Nevertheless, undetected CAS remains clinically important.[55] Longitudinal studies indicate that 9-29% of individuals with asymptomatic CAS experience disease progression and become symptomatic,[56] with annual stroke risk ranging from 1.6% to 3.2% depending on stenosis severity and plaque characteristics.[57] Importantly, CAS prevalence increases markedly with age, reaching 12.5% in men and 6.9% in women aged ≥70 years.[46] Established predictors include advancing age, male sex, smoking, hypercholesterolemia, and elevated systolic blood pressure.[58] Consistent with this, a Japanese cohort study demonstrated that higher atherosclerotic risk scores are associated with greater likelihood of stenosis >50%, including among patients referred for coronary artery bypass grafting, where nearly 22% have CAS >50%.[55] Moreover, stenosis >75% has also been identified as an independent predictor of perioperative stroke during cardiac surgery.[55] These observations inform guidelines from multiple societies, supporting screening in selected high-risk asymptomatic individuals, such as those with carotid bruits, peripheral arterial disease, coronary artery disease, or multiple vascular risk factors (Table 1).[59]

In addition, several clinical and imaging features have been proposed to identify asymptomatic patients at elevated stroke risk, including contralateral stroke, microemboli on transcranial Doppler, plaque echolucency, silent cerebral infarction, stenosis progression, impaired cerebrovascular reserve, plaque ulceration, and intraplaque hemorrhage on magnetic resonance imaging (MRI). In this context, the 2023 European Society for Vascular Surgery (ESVS) guidelines emphasize that carotid revascularization may be most appropriate in asymptomatic patients who exhibit one or more high-risk features for stroke (Table 2).[60]

Diagnosis of carotid artery stenosis

Accurate diagnosis and classification of CAS are critical for appropriate clinical management.[61] Advances in scientific research and imaging technology have substantially improved diagnostic capabilities; however, the diagnostic approach may differ between asymptomatic and symptomatic patients.[62]

Carotid auscultation should remain part of the routine physical examination in patients with vascular risk factors. Although

Table 1. Guideline recommendations on screening for asymptomatic carotid artery stenosis.

Guideline/Organization	Year	Recommendations
14-Societies	2011	CDUS is reasonable to screen for hemodynamically significant stenosis in asymptomatic patients with a carotid bruit. It may also be considered in asymptomatic individuals with symptomatic PAD, CAD, or atherosclerotic aortic aneurysms. However, because these patients already warrant medical therapy, the additional diagnosis of CAS may not alter clinical outcomes. Screening might further be considered in asymptomatic patients without known atherosclerosis who have ≥2 risk factors (hypertension, hyperlipidemia, tobacco use, or a family history of atherosclerosis or ischemic stroke), though clinical benefit of detecting CAS in this group remains uncertain.
USPSTF	2021	The USPSTF advises against routine screening for asymptomatic CAS in the general adult population.
SVS	2022	Routine screening for asymptomatic CAS is not recommended in individuals without cerebrovascular symptoms or major risk factors. Screening may be considered in selected high-risk asymptomatic patients, particularly those open to intervention if significant stenosis is detected including those with lower extremity PAD, undergoing CABG, age ≥55 years, with ≥2 atherosclerotic risk factors or active smoking, or those with diabetes, hypertension, CAD, or incidentally identified silent cerebral infarction on imaging.
ESVS	2023	Routine population screening for asymptomatic CAS is not recommended. Selective screening may be considered in patients with ≥2 vascular risk factors to guide risk-factor optimization and medical therapy, with goal of reducing long-term cardiovascular morbidity and mortality rather than identifying candidates for carotid intervention.

CDUS, carotid duplex ultrasound; PAD, peripheral arterial disease; CAD, coronary artery disease; CAS, carotid artery stenosis; USPSTF, United States Preventive Services Task Force; *SVS*, Society for Vascular Surgery; CCABG, coronary artery bypass graft; ES*VS*, European Society for Vascular Surgery.

Table 2. Features indicating high stroke risk in patients with asymptomatic high-grade carotid artery stenosis.

Clinical features	Contralateral TIA or stroke
Imaging features	Plaque cross-sectional area >40 sq.mm
	Progressive stenosis (>20%)
	Increased juxta-luminal black area
	Silent brain infarction on MRI
	≥1 micro-embolic signal in ≥1 hour of TCD examination
	Intraplaque hemorrhage on MRI
	Predominantly echolucent plaques
	Impaired cerebrovascular reserve

Adapted from the 2023 European Society for Vascular Surgery Guidelines.
TIA, transient ischemic attack; TCD, transcranial doppler; mm, millimeters; MRI, magnetic resonance imaging.

carotid bruits have limited diagnostic accuracy for CAS, they are useful markers of generalized atherosclerosis and are associated with increased risks of stroke, myocardial infarction, and cardiovascular death.[63] In asymptomatic individuals, auscultation may serve as an initial screening step; however, in patients presenting with TIA or stroke, evaluation cannot rely on auscultation alone, as carotid bruits have low sensitivity for detecting moderate or severe CAS.[64] While specificity is acceptable for carotid artery disease overall, it declines with increasing stenosis severity.[64] Moreover, since bruits result from turbulent flow, they may be present in mild stenosis and diminish or disappear in critical disease, necessitating vascular imaging in symptomatic patients.[39]

Four primary imaging modalities are used to evaluate CAS: noninvasive carotid duplex ultrasound (CDUS), CTA, MRA, and invasive digital subtraction angiography (DSA).[65] In asymptomatic patients, an evidence-based imaging strategy may follow a pragmatic diagnostic algorithm (Figure 2).[66]

The American Heart Association (AHA) recommends CDUS as the initial imaging modality to detect CAS, determine disease severity, and serve as the primary tool for longitudinal surveillance in both symptomatic and asymptomatic patients.[66,67] CDUS offers several advantages. It is noninvasive, widely available, does not require contrast administration, and is lower in cost than CTA or MRA, making it well suited for screening and repeated follow-up.[68,69] Technological advances, including high-resolution portable ultrasound systems, now permit reliable bedside evaluation of CAS comparable to larger units.[42] CDUS readily identifies atherosclerotic plaques, defined as focal wall thickening ≥50% greater than the surrounding vessel wall or intima-media protrusion ≥1.5 mm into the lumen.[70] Meta-analyses demonstrate high diagnostic performance, with sensitivities of up to 98% and specificities of 88% for detecting extracranial stenosis >50% when performed by experienced operators,[71] and sensitivity and specificity of 86% and 87%, respectively, compared with DSA for hemodynamically significant CAS.[72] Beyond stenosis grading, CDUS also helps characterize plaque morphology, which can refine risk stratification beyond luminal narrowing alone. Low gray-scale median values identify lipid-rich plaques with increased embolic potential.[73] In this regard, the recently introduced Plaque-Reporting and Data System (RADS) score offers a standardized framework for assessing plaque vul-

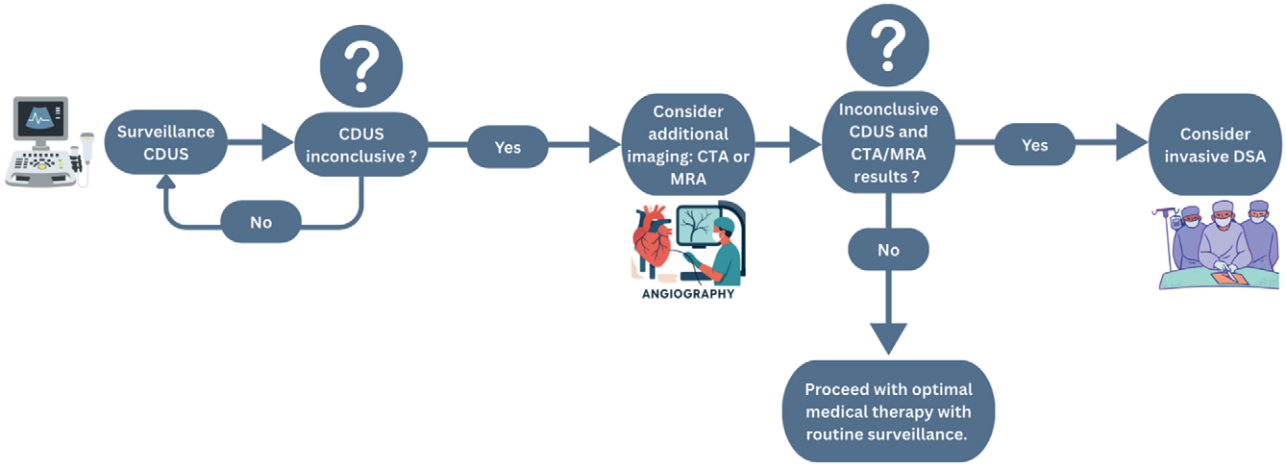

Figure 2. Flow diagram of imaging in asymptomatic carotid artery stenosis.
CDUS, carotid duplex ultrasound; CTA, computed tomographic angiography; MRA, magnetic resonance angiography; DSA, digital subtraction angiography.

nerability using ultrasound (Table 3).[74] Duplex ultrasound also supports stroke risk stratification in asymptomatic patients through detection of microemboli using transcranial Doppler, a marker of plaque instability and future stroke risk.[75-77] Additional applications include detection of carotid ulceration using three-dimensional ultrasound and longitudinal monitoring of plaque stability or stenosis progression.[74,78] Severity of CAS on CDUS is assessed using peak systolic velocity (PSV), end-diastolic velocity (EDV), gray-scale imaging, and spectral waveform analysis,[79] most commonly applying criteria established by the Society of Radiologists in Ultrasound Consensus Conference (Table 4).[80] However, Doppler ultrasound may overestimate or underestimate stenosis severity, and confirmatory imaging with CTA or MRA is recommended when results are equivocal or when revascularization is being considered.[38] Accordingly, individual ultrasound laboratories should validate diagnostic criteria against CTA or MRA and adopt standardized thresholds for CAS severity.[38] A major limitation of CDUS is its strong dependence on operator skill and experience,[39] and imaging is restricted to extracranial vessels, with the potential to overlook severely narrowed lumens.[81] In symptomatic patients, hemodynamically significant stenosis identified on CDUS warrants subsequent angiographic evaluation to exclude distal disease.[55] Despite these limitations, CDUS remains a rapid, inexpensive, and non-invasive first-line modality for CAS detection and surveillance, while emerging techniques such as contrast-enhanced ultrasound may further enhance plaque characterization, they are not yet used in routine clinical practice.[81]

CTA and MRA provide complementary noninvasive alternatives to CDUS by enabling visualization of both extracranial and intracranial vessels and allowing more direct measurement of CAS.[55] These modalities facilitate more precise assessment of stenosis severity and detailed evaluation of aortic arch anatomy, which is particularly valuable for procedural planning and selection of revascularization strategies.[65] Reported diagnostic performance varies by modality, with MRA demonstrating sensitivities of 91-95% and specificities of 88-99% for stenosis detection and plaque characterization, while CTA shows a sensitivity of approximately 77% and specificity of 95%. Importantly, the accuracy of both techniques is institution dependent, underscoring the need for clinicians to select imaging strategies based on physician expertise and validated protocols.[38] CTA offers rapid, high-resolution evaluation of the carotid system and permits direct assessment of plaque morphology and stenosis severity using the NASCET criteria (Table 5).[55,79] Further, the acquisition of three-dimensional dataset allows measurement in any projection, enhancing anatomic precision.[79] CTA is particularly advantageous in patients with complex anatomy, including severe vessel kinking, high carotid bifurcation stenosis, carotid dissection with intimal flap, pseudoaneurysm, or near-occlusive atherosclerotic disease that may be difficult to assess with CDUS or MRA.[55] In addition to evaluating the carotid bifurcation, CTA

Table 3. Carotid Plaque Reporting and Data System classification with corresponding cerebrovascular risk and imaging features.

Plaque-RADS score	Imaging features	Risk of cerebrovascular events
1	Normal vessel wall	Absent
2	Medial wall thickness <3mm	Low
3	Medial wall thickness >3mm or healed ulcerated plaque	Moderate
3a	Medial wall thickness >3mm + lipid rich necrotic core + thick fibrous cap	Moderate
3b	Medial wall thickness >3mm + lipid rich necrotic core + thin fibrous cap	Moderate
3c	Healed ulcerated plaque	Moderate
4	Complicated plaque	High
4a	Intraplaque hemorrhage	High
4b	Ruptured fibrous cap + necrotic core	High
4c	Intraluminal thrombus	High

Plaque-RADS, Carotid Plaque Reporting and Data System; mm, millimeters.

Table 4. The Society of Radiologists in Ultrasound blood flow velocity criteria for diagnosis of carotid artery stenosis.

Category	ICA PSV (cm/s)	ICA/CCA PSV ratio	ICA EDV (cm/s)	Sonographic/Doppler findings
Normal	<125	<2.0	<40	No plaque or intimal thickening
<50% stenosis	<125	<2.0	<40	Plaque or intimal thickening present
50-69% stenosis	125-230	2.0-4.0	40-100	Visible plaque on grayscale ultrasound
≥70% stenosis	>230	>4.0	>100	Plaque with luminal narrowing on grayscale and color Doppler
Near occlusion	Variable (high/low/undetectable)	Variable	Variable	Markedly narrow lumen with “trickle flow” on color or power Doppler
Total occlusion (100%)	No detectable flow	-	-	No luminal patency and no flow on color, spectral, or power Doppler

ICA, internal carotid artery; PSV, peak systolic volume; CCA, common carotid artery; EDV, end-diastolic volume; cm/s, centimeters per second.

provides comprehensive assessment of aortic arch plaque burden, great vessel origins, common carotid artery disease and tortuosity, distal internal carotid artery anatomy, and vessel diameters. Critically, CTA allows identification of dense and concentric calcification that may be underappreciated with conventional angiography,[79] making it particularly useful for procedural planning. However, CTA has important limitations. Heavy calcification may result in overestimation of stenosis severity, as calcium can obscure the lumen and limit accurate measurement. In such cases, CDUS or MRA may provide more reliable noninvasive assessment. Thus, although CTA is often regarded as the 'gold standard' among noninvasive imaging modalities, careful interpretation is required, particularly in heavily calcified lesions.[79] Additional well-recognized drawbacks of CTA include exposure to ionizing radiation and the risk of contrast-induced nephropathy.[55]

MRA demonstrates diagnostic performance comparable to CTA for identifying CAS and high-grade occlusion, while being less affected by surrounding bone or vascular calcification and allowing characterization of plaque features such as ulceration or fissuring, which may inform plaque stability.[82] Importantly, MRA provides reliable assessment of vessel stenosis in the setting of extensive arterial calcification without exposing patients to ionizing radiation.[81] Accordingly, MRA is particularly well suited for patients in whom radiation exposure is a concern or for evaluation of intracranial stenosis, where adjacent bone may obscure the vessel lumen on CTA.[55] Wardlaw and colleagues demonstrated that contrast-enhanced MRA was more sensitive and specific for detecting carotid occlusion or severe stenosis (sensitivity 0.94; specificity 0.93) than CDUS, non-contrast MRA, or CTA.[83] Additionally, three-dimensional time-of-flight MRA does not require contrast administration and offers the highest spatial resolution among commonly used MRA techniques, making it a valuable option for patients who cannot receive gadolinium-based contrast agents.[65,79] Despite these advantages, MRA has notable limitations. Its inability to visualize calcium restricts its utility for procedural planning, as calcified plaques and mural atheroma features are more clearly depicted by CTA and are less conspicuous on MRA, rendering CTA the preferred modality for planning carotid interventions.[79] Additional limitations include that MRA is also more time-consuming than CTA,[55] gadolinium contrast carries a risk of nephrotoxicity, and the technique may overestimate stenosis severity compared with CDUS or CTA, necessitating caution in interpretation.[84,85]

Nonetheless, MRA is suboptimal for screening asymptomatic CAS because it may overestimate stenosis severity, is time-consuming, and costly.[86] CTA, although highly accurate for stenosis quantification, is similarly unsuitable for screening due to cost, radiation exposure, and iodinated contrast risk, but is preferred over MRA in the presence of vascular calcification.[87] Accordingly, CTA and MRA are primarily used as second-line modalities following ultrasound detection of CAS.[88] Overall, CDUS, CTA, and MRA demonstrate high accuracy for severe (70-99%) stenosis, with lower performance for moderate (50-69%) disease.[83]

DSA is traditionally regarded as the 'gold standard' imaging modality for diagnosing CAS.[79] It generates high-contrast vascular images by subtracting pre- and post-contrast X-ray acquisitions, allowing detailed visualization with reduced contrast volume and smaller catheter sizes.[68] DSA provides comprehensive assessment of the head and neck vasculature, including collateral circulation, adjacent arterial disease, and plaque morphology and severity.[81] Although DSA offers the most accurate measurement of luminal stenosis, mural plaque burden is better characterized with CTA or CDUS.[79] Major limitations include higher cost, invasiveness, and a small but finite risk of serious complications, including stroke.[55,79] Consequently, noninvasive imaging has largely replaced DSA for initial evaluation, and it has no role as a screening tool.[6,65] DSA is now reserved for select problem-solving scenarios when uncertainty regarding disease severity or symptom etiology persists after noninvasive imaging.[79]

Table 5. Carotid artery stenosis grading according to the North American Symptomatic Carotid Endarterectomy Trial criteria.

Severity grade	Percent stenosis
Mild	0-49
Moderate	50-69
Severe	70-99
Complete occlusion	100

Plaque morphology and vulnerability

Luminal stenosis does not fully predict stroke risk in CAS. High-risk plaque features, including intraplaque hemorrhage, a lipid-rich necrotic core, fibrous cap thinning or rupture, and ulceration, account for carotid-territory ischemia even when stenosis is less than 50%.[89,90] Multimodality plaque phenotyping, as standardized by Plaque-RADS, improves stroke risk stratification beyond traditional stenosis grading, particularly in mild and moderate stenosis.[90,91] In asymptomatic CAS, plaque vulnerability identifies the small subgroup at higher risk despite optimal medical therapy. In symptomatic CAS, vulnerable plaques signal greater embolic potential and increased risk of recurrent events.[89,91] Plaque morphology may guide future treatment by supporting more selective revascularization, clearer risk communication, and morphology-based trial design, although this approach remains under investigation.

Treatment of asymptomatic carotid artery stenosis

Treatment recommendations for CAS are guided by clinical practice guidelines from the American and European Societies of Vascular Surgery and the American Heart Association/American Stroke Association (AHA/ASA).[60,67,92,93] Regardless of revascularization status, all patients with asymptomatic CAS should receive optimal medical therapy to address risk factors and co-

morbidities.[94] Optimal medical therapy focuses on comprehensive cardiovascular risk reduction through dietary and lifestyle modification and pharmacologic treatment, aiming to reduce both cerebrovascular and overall cardiovascular events (Table 6).[95,96] Contemporary evidence suggests that aggressive lifestyle modification and optimal medical therapy can reduce annual stroke rates in asymptomatic CAS to approximately 1-2%.[52,97,98] Thus, optimal medical therapy remains the cornerstone of management for asymptomatic CAS (Figure 3).

Optimal medical therapy: lifestyle modifications

Medical therapy begins with smoking cessation,[99] as tobacco use is a major driver of CAS progression, ipsilateral cerebrovascular events, and the need for revascularization.[100] A meta-analysis of 14 studies showed a 12% increase in stroke risk for every additional five cigarettes smoked per day.[101] Other forms of smoking are also harmful. Cannabis use has been independently associated with atherosclerotic stroke risk.[102] Accordingly, all asymptomatic patients with CAS who smoke should receive structured cessation counseling and pharmacologic therapy, including varenicline or bupropion with nicotine replacement.[94] Additionally, patient's visualization of carotid plaque using ultrasound images has been shown to increase smoking cessation rates more than sixfold.[103]

Lifestyle modification is central to risk reduction and includes regular physical activity, healthy diet, weight loss, moderation of alcohol intake, and optimal blood pressure and glycemic control.[95] In the Health Professionals Study and Nurses' Health Study, adherence to five healthy lifestyle behaviors: non-smoking, moderate alcohol intake, BMI <25, regular physical activity, and a healthy diet, was associated with an 80% reduction in stroke risk.[104] Physical activity is particularly important, as poor cardiorespiratory fitness predicts long-term vascular events and mortality, and exercise has been shown to slow carotid atherosclerosis progression on imaging studies.[105-107] Current recommendations support ≥30 minutes of aerobic exercise on at least five days per week, combined with a diet low in saturated fat.[35]

Dietary composition also influences stroke risk.[108] A meta-analysis of approximately 258,000 individuals found that intake of more than five daily servings of fruits and vegetables was associated with lower ischemic stroke risk compared with fewer than three servings.[109] High sodium intake has consistently been linked to increased stroke risk, likely mediated by blood pressure effects, supporting sodium restriction and increased fruit and vegetable consumption in patients with CAS.[108] The Mediterranean diet has the strongest evidence base for vascular prevention and emphasizes fruits,[105] vegetables, whole grains, fish, olive oil, low-fat dairy products, and moderate alcohol intake.[110,111] Two trials demonstrated significant reductions in cardiovascular events with Mediterranean-style diets in both primary and secondary prevention settings.[112,113]

Although data linking obesity specifically to CAS are limited, increased adiposity has been associated with carotid atherosclerosis. In a cohort of Italian women, elevated BMI and waist-to-hip ratio were independently associated with carotid wall thickening.[114] While evidence for stroke reduction with weight loss is limited,[108] a meta-analysis of more than 2.2 million individuals showed a 64% higher ischemic stroke risk with BMI >30 compared with BMI 18.5-24.9.[115] Accordingly, patients with CAS should be counseled to pursue weight reduction with a target BMI <25 kg/m².[116]

Table 6. Summary of optimal medical therapy.

Domain	Details
Diet	Mediterranean-style diet
Physical activity	Moderate intensity ≥150min/week
Smoking	Cessation counseling + pharmacotherapy (varenicline, bupropion, nicotine replacement)
Antithrombotic therapy	1. Aspirin 75-325mg daily 2. Aspirin + rivaroxaban 2.5mg BID 3. Clopidogrel 75mg daily or ticagrelor 90mg BID if aspirin-intolerant
Lipid lowering therapy	1. LDL target <70mg/dl (<54 mg/dl very high-risk) 2. High-intensity statin 3. Add ezetimibe or PCSK9 inhibitor if needed 4. Consider icosapent ethyl for elevated triglycerides
Blood pressure control	1. Target <13080mmHg 2. Prefer ACEi/ARB due to high prevalence of renovascular hypertension 3. May require combination therapy
Glucose control	1. Target HbA1c <7.0% 2. Metformin, GLP-1RA, SGLT2-i are preferred

LDL, low-density lipoprotein; mg, milligrams; min, minute; BID, twice daily; HbA1c, hemoglobin A1c; mmHg, millimeters of mercury; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GLP-1RA, glucagon-like peptide-1 receptor antagonist; SGLT2-i, sodium-glucose cotransporter-2 inhibitor, PCSK9, proprotein convertase subtilisin/kexin type 9.

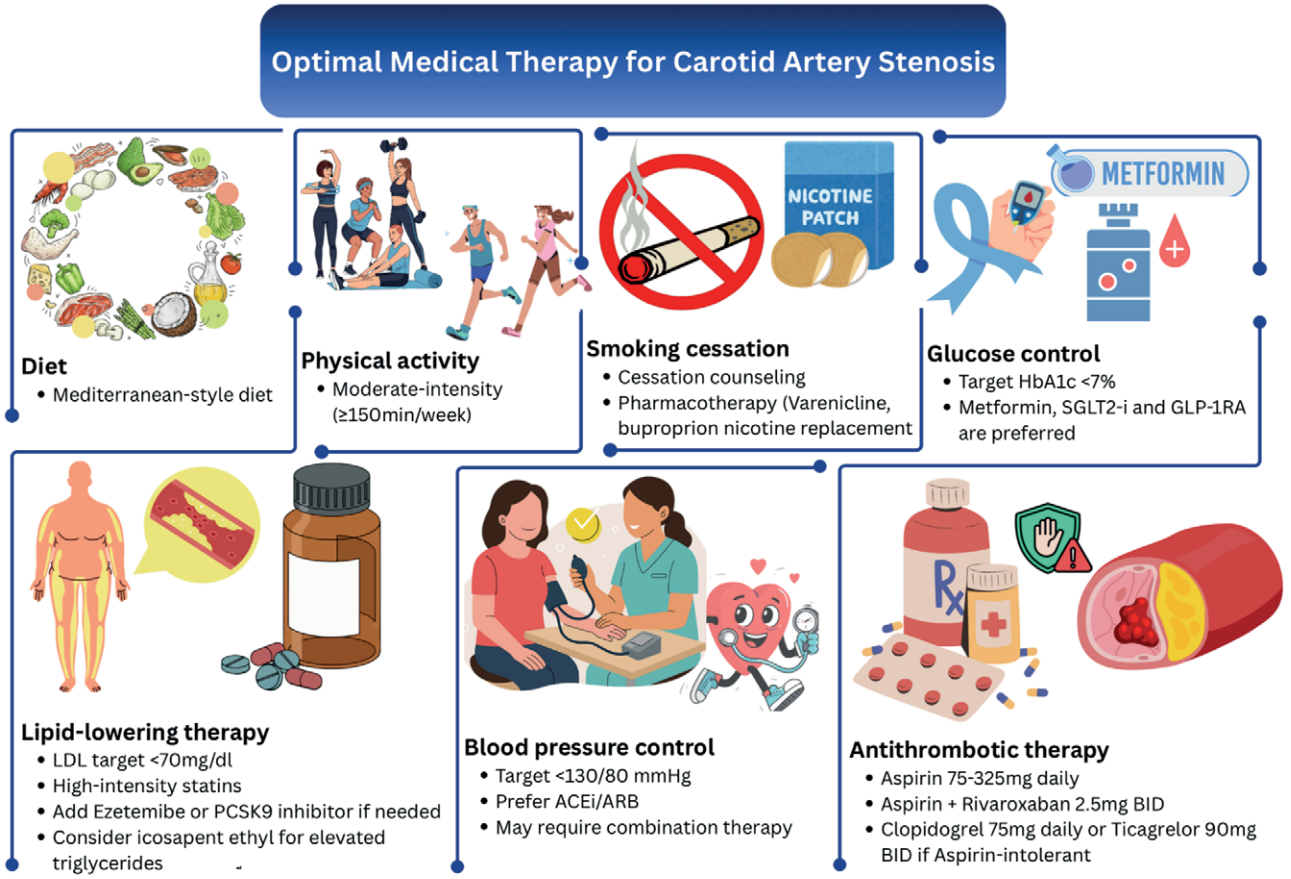

Figure 3. Optimal medical therapy.
Min, minutes; HbA1c, hemoglobin A1c; SGLT2-i, sodium-glucose co-transporter-2 inhibitor; GLP1-1RA, glucagon-like peptide-1 receptor antagonist; LDL, low-density lipoprotein; mg/dl, milligrams per deciliter; mmHg, millimeters of mercury; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; mg, milligrams; BID, twice a day; PCSK9, proprotein convertase subtilisin/kexin type 9.

Optimal medical therapy: pharmacological strategies

Blood pressure control is associated with slowed progression and partial regression of CAS.[68] In a longitudinal cohort with 44 months of follow-up, hypertension was consistently linked to higher stroke risk across all degrees of stenosis.[117] Several antihypertensive classes including thiazides, calcium channel blockers (CCB), ACE inhibitors (ACE-i), and angiotensin receptor blockers (ARB) effectively reduce blood pressure and stroke risk.[118] Given the frequent coexistence of renal artery stenosis in asymptomatic patients, renin-angiotensin system inhibitors are particularly relevant and have demonstrated benefits in attenuating carotid atherosclerosis progression and reducing vascular events.[119-121] Perindopril lowers blood pressure without compromising cerebral perfusion in patients with hypertensive stroke and moderate-to-severe carotid disease.[122] A target blood pressure <140/90 mmHg is recommended, with lower goals (<130/80 mmHg) appropriate for selected high-risk patients, including those with diabetes or chronic kidney disease.[116]

Diabetes mellitus is a well-established risk factor for both stroke and CAS.[108] In a cohort of 1058 asymptomatic individuals undergoing carotid duplex screening, diabetes emerged as the strongest predictor of severe stenosis (>70%), conferring more than a threefold increased risk.[123] Similarly, severe CAS was markedly more prevalent among patients with non-insulin-dependent diabetes and elevated fasting glucose than in controls (8.2% *vs*. 0.7%).[108] Although direct evidence that glycemic control modifies CAS progression is lacking, its established microvascular and macrovascular benefits justify routine diabetes screening in asymptomatic CAS and targeting a hemoglobin A1c <7.0%.[108] Glucose-lowering agents with proven cardiovascular benefit including metformin, sodium-glucose cotransporter-2 inhibitors (SGLT2-i), and glucagon-like peptide-1 receptor agonists (GLP-1RA) are preferred.[94]

Oral antiplatelet therapy remains central to the management of atherosclerotic disease, including asymptomatic CAS.[94] The AHA recommends daily low-dose aspirin (81 mg) for primary stroke prevention in adults aged 40-59 years with a ≥20% 10-year stroke risk,[94] while the 2023 ES*VS* guidelines

endorse aspirin (81-325 mg daily) as first-line therapy, followed by clopidogrel (75 mg daily) or dipyridamole (200 mg twice daily) as alternatives.[60] Dual antiplatelet therapy with aspirin and clopidogrel is recommended after carotid stenting.[60,67] In the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial, among nearly 2000 patients with asymptomatic CAS ≥50% or prior carotid revascularization, low-dose rivaroxaban plus aspirin reduced major cardiovascular events compared with aspirin alone, without excess major bleeding in the carotid subgroup.[124,125] These results suggest that the aspirin/rivaroxaban combination is a reasonable alternative therapy for individuals with asymptomatic CAS.[116] However, given ongoing uncertainty regarding net benefit in asymptomatic CAS, antiplatelet therapy may be best targeted to individuals with high-risk plaque features identified on imaging.[94]

Treatment of dyslipidemia, particularly with statins, has had a substantial impact on stroke prevention.[108] Evidence from 18 RCTs including 56,934 participants indicates that statin therapy confers significant reductions in mortality, stroke, and revascularization outcomes.[126] In a meta-analysis of nine statin trials, every 10% reduction in LDL-C corresponded to a 0.73% annual reduction in carotid intima-media thickness, however it was statistically non-significant.[127] Moreover, statin use during carotid revascularization was associated with threefold lower 30-day stroke risk and fivefold lower mortality.[128-131] Accordingly, combination lipid-lowering therapy with statins and ezetimibe is recommended for asymptomatic individuals to reduce long-term risks of stroke and cardiovascular events.[60,132] For patients with persistently elevated triglycerides despite statin therapy, icosapent ethyl may provide additional cardiovascular risk reduction. In the REDUCE-IT (Reduction of Cardiovascular Events With Icosapent Ethyl-Intervention Trial), icosapent ethyl significantly reduced major adverse cardiovascular events, including ischemic stroke, in statin-treated patients with established atherosclerotic cardiovascular disease or high cardiovascular risk and elevated triglyceride levels.[133] This supported its use as an adjunctive therapy in appropriately selected patients with asymptomatic CAS and residual lipid-related risk. The 2018 AHA cholesterol guidelines endorse an LDL-C target of <70 mg/dL in patients with atherosclerotic disease, including asymptomatic CAS,[134] while high-intensity statins provide superior plaque regression and stroke prevention, typically achieving ≥50% LDL-C reduction.[116,135] For very high-risk patients, a more stringent LDL-C goal of <54 mg/dL is recommended (94). PCSK9 inhibitors represent an adjunctive therapy in advanced atherosclerosis, lowering LDL-C by up to 70% in high-risk patients already receiving statins.[136-138] The 2023 ES*VS* carotid guidelines provide a weak recommendation for PCSK9 inhibitors in statin-intolerant asymptomatic CAS, with or without ezetimibe.[60] Nonetheless, given the heterogeneity of asymptomatic CAS with respect to patient risk, patients with vulnerable plaques may warrant particularly intensive lipid-lowering strategies to further mitigate stroke risk.[94]

Revascularization in asymptomatic carotid artery stenosis

Selection of asymptomatic patients for carotid revascularization remains contentious, particularly as contemporary data show a marked decline in annual ipsilateral stroke risk among individuals with >50% asymptomatic CAS receiving optimal medical therapy.[139] These trends have prompted renewed scrutiny of prophylactic intervention in the modern medical therapy era.[52,97,140] Nonetheless, current practice remains largely grounded in historical level 1 evidence from RCTs conducted more than two decades ago.[141-148] Table 7, which demonstrated a modest but consistent benefit of CEA in carefully selected patients, namely those with 60-99% stenosis, ≥5-year life expectancy, and limited competing comorbidity.[32,69,141,146,149] Reflecting ongoing uncertainty, contemporary guidelines vary considerably.[116] A review of four European guidelines published between 2017 and 2021 revealed discordant recommendations, ranging from broad endorsement of CEA in surgically fit patients to more restrictive use limited to individuals with additional high-risk features despite optimal medical therapy.[150] Subsequent reanalysis of these studies and observational data have contributed to more broadened criteria, allowing consideration of revascularization in selected patients with >70% stenosis and reasonable life expectancy.[66]

Most contemporary evidence on medical therapy in asymptomatic CAS is derived from patients with moderate stenosis, limiting applicability to severe disease. Despite overall reductions in stroke risk with modern medical therapy, systematic reviews show that patients with severe asymptomatic CAS (70-99%) continue to experience significantly higher ipsilateral stroke rates than those with moderate stenosis (50-69%), confirming a severity-dependent risk gradient.[151] Meta-analytic data further demonstrate a graded relationship between stenosis severity and stroke risk, with severe, particularly 80-99% stenosis, conferring more than a twofold higher risk, while medically treated moderate disease carries very low event rates.[152] These observations suggest that any incremental benefit of revascularization is largely confined to severe disease, a position reflected in the 2022 Society for Vascular Surgery guidelines, which strongly recommend CEA plus optimal medical therapy over medical therapy alone in low surgical-risk patients with >70% asymptomatic CAS.[67,153] Nonetheless, the landmark trials supporting revascularization for asymptomatic CAS are now 20-30 years old and predate major advances in medical therapy and procedural techniques.[69] Contemporary improvements in risk-factor control appears to have substantially lowered baseline stroke risk, with recent data showing a 5-year stroke risk of approximately 3.1% with medical therapy alone, far lower than rates reported in earlier trials.[141,144,146] By comparison, ACAS and ACST reported 5-year stroke risks of 11% and 11.8%, respectively Consistent with this evolution, subsequent randomized and observational studies demonstrate progressively lower event rates in patients with high-grade asymptomatic CAS.[45,154] To-

gether, these trends have reignited debate regarding the risk-benefit balance of prophylactic carotid revascularization in asymptomatic patients.[69]

Recent trials have sought to address this evidence gap. In the Stent-Protected Angioplasty versus Carotid Endarterectomy 2 (SPACE-2) trial, which compared CEA, carotid stenting, and optimal medical therapy in just over 500 asymptomatic patients, no significant differences were observed in periprocedural or long-term ipsilateral stroke outcomes, although the trial was limited by small sample size.[145] Similarly, the Second European Carotid Surgery Trial (ECST-2), found no added benefit of revascularization over optimal medical therapy at two years in patients with asymptomatic or symptomatic CAS ≥50% and low predicted stroke risk.[147] Consistent with these findings, a contemporary retrospective cohort study reported similar 5-year fatal and nonfatal stroke rates between asymptomatic patients managed with carotid stenting and those treated medically.[155] Collectively, data from SPACE-2, ECST-2, Second asymptomatic carotid surgery trial (ACST-2), and contemporary observational studies suggest broad equipoise among CEA, carotid stenting, and optimal medical therapy for asymptomatic CAS, underscoring the diminishing incremental benefit of revascularization in the modern medical therapy era. Although factors such as advanced age, prior infarction, stenosis severity or progression, and high-risk plaque features are associated with increased stroke risk and often guide intervention, none have consistently identified subgroups that derive added benefit from revascularization in RCTs incorporating optimal medical therapy alone.[139,156] Accordingly, a central unresolved question is whether revascularization still offers meaningful net benefit in a carefully selected "high-risk" asymptomatic subgroup despite contemporary optimal medical therapy?

The recently published Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2),[148] was designed to determine whether carotid revascularization provides incremental benefit over intensive optimal medical therapy alone in patients with high-grade (≥70%) asymptomatic CAS. In two parallel randomized comparisons in which all participants received protocol-driven optimal medical therapy, the carotid stenting comparison suggested a modest reduction in the primary composite endpoint (any stroke or death, or ipsilateral ischemic stroke) relative to medical therapy alone, whereas the CEA did not demonstrate a statistically significant advantage over medical therapy alone. This raises the question of whether carotid stenting should be widely adopted? However, interpretation should remain cautious. The absolute event rates were low, and the observed differences were driven by relatively few outcome events, making estimates vulnerable to small changes in event counts. In addition, outcomes were achieved in the setting of highly selected participants and expert

Table 7. Randomized controlled trials of asymptomatic carotid artery stenosis.

Trial	Year	No.	Population	Endpoint	Arm 1	Arm 2	Arm 3
VACS	1993	444	Asymptomatic patients with >50% stenosis	Ipsilateral TIA or stroke under follow-up	OMT: 20.6%	CEA: 8.0%	-
ACAS	1995	1659	Asymptomatic patients with ≥60% stenosis	Perioperative stoke or death, ipsilateral stroke under follow-up	OMT: 11.0%	CEA: 5.1%	-
ACST	2004	3120	Asymptomatic patients with ≥60% stenosis	Perioperative stroke or death, any stoke under follow-up	OMT: 11.8%	CEA: 6.4%	-
ACT-1	2016	1453	Asymptomatic patients with ≥70% stenosis	Perioperative stroke, death, MI, or ipsilateral stroke at 1 year	CEA: 3.4%	TF-CAS: 3.8%	-
ACST-2	2021	3625	Asymptomatic patients with ≥60% stenosis	Perioperative stroke or death, any stroke under follow-up	CEA: 7.2%	TF-CAS: 9.0%	-
SPACE-2	2022	513	Asymptomatic patients with ≥70% stenosis	Perioperative stroke or death, ipsilateral stroke within 5 years	CEA: 2.5%	TF-CAS: 4.4%	OMT: 3.1%
ECST-2	2025	258	Asymptomatic or low to medium-risk symptomatic patients with ≥50% stenosis	Composite of periprocedural stroke, MI, or death	OMT: 21%	CEA or TF-CAS: 22%	-
CREST-2 Trial (N=1240)	2026	2485	Asymptomatic patients with ≥70% stenosis	Periprocedural stroke or death, or postprocedural ipsilateral stroke within 4 years	Stenting trial (N=1245) OMT alone: 6.0% OMT + TF-CAS: 2.8%	CEA trial OMT alone: 5.3% OMT + CEA: 3.7%	-

VACS, Veterans Administrative Cooperative Study; ACAS, Asymptomatic Carotid Atherosclerosis Study; ACST, Asymptomatic Carotid Surgery Trial; ACT-1, Carotid Angioplasty and Stenting Versus Endarterectomy; ACST-2, Second Asymptomatic Carotid Surgery Trial; SPACE-2, Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis; ECST-2, Second European Carotid Surgery Trial; CREST-2, Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis; TIA, transient ischemic attack; MI, myocardial infarction; OMT, optimal medical therapy; CEA, carotid endarterectomy; TF-CAS, transfemoral carotid artery stenting.

operators, which may limit generalizability to routine practice where peri-procedural performance varies across centers. While intensive medical therapy targets were protocolized, real-world achievement of risk-factor goals (*e.g.*, systolic blood pressure, LDL-C, and glycemic control) remains imperfect and may influence comparative effectiveness. Finally, any potential long-term reduction in ipsilateral stroke must be weighed against early procedural risk, as revascularization introduces a non-zero peri-procedural stroke/death risk that does not exist with medical therapy alone.[157]

Overall, contemporary evidence indicates that routine revascularization for asymptomatic CAS confers only limited incremental benefit beyond optimal medical therapy. Findings from SPACE-2, ECST-2, and CREST-2 support an initial strategy of intensive medical management for most patients, given the low absolute stroke risk achieved with modern risk-factor control. Revascularization may still be appropriate in carefully selected individuals with severe stenosis (≥70-80%), good life expectancy (≥5 years), low procedural risk (perioperative stroke or death <3%), intolerance to medical therapy, or strong informed preference, although current data are insufficient to establish the superiority of carotid stenting over CEA, and ongoing follow-up from contemporary trials will further clarify the comparative benefits and risks of each approach. Future advances will depend on identifying the small subset of asymptomatic patients who develop symptoms despite optimal medical therapy, particularly through MRI-based detection of intraplaque hemorrhage as a potent marker of stroke risk.[157]

Treatment of symptomatic carotid artery stenosis

Management of symptomatic CAS is more straightforward than that of asymptomatic disease because stroke risk correlates more directly with stenosis severity, and the absolute risk of recurrence is higher, making the benefits of revascularization more readily apparent.[65] Regardless of symptom status, all patients should receive optimal medical therapy, including antiplatelet agents, intensive lipid-lowering therapy, and antihypertensive treatment.[66,86,108] Revascularization is not recommended for complete carotid occlusion or for symptomatic patients with mild (<50%) stenosis.[158]

Following a TIA or minor stroke, rapid evaluation and initiation of secondary prevention are critical as it can reduce early stroke recurrence by up to 80%.[159] Patients presenting within 4.5 hours of symptom onset should be assessed for intravenous thrombolysis, while those with large-vessel occlusion within 24 hours should be considered for mechanical thrombectomy to limit neurologic injury.[60] Aspirin should be initiated promptly, and early dual antiplatelet therapy with aspirin and clopidogrel may provide additional benefit over aspirin alone after TIA or minor stroke.[160] Carotid revascularization (CEA or stenting) within 6-14 days after thrombolysis may be considered in symptomatic patients with >50% stenosis, provided there is no intracranial hemorrhage or significant edema, neurologic recovery is rapid (modified Rankin score ≤2), infarct size involves <30% of the ipsilateral middle cerebral artery territory, and vessel patency has been restored.[139,161] Patients with carotid stenosis presenting with stroke in evolution or crescendo TIAs may require urgent revascularization with CEA or stenting.[60] However, perioperative risk is substantial, with stroke or death rates reaching up to 20% for stroke-in-evolution and approximately 11% for crescendo TIA, depending on age and comorbidity burden.[67,162] In carefully selected patients with infarct volumes <30% of the middle cerebral artery territory, emergency CEA performed at specialized centers can be undertaken with lower risks, approximating 8% for stroke in evolution and 2-7% for crescendo TIAs.[67,163] Nonetheless, potential benefits of restoring cerebral perfusion must be weighed against risks of hemorrhagic transformation and reperfusion injury.[60] Accordingly, revascularization is generally avoided after recent severe disabling stroke, particularly when infarction exceeds 30% of the ipsilateral middle cerebral artery territory, the modified Rankin score is >3, or consciousness is significantly impaired.[60]

Patients with stroke within the preceding six months attributable to CAS require optimal medical therapy and multidisciplinary evaluation for potential carotid revascularization to prevent recurrence. Dual antiplatelet therapy with aspirin plus clopidogrel or ticagrelor is central to secondary prevention in symptomatic CAS but necessitates careful monitoring for extracranial and gastrointestinal bleeding.[139] In patients not undergoing CEA or stenting after TIA or stroke, dual antiplatelet therapy for 90 days is recommended. Dipyridamole or ticagrelor monotherapy may be used in those intolerant of aspirin or clopidogrel.[67,139,164] RCTs have demonstrated comparable efficacy among aspirin-extended-release dipyridamole, clopidogrel, and aspirin-based dual regimens for embolic reduction and secondary stroke prevention.[165,166] For candidates with 50-99% stenosis undergoing CEA or stenting, aspirin plus clopidogrel should be initiated after exclusion of intracranial hemorrhage and continued for at least four weeks following stenting, with vigilance for bleeding complications. Patients with recurrent events despite dual therapy should be evaluated for clopidogrel resistance, considered for ticagrelor, or reassessed for revascularization.[67,139,167-169] Dual antiplatelet therapy is also indicated in patients with concomitant symptomatic coronary disease, recent coronary stenting, or severe peripheral arterial disease.[170]

Lipid-lowering therapy with statins, with or without ezetimibe, is recommended for long-term prevention of stroke and cardiovascular events in patients with symptomatic CAS.[139] Beyond lipid reduction, statins stabilize carotid plaque by reducing angiogenic vascular endothelial growth factor (VEGF) expression and intraplaque neovascularization, thereby attenuating vascular inflammation and significantly lowering mortality and fatal and nonfatal stroke risk.[126,171] Therefore, statins should be continued peri- and post-intervention to reduce the risk of stroke, myocardial infarction, and heart failure.[60] When LDL-C targets are not achieved with maximally tolerated statins, ezetimibe may be added, with PCSK9 inhibitors considered for persistent dyslipidemia despite combination therapy.[60] In patients with

multiple vascular risk factors or concomitant symptomatic coronary artery disease, targeting an LDL-C level <70 mg/dL may be particularly appropriate.[170] Blood pressure reduction in patients with CAS is generally safe when performed gradually; however, individuals with severe bilateral or critical unilateral stenosis should avoid abrupt lowering and require cautious antihypertensive titration.[172] Antihypertensive therapy confers a significant reduction in stroke risk, as demonstrated in a meta-analysis of 13 trials, although perioperative hypotension is more common in patients receiving ≥2 antihypertensive agents.[173,174] Moreover, in symptomatic CAS, meticulous glycemic control is essential to avoid both hyperglycemia and hypoglycemia.[38] Further, beta-blockers should be continued in patients already receiving them and considered perioperatively in those at intermediate or high ischemic risk or with ≥3 cardiac risk factors, given that myocardial infarction remains the most common non-neurologic complication after CEA. Nonetheless, initiation of beta-blockers should occur only with close hemodynamic monitoring and not within 24 hours of surgery to minimize hypotension and bradycardia.[38]

Revascularization should be considered in symptomatic patients with moderate to severe CAS.[38] Two landmark multicenter RCTs established the superiority of CEA over medical therapy alone in this population.[175,176] In the NASCET trial, CEA reduced the 5-year risk of death or stroke by 29% among patients with 50-69% stenosis and provided a marked benefit in those with ≥70% stenosis, prompting early trial termination due to significantly lower rates of major stroke or death (8.0% *vs*. 19.1%) and ipsilateral stroke (9.0% *vs*. 26.0%) compared with medical therapy.[175] Similarly, the European Carotid Surgery Trial (ECST) demonstrated a significant reduction in major stroke or death with CEA in symptomatic patients with ≥80% stenosis.[176] Accordingly, current AHA/ASA guidelines recommend CEA for patients with symptomatic 70-99% stenosis within the prior six months when perioperative risk is <6%, and for selected patients with 50-69% stenosis based on age, sex, and comorbidities. Revascularization is not recommended for stenosis <50%, for which optimal medical therapy is indicated.[177] Table 8 lists the results of trials in symptomatic and some asymptomatic patients with moderate or severe stenosis.[175,176,178-181]

In a meta-analysis of 10 RCTs comparing CEA and carotid stenting in symptomatic patients, peri-procedural outcomes favored CEA for stroke and stenting for myocardial infarction. At 30 days, CEA was associated with lower rates of death (1.4% *vs*. 1.9%) and stroke (4.6% *vs*. 8.5%), whereas myocardial infarction was more frequent after CEA than stenting (1.6% *vs*. 0.8%) (176). These findings indicate higher death and ischemic stroke rates with stenting, particularly in patients >70 years, while CEA carries a higher early myocardial infarction risk. Moreover, carotid stenting was associated with higher rates of severe restenosis (>70%) at five years compared with CEA (≥10% *vs*. 5.8%).[182] Across treatment strategies, restenosis is more common among women and patients with hypertension, diabetes, renal disease, and dyslipidemia.[38] Accordingly, CEA remains the preferred revascularization strategy for most symptomatic patients, particularly those aged >70 years, those requiring intervention within 14 days of symptom onset, and those with high-risk plaque morphology, provided surgical risk is acceptable. In contrast, carotid stenting may be preferred in patients with prior neck surgery, previous cervical irradiation, high carotid bifurcation lesions, restenosis after prior CEA, contralateral recurrent laryngeal nerve palsy, tracheostomy, or other anatomic factors that increase operative difficulty or cranial nerve injury risk during CEA.[183] Procedure-specific compli-

Table 8. Randomized controlled trials of symptomatic carotid artery stenosis.

Trial	Year	No.	Population	Endpoint	Arm 1	Arm 2
VACS 309	1991	189	Symptomatic patients with 50% stenosis	Cerebral infarction or crescendo TIAs within 30 days	CEA + OMT: 7.7%	OMT alone: 19.4%
ECST	1998	3024	Symptomatic patients	Major stroke or death	CEA: 37.0%	Control: 36.5%
NASCET	1999	1415	Symptomatic patients with ≥30% stenosis	Disabling stroke, non-disabling stroke or death	CEA: disabling stroke (0.9%), non-disabling stroke (4.5%), death (1.1%), at 90 days	-
SPACE	2008	1214	Symptomatic patients with ≥70% stenosis	Ipsilateral stroke or death of any cause	CEA: 5.5%	CAS: 6.8%
SAPPHIRE	2008	334	Symptomatic patients with ≥70% stenosis or asymptomatic patients with ≥80% stenosis	Periprocedural stroke, MI, or death	CEA: 9.8%	CAS: 4.8%
CREST	2016	2502	Symptomatic patients with ≥50% stenosis or asymptomatic patients with ≥60% stenosis	Periprocedural MI and stroke Stroke, MI, or death at 4 years	CEA: MI (2.3%), stroke (2.3%) CEA: 6.8%%	CAS: MI (1.1%), stroke (4.1%) CAS: 7.2%

VACS, Veterans Affairs Cooperative Studies Program 309 Trialist Group; ECST, European Carotid Surgery Trial; NASCET, North American Symptomatic Carotid Endarterectomy Trial; SPACE, Stent-Supported Percutaneous Angioplasty of the Carotid Artery vs. Endarterectomy Trial; SAPPHIRE, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; CREST, Carotid Revascularization Endarterectomy Versus Stent Trial; TIA, transient ischemic attack; MI, myocardial infarction; CEA, carotid endarterectomy; CAS, carotid artery stenting; OMT, optimal medical therapy.

cations should also influence treatment selection. CEA is associated with cervical hematoma, cranial nerve injury, wound complications, and myocardial infarction, whereas carotid stenting is associated with access-site complications, periprocedural embolization, and a higher risk of early stroke, particularly in older patients.[184] Most cranial nerve injuries after CEA are transient; however, permanent deficits may occur in a small proportion of patients. Among patients <70 years of age, carotid stenting yields outcomes comparable to CEA, although long-term benefit depends on sustained medical therapy and continued improvements in stent technology and procedural technique.[178,185]

Transcarotid artery revascularization

Transcarotid artery revascularization (TCAR) has been rapidly adopted in the U.S. since FDA approval in 2015, with expanded indications to standard-risk patients in 2023 further increasing its adoption.[59,69] TCAR is less invasive than CEA, requiring a smaller incision, and has demonstrated favorable perioperative outcomes in nonrandomized studies, with lower stroke and death rates than carotid stenting and comparable outcomes to CEA.[186-189] In Vascular Quality Initiative data analysis, perioperative stroke or death rates in asymptomatic CAS were 1.1% with CEA, 1.2% with TCAR, and 1.8% with stenting, with corresponding 1-year rates of 3.8%, 4.9%, and 6.6%, respectively.[142] TCAR was also associated with lower in-hospital stroke/TIA risk than stenting.[190] TCAR offers particular advantages in patients with restenosis after prior CEA, hostile neck anatomy, severe peripheral arterial disease, challenging aortic arch anatomy, or heavy aortic calcification, and in those with prior neck surgery, by avoiding reoperation.[65,69] While early outcomes are encouraging, long-term stroke rates and stent durability remain uncertain.[69]

Despite promising perioperative outcomes and technical advantages over CEA and stenting in selected settings, TCAR's rapid adoption has occurred in the absence of RCT evidence.[69] Unlike CEA and stenting, TCAR has not been compared with alternative revascularization strategies or optimal medical therapy in a RCT, and current practice is therefore informed exclusively by observational data that also underpinned recent FDA approvals.[69] Interestingly, observational studies further suggest superior outcomes at centers offering TCAR alongside CEA than those offering CEA alone, likely reflecting improved procedure selection tailored to patient anatomy and comorbidity profiles.[191] Accordingly, management of CAS should remain individualized, integrating clinical presentation, imaging findings, patient preferences, and social factors. Future research should prioritize RCTs and long-term follow-up to define TCAR's durability and clarify its role relative to CEA, stenting, and contemporary optimal medical therapy, with refinement of patient- and anatomy-specific selection criteria. Key indications, advantages, limitations, and procedure-specific complications of revascularization strategies for CAS are summarized in Table 9.

Future directions

Declining stroke rates with optimal medical therapy have reduced the absolute benefit of prophylactic revascularization, particularly in asymptomatic patients, emphasizing the need for risk stratification beyond luminal stenosis alone. Future efforts should focus on identifying the small subset of asymptomatic patients who develop symptoms despite optimal medical therapy and may benefit from early intervention. Advances in imaging will be central to this shift, with multimodal evaluation of plaque composition, biological activity, as well as MRI-detected intraplaque hemorrhage, CTA-based plaque characterization, ultrasound-derived plaque vulnerability metrics, transcranial Doppler microemboli, and markers of impaired cerebrovascular reserve, offering promise for identifying high-risk phenotypes. Artificial intelligence may further enable individualized risk prediction models by integrating clinical, laboratory, and imaging data. Therapeutically, continued refinement of optimal medical therapy, including more intensive lipid lowering, wider use of cardioprotective glucose-lowering agents, and tailored antithrombotic strategies will likely further reduce stroke risk across both symptomatic and asymptomatic populations. Procedurally, long-term randomized data are needed to define the durability and role of TCAR relative to CEA, carotid stenting, and medical therapy alone. Moreover, future trials should extend beyond periprocedural safety to assess long-term stroke prevention, cognitive outcomes, quality of life, and cost-effectiveness. Finally, ongoing improvements in stent delivery systems and stent design, including micromesh platforms and retrograde flow protection will continue to enhance procedural safety.

Conclusions

CAS remains a major contributor to ischemic stroke and a marker of systemic atherosclerosis with important cerebrovascular and cardiovascular implications. Contemporary evidence supports optimal medical therapy as the cornerstone of care across the CAS spectrum, with aggressive risk-factor control and modern pharmacotherapy achieving low absolute stroke rates, particularly in asymptomatic disease. Timely revascularization provides clear benefit for appropriately selected symptomatic patients with hemodynamically significant stenosis, whereas in asymptomatic individuals, the role of revascularization remains one of the most important unresolved controversies in the field. Although selected patients with severe stenosis, favorable procedural risk, meaningful life expectancy, or high-risk plaque features may benefit from intervention, the incremental benefit of revascularization over contemporary optimal medical therapy remains uncertain and continues to be evaluated in ongoing clinical trials. Current evidence is insufficient to establish the superiority of carotid stenting over CEA in asymptomatic CAS, and treatment decisions should therefore be individualized according to patient characteristics, procedural risk, and local expertise. Diagnosis and procedural planning rely primarily on

Table 9. Comparison of revascularization strategies for carotid artery stenosis.

	Carotid endarterectomy	Transfemoral carotid artery stenting	Transcarotid artery revascularization
Principal role	Surgical removal of carotid plaque through open arterial reconstruction	Endovascular treatment using transfemoral stent placement and embolic protection	Hybrid surgical-endovascular approach using direct carotid access with flow reversal neuroprotection
Preferred patient population	Most symptomatic patients with 50-99% stenosis, particularly those aged >70 years and those requiring intervention within 14 days of symptom onset	Patients with anatomy unfavorable for CEA or prior cervical interventions	Patients with hostile neck anatomy, prior neck surgery, prior cervical irradiation, or restenosis after CEA
Major advantages	Most established evidence base; lower peri-procedural stroke risk than transfemoral stenting; durable long-term results; lower restenosis rates	Less invasive than CEA; lower peri-procedural myocardial infarction risk than CEA	Direct carotid access avoids aortic arch manipulation; flow reversal provides cerebral embolic protection; less invasive than CEA; favorable peri-procedural outcomes in observational studies
Potential limitations	Requires open surgical exposure and carries risk of local surgical complications	Higher peri-procedural stroke risk, particularly in older patients; higher long-term restenosis rates; outcomes influenced by arch anatomy and operator experience	Limited long-term data; absence of randomized controlled trial evidence comparing T CAR with CEA, transfemoral stenting, or optimal medical therapy
Situations favoring procedure selection	Age >70 years; intervention within 14 days of symptoms; acceptable surgical risk	Prior neck surgery; previous cervical irradiation; high carotid bifurcation lesions; restenosis after prior CEA; contralateral recurrent laryngeal nerve palsy; tracheostomy; other conditions increasing operative difficulty	Restenosis after prior CEA; hostile neck anatomy; prior neck surgery
Peri-procedural stroke risk	Lower than transfemoral carotid stenting in randomized trials	Higher than CEA, particularly in patients >70 years	Favorable peri-procedural stroke outcomes in registry and observational studies
Peri-procedural myocardial infarction risk	Higher than transfemoral carotid stenting	Lower than CEA	Limited comparative data available
Restenosis risk	Lower long-term restenosis rates	Higher rates of severe restenosis than CEA	Long-term restenosis rates remain incompletely defined
Important procedure-specific complications	Cranial nerve injury, cervical hematoma, wound complications, myocardial infarction	Access-site complications, distal embolization, peri-procedural stroke, restenosis	Access-site and stent-related complications may occur

CAS, Carotid artery stenosis; CEA, Carotid endarterectomy; TCAR, Transcarotid artery revascularization.

noninvasive imaging with CDUS as first-line and CTA and MRA as complementary modalities, while DSA is reserved for problem-solving when findings are inconclusive. Because luminal stenosis alone inadequately captures stroke risk, integration of plaque vulnerability markers and patient-level factors is essential to refine selection and outcomes. Although TCAR shows promising perioperative safety and applicability, its durability and effectiveness require randomized evidence in comparison to other techniques and optimal medical therapy. Ultimately, CAS management should be individualized and multidisciplinary, balancing procedural risk against expected benefit and anchored in sustained, target-driven medical therapy.

Authors' contributions

All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare no potential conflicts of interest.

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Ethics approval and consent to participate

Not required.

Availability of data and materials

The datasets used and/or analyzed during the current study are available upon reasonable request from the corresponding author.

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