

Screening for Asymptomatic Carotid Artery Stenosis in Adult Patients Unclear Benefit but Downstream Risks

Salomeh Keyhani, MD, MPH; Eric M. Cheng, MD

Carotid artery stenosis is a risk factor for stroke, but a relatively small proportion of strokes (approximately 11%) can be attributed to atherosclerosis of the internal carotid arteries. There is no evidence that screening for carotid artery stenosis in the asymptomatic adult population (ie, no history or symptoms of stroke or transient ischemic attack) will reduce the risk of stroke, but there are downstream risks from identifying patients with carotid stenosis. Thus, in a recommendation statement¹ and updated evidence report and systematic review,² the US Preventive Services Task Force (USPSTF) has reaffirmed its 2014 recommendation³ against screening for asymptomatic carotid artery stenosis in the general adult population (D recommendation) based on an assessment of no benefit and possible harm.



Multimedia



Related articles at

[jama.com](https://www.jama.com)

[jamanetworkopen.com](https://www.jamanetworkopen.com)

[jamaneurology.com](https://www.jamaneurology.com)

Patients identified with carotid artery stenosis are referred to surgeons or other specialists who must make the decision to revascularize based on outdated trial data.⁴ Carotid revascularization involves the up-front perioperative risks of stroke and death. Stroke risk from carotid artery stenosis has been declining since the original asymptomatic carotid trials were completed.⁵ The National Institute of Neurological Disease and Stroke funded the Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2) to determine if revascularization offers any benefit beyond cardiovascular risk factor control.⁶ CREST-2 was launched in 2014 and is an ongoing trial that involves 2 parallel randomized clinical trials: (1) carotid endarterectomy (CEA) plus intensive medical therapy vs intensive medical therapy alone and, similarly, (2) carotid artery stenting (CAS) plus intensive medical therapy vs intensive medical therapy alone. Results are expected in 2025.

A Multitude of Recommendations Against Carotid Imaging
The USPSTF first published its recommendation against screening for carotid artery stenosis in the general population in 2007.⁷ Additional evidence reviews reaffirmed this guidance in 2014⁸ and again in 2021.² Guidelines from other medical societies also recommend against screening healthy adults, and some specialty societies rely on expert opinion to endorse screening for select high-risk populations (eg, those with coronary artery disease) in guidelines published 10 years ago.^{9,10} Many specialty societies participating in Choosing Wisely have included carotid imaging on their “do not do” list.¹¹ The American Academy of Family

Physicians recommends against screening for asymptomatic carotid artery stenosis in adult patients. The Society of Vascular Surgery recommends against routine surveillance of carotid arteries in the asymptomatic healthy population. The Society of Thoracic Surgeons recommends against routine evaluation of carotid artery disease prior to cardiac surgery in the absence of symptoms or other high-risk criteria. The American Academy of Neurology recommends against imaging of the carotid arteries for simple syncope without other neurologic symptoms. There is no national data available on how the USPSTF and other recommendations against use of screening for carotid artery stenosis have affected practice. The billing codes for screening are non-specific, and obtaining national estimates is challenging. However, Medicare data suggest that the number of patients who underwent CEA for asymptomatic carotid stenosis declined from 1999 through 2000 to 2013 through 2014, and CAS declined from 2005 through 2006 to 2013 through 2014, although this drop may be related to decreased reimbursement.¹²

Identifying Patients With Carotid Artery Stenosis

Patients may receive head and neck imaging for other indications in which carotid artery stenosis is also identified. Patients may still receive carotid imaging as part of a syncope evaluation, for a carotid bruit, or because of direct-to-consumer advertising. None of these reasons is supported by evidence.^{13,14}

Declining Risk of Stroke and Declining Benefit of Revascularization

Carotid revascularization among asymptomatic patients is a primary prevention surgery/procedure. Revascularization with CEA or CAS is a trade-off between higher perioperative short-term risks (stroke and death) in exchange for a lower long-term risk of stroke. The evidence against screening for carotid disease outlined in the USPSTF recommendations are largely based on 2 pillars of evidence regarding treatment: (1) the benefit of revascularization in asymptomatic patients is unclear, and (2) there are significant risks associated with revascularization. The stroke risk from carotid arteries appears to be declining, which fundamentally alters the risk-benefit ratio of revascularization. Improved medical therapy such as statins, improved antiplatelet regimens, and improved treatment of hypertension and diabetes may have resulted in a reduced stroke risk among patients with asymptomatic carotid stenosis.¹⁵ Stroke has dropped from the third to the fifth leading cause of mortality.¹⁶ Existing data support a declin-

ing stroke risk from carotid artery stenosis. The Asymptomatic Carotid Surgery Trial,¹⁷ which was initiated in 1993, reported a 5-year stroke risk of 11% in the medical therapy arm (2.2% annually), and the Endarterectomy for Asymptomatic Carotid Artery Stenosis trial,¹⁸ initiated in 1987, reported a 2.3% annual stroke risk in the medical therapy arm. However, later studies reported an annual stroke risk as low as 0.6% for medically treated asymptomatic carotid stenosis, which over 5 years is close to the perioperative complication risk reported for CEA in community settings.⁵ Furthermore, the unexpectedly lower risk of stroke in the medical therapy arm of the Stenting vs Aggressive Medical Therapy for Intracranial Stenosis trial,¹⁹ published in 2011, provided further support that advances in medical therapy have had a considerable effect on stroke risk reduction. The ongoing CREST-2 trial⁶ will inform our understanding of contemporary stroke risk from asymptomatic carotid artery stenosis.

Perioperative Risks of Revascularization

Surgery in asymptomatic persons should offer a clear chance that benefits will outweigh the known surgical risks. Perioperative complications of CEA (stroke and death) in community settings range from 1.7% to 3.2%,²⁰ which is consistent with stroke and death rates from 2 large randomized clinical trials.⁴ Perioperative stroke and/or death rates as high as 4.0% among asymptomatic patients undergoing CAS have been reported outside of trials.²¹ These up-front risks are serious and dwarf the possible small long-term benefits associated with revascularization, especially given the declining stroke risk from asymptomatic carotid artery stenosis.

Do Carotid Trials Extend to Community Practice?

Trials are necessary to inform our understanding of the risks and benefits of screening. The new USPSTF recommendation¹ notes there have been no trials specifically looking at the benefits of carotid screening in the general population or in high-risk groups. The trials have all been focused on revascularization. Benefits observed in carotid trials may not extend to practice given the rigorous patient and surgeon selection instituted in trials but not required in practice.²² Surgeons and interventionalists are recruited into trials from leading academic medical centers. Trials typically have a training, or run-in, phase to ensure a low perioperative complication rate. Patients with considerable comorbidities are excluded from trials; however, in practice, many patients who are revascularized do not live long enough to benefit from stroke reduction.²³ This concern about the generalizability of trials is supported empirically by recent comparative effectiveness research, which demonstrated no benefit to CEA in community settings.²³ Similarly CREST-2 differs from real-world practice in patient selection, surgeon selection, and rigorous participant monitoring.^{24,25}

Conclusions

Carotid artery screening among asymptomatic patients makes it more likely for carotid artery revascularization to occur, even though the benefits in stroke risk reduction are not established and the up-front risks are clear (stroke and death). The USPSTF has once again reaffirmed its message that the evidence does not support screening in the general adult population. In addition, if a patient with carotid artery stenosis is identified through imaging for other reasons, a focus on cardiovascular risk factor control is the best treatment strategy.

ARTICLE INFORMATION

Author Affiliations: Department of Medicine, University of California, San Francisco (Keyhani); San Francisco VA Medical Center, San Francisco, California (Keyhani); Department of Neurology, University of California, Los Angeles (Cheng); VA Greater Los Angeles Healthcare System, Los Angeles, California (Cheng).

Corresponding Author: Salomeh Keyhani, MD, MPH, San Francisco VA Medical Center, 4150 Clement St, San Francisco, CA 94121 (salomeh.keyhani@ucsf.edu).

Published Online: February 2, 2021.
doi:10.1001/jamainternmed.2021.0029

Conflict of Interest Disclosures: None reported.

REFERENCES

- US Preventive Services Task Force. Screening for asymptomatic carotid artery stenosis: US Preventive Services Task Force recommendation statement. *JAMA*. Published online February 2, 2021. doi:10.1001/jama.2020.26988
- Guirgis-Blake JM, Webber EM, Coppola EL. Screening for asymptomatic carotid artery stenosis in the general population: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. Published online February 2, 2021. doi:10.1001/jama.2020.20364
- LeFevre ML; US Preventive Services Task Force. Screening for asymptomatic carotid artery stenosis: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014; 161(5):356-362. doi:10.7326/M14-1333
- Chaturvedi S, Bruno A, Feasby T, et al; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Carotid endarterectomy—an evidence-based review: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2005; 65(6):794-801. doi:10.1212/01.wnl.0000176036.07558.82
- Abbott AL. Medical (nonsurgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. *Stroke*. 2009;40(10):e573-e583. doi:10.1161/STROKEAHA.109.556068
- Carotid revascularization and medical management for asymptomatic carotid stenosis trial (CREST-2). ClinicalTrials.gov identifier: NCT02089217. Updated June 9, 2020. Accessed January 12, 2021. <https://clinicaltrials.gov/ct2/show/NCT02089217>
- Carotid Artery Stenosis: Screening, December 2007. US Preventive Services Task Force. December 15, 2007. Accessed January 12, 2021. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/carotid-artery-stenosis-screening-december-2007>
- Jonas DE, Feltner C, Amick HR, et al. Screening for asymptomatic carotid artery stenosis: a systematic review and meta-analysis for the US Preventive Services Task Force. In: *U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews*. Agency for Healthcare Research and Quality; 2014.
- Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK; Society for Vascular Surgery. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. *J Vasc Surg*. 2011;54(3):e1-e31. doi:10.1016/j.jvs.2011.07.031
- Brott TG, Halperin JL, Abbara S, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Stroke Association; American Association of Neuroscience Nurses; American Association of Neurological Surgeons; American College of Radiology; American Society of Neuroradiology; Congress of Neurological Surgeons; Society of Atherosclerosis Imaging and Prevention; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society of NeuroInterventional Surgery; Society for Vascular Medicine; Society for Vascular Surgery; American Academy of Neurology and Society of Cardiovascular Computed Tomography. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the

management of patients with extracranial carotid and vertebral artery disease: executive summary. *Stroke*. 2011;42(8):e420-e463.

11. Clinician lists. Choosing Wisely. Accessed January 12, 2021. <https://www.choosingwisely.org/clinician-lists/>

12. Lichtman JH, Jones MR, Leifheit EC, et al. Carotid endarterectomy and carotid artery stenting in the US Medicare population, 1999-2014. *JAMA*. 2017;318(11):1035-1046. doi:10.1001/jama.2017.12882

13. Keyhani S, Cheng EM, Naseri A, et al. Common reasons that asymptomatic patients who are 65 years and older receive carotid imaging. *JAMA Intern Med*. 2016;176(5):626-633. doi:10.1001/jamainternmed.2016.0678

14. Scott JW, Schwartz AL, Gates JD, Gerhard-Herman M, Havens JM. Choosing wisely for syncope: low-value carotid ultrasound use. *J Am Heart Assoc*. 2014;3(4):e001063. doi:10.1161/JAHA.114.001063

15. Lackland DT, Roccella EJ, Deusch AF, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; Council on Functional Genomics and Translational Biology. Factors influencing the decline in stroke mortality: a statement from the American Heart Association/American Stroke Association. *Stroke*.

2014;45(1):315-353. doi:10.1161/01.str.0000437068.30550.cf

16. Leading causes of death. Centers for Disease Control and Prevention. Updated October 30, 2020. Accessed December 30, 2020. <https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm>

17. Halliday A, Mansfield A, Marro J, et al; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet*. 2004;363(9420):1491-1502. doi:10.1016/S0140-6736(04)16146-1

18. Walker MD, Marler JR, Goldstein M, et al. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA*. 1995;273(18):1421-1428. doi:10.1001/jama.1995.03520420037035

19. Chimowitz MI, Lynn MJ, Derdeyn CP, et al; SAMMPRIS Trial Investigators. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med*. 2011;365(11):993-1003. doi:10.1056/NEJMoa1105335

20. Boitano LT, DeCarlo C, Schwartz MR, et al. Surgeon specialty significantly affects outcome of asymptomatic patients after carotid

endarterectomy. *J Vasc Surg*. 2020;71(4):1242-1252. doi:10.1016/j.jvs.2019.04.489

21. Liang P, Solomon Y, Swerdlow NJ, et al. In-hospital outcomes alone underestimate rates of 30-day major adverse events after carotid artery stenting. *J Vasc Surg*. 2020;71(4):1233-1241. doi:10.1016/j.jvs.2019.06.201

22. Wennberg DE, Lucas FL, Birkmeyer JD, Bredenberg CE, Fisher ES. Variation in carotid endarterectomy mortality in the Medicare population: trial hospitals, volume, and patient characteristics. *JAMA*. 1998;279(16):1278-1281. doi:10.1001/jama.279.16.1278

23. Keyhani S, Cheng EM, Hoggatt KJ, et al. Comparative effectiveness of carotid endarterectomy vs initial medical therapy in patients with asymptomatic carotid stenosis. *JAMA Neurol*. 2020;77(9):1110-1121. doi:10.1001/jamaneurol.2020.1427

24. Lal BK, Meschia JF, Roubin GS, et al; CREST-2 Investigators. Factors influencing credentialing of interventionists in the CREST-2 trial. *J Vasc Surg*. 2020;71(3):854-861. doi:10.1016/j.jvs.2019.05.035

25. Turan TN, Voeks JH, Chimowitz MI, et al. Rationale, design, and implementation of intensive risk factor treatment in the CREST2 trial. *Stroke*. 2020;51(10):2960-2971. doi:10.1161/STROKEAHA.120.030730