

Arterial Atherosclerosis: Vascular Surgery Interventions

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Atherosclerotic vascular disease is a leading cause of death worldwide. Atherosclerotic stenosis of the internal carotid or intracranial arteries causes up to 15% of strokes. Peripheral artery disease affects up to one in five people in the United States who are 60 years and older and nearly one-half of those who are 85 years and older. Renal artery stenosis may affect up to 5% of people with isolated hypertension and up to 40% of people with other atherosclerotic diseases. All patients with atherosclerotic vascular disease should receive a comprehensive program of guideline-directed medical therapy, including structured physical activity and lifestyle modification, an antiplatelet agent, a statin, antihypertensive therapy, and smoking cessation counseling. The U.S. Preventive Services Task Force recommends one-time screening for abdominal aortic aneurysm with ultrasonography in men 65 to 75 years of age who have smoked at least 100 cigarettes, but screening is not recommended for carotid, peripheral, and renal disease. Surgical revascularization decreases adverse outcomes and mortality in selected patients with advanced vascular disease. Endovascular repair has become more common for patients younger than 70 years because of decreased short-term mortality. Carotid revascularization with carotid endarterectomy or carotid artery stenting is recommended for symptomatic patients with greater than 50% internal carotid artery stenosis. Carotid artery stenting is preferred in patients with multiple comorbidities, tracheostomy, or previous neck radiation or dissection. In patients older than 70 years, carotid endarterectomy is associated with a lower risk of periprocedural stroke or death than carotid artery stenting. Revascularization is a reasonable treatment option for patients with lifestyle-limiting claudication and an inadequate response to guideline-directed therapies. Revascularization is indicated for patients with critical limb ischemia and is emergently indicated for acute limb ischemia. Renal artery revascularization offers no proven clinical benefit when added to optimal medical therapy. (*Am Fam Physician*. 2022;105(1):65-72. Copyright © 2022 American Academy of Family Physicians.)

Atherosclerotic vascular disease is a leading cause of death worldwide. However, over the past few decades, the incidence of vascular disease and resultant mortality have declined in higher-income countries. The most significant risk factors for atherosclerotic vascular disease are hypertension, diabetes mellitus, hyperlipidemia, and smoking.¹ For abdominal aortic aneurysm (AAA), smoking is the strongest predictor of prevalence, growth, and rupture, with a clear dose-response relationship.² A family history of vascular disease increases risk, and the risk of developing AAA is doubled if a first-degree relative has an AAA. Standard medical treatment of atherosclerotic vascular disease, or guideline-directed medical therapy, includes structured

physical activity and lifestyle modification, an antiplatelet agent, a statin, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and smoking cessation counseling with medical and psychological support (*Table 1*).³ Surgical revascularization decreases adverse outcomes and mortality in some patients with advanced vascular disease.

Abdominal Aortic Disease

AAA affects 1% of women and nearly 10% of men between 65 and 80 years of age.⁴ AAA is rare in people younger than 50 years.⁴ The prevalence of AAA in European countries has declined, likely due to decreased smoking. Because recommended screening is rarely performed, the current prevalence of AAA in the United States is uncertain.²

Screening for AAA with ultrasonography has a sensitivity of 94% or greater and a specificity of 98% or greater.² The U.S. Preventive Services Task

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 15.

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TABLE 1

Elements of Guideline-Directed Therapy for Atherosclerotic Vascular Disease

Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker
 Lifestyle modification, preferably including a structured exercise program
 Low-dose aspirin
 Smoking cessation with medical and psychological support
 Statin, at least moderate intensity

Information from reference 3.

Force (USPSTF) recommends one-time screening for AAA with ultrasonography in men 65 to 75 years of age who have smoked 100 or more cigarettes in their lifetime.² One-time screening for AAA with ultrasonography may be considered in men 65 to 75 years of age who have never smoked, but screening is not recommended in women who have never smoked or do not have a family history of AAA. The evidence is insufficient to recommend for or against screening women who have ever smoked or have a family history of AAA. Consider not screening patients with a lower life expectancy or those who are not

good candidates for surgical intervention. The USPSTF recommends using sex and not gender identity for screening decisions.² The American Academy of Family Physicians (AAFP) endorses the USPSTF recommendations.⁵

For men 65 to 79 years of age, screening for AAA prevents aneurysm rupture (number needed to screen = 294) and mortality from AAA (number needed to screen = 917). These benefits have not been demonstrated in women.⁶

Rupture of AAA is a surgical emergency with high mortality. For patients who survive long enough to reach a hospital, 80% die before discharge.⁴ The annual risk of rupture is 1% for smaller aneurysms but increases to 11% when the diameter reaches 5 cm (2 in).⁷ Elective repair of an AAA less than 5.5 cm (2.2 in) has not been shown to decrease mortality.⁸

Surgical repair is standard practice for patients with an AAA of 5.5 cm (2.2 in) or larger in diameter or any AAA larger than 4.0 cm (1.6 in) that has increased by 1.0 cm (0.4 in) or more over one year.² Because most trials were conducted in men, the threshold for surgical intervention in women is not well established.²

Open surgical repair has been the traditional approach when a repair is indicated; however, endovascular aneurysm repair (EVAR) has become more common than open repair over the past two decades.⁷ During the EVAR procedure, bilateral femoral artery catheters are used to place an endograft across the aneurysmal portion to act as an artificial lumen and protect the aneurysm from vascular pressure (*Figures 1 and 2*).

In the United States, EVAR is currently used for 80% of intact AAA repairs and 52% of ruptured AAA repairs.⁷ EVAR has about one-third of the 30-day mortality rate vs. open repair.⁹ EVAR has lower mortality rates compared with open repair until approximately four years, when survival after both procedures is equivalent.¹⁰ When outcomes are separated by age, overall survival is higher with EVAR for patients younger than 70 years, and the two procedures are equivalent in people 70 years and older.¹¹ Repeat interventions to address complications such as a leak or device migration are more common with EVAR.⁹

Carotid Artery Disease

Stroke is the second leading cause of death worldwide and the fourth leading cause of death in the

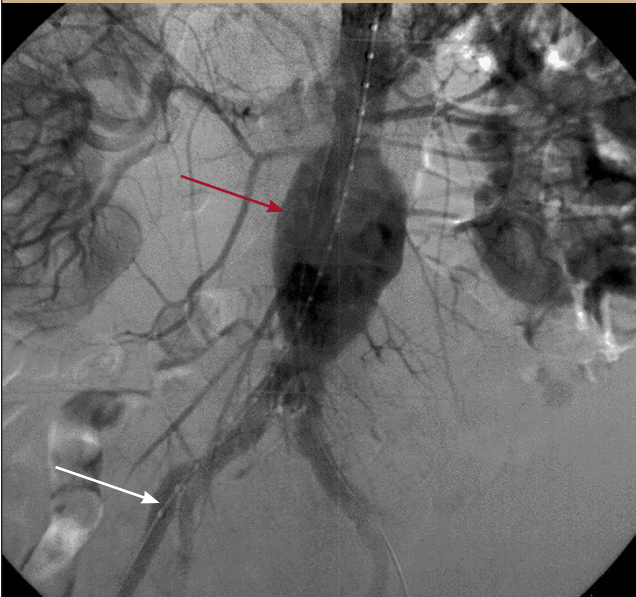
BEST PRACTICES IN VASCULAR MEDICINE

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not screen for carotid artery stenosis in adult patients who are asymptomatic.	American Academy of Family Physicians
Do not screen for renal artery stenosis in patients without resistant hypertension and with normal renal function, even if known atherosclerosis is present.	Society for Vascular Medicine

Source: For more information on the Choosing Wisely Campaign, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/afp/recommendations/search.htm>.

FIGURE 1



Large infrarenal abdominal aortic aneurysm (*red arrow*) during an endovascular repair with a traversing guide wire (*white arrow*) from the right femoral artery.

FIGURE 2



Large infrarenal abdominal aortic aneurysm during an endovascular repair with a normal caliber aorta (*arrow*) after endovascular graft placement.

United States.¹² Although mortality after a first stroke can be as high as 35%, subsequent strokes are associated with a mortality of nearly 70%.¹³ Repeat strokes commonly occur within one year. Up to 15% of strokes are caused by atherosclerotic stenosis of the internal carotid or intracranial arteries.¹⁴

In patients without symptoms, screening for carotid artery stenosis does not improve outcomes and is not recommended by the USPSTF or the AAFP.^{15,16} The low prevalence of carotid artery stenosis in the population leads to a high rate of false-positive results. No reliable method exists to estimate stroke risk for patients who are asymptomatic with carotid artery stenosis.¹⁵

Carotid auscultation is also not useful to diagnose or rule out carotid artery stenosis. In addition to stenosis, bruits are commonly caused by transmitted cardiac murmurs, external carotid stenosis, venous hum, and tortuous arteries.

Imaging can be helpful for symptoms that suggest carotid disease. Carotid stenosis is considered symptomatic if patients have a history of transient ischemic attack, amaurosis fugax, or stroke in the distribution of the narrowed artery.¹⁷ Duplex ultrasonography is the most commonly used study to evaluate for stenosis. The degree of stenosis is estimated by measuring blood flow velocity at multiple points across the artery. The severity of the obstruction correlates with carotid flow velocity: the narrower the lumen of the vessel, the higher the flow rate through the stenotic segment. Tortuosity and heavy calcification of the artery may affect flow velocity measurements and estimation of stenosis. Computed tomographic angiography and magnetic resonance angiography can add to ultrasonography results by showing plaque morphology, intracranial collateralization, and brain perfusion that can affect stroke risk.

Without surgical intervention, strokes will affect approximately 1% of patients with carotid artery stenosis of 70% or more who receive guideline-directed medical therapy.¹⁷ Because older studies reported annual stroke rates of approximately 2% without surgical intervention, the current benefit from surgery is less clear. An ongoing trial (CREST-2) comparing carotid endarterectomy, carotid artery stenting, and medical management alone should clarify the relative benefit of intervention.^{18,19}

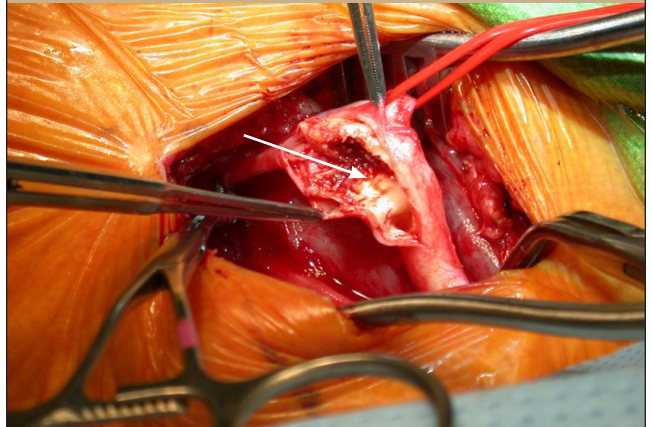
The most recent guidelines for stroke prevention are from 2021. Carotid endarterectomy is recommended for patients with transient ischemic attack or ischemic stroke within the past six months and ipsilateral severe (i.e., 70% to 99%) carotid artery stenosis when the estimated perioperative morbidity and mortality risk is less than 6%²⁰ (Figure 3). The National Surgical Quality Improvement Program surgical risk calculator (<https://riskcalculator.facs.org/RiskCalculator>) is a validated tool to estimate the risk of postoperative complications.¹⁹ Carotid endarterectomy can be considered for symptomatic carotid stenosis of greater than 70% by noninvasive imaging or 50% by angiography unless medical comorbidities or anatomic conditions increase surgical risk.²⁰ Conditions that increase surgical risk include multiple comorbidities, tracheostomy, previous neck radiation or dissection, or restenosis after previous carotid endarterectomy^{20,21} (Figure 4).

Stenting has more short-term complications than surgery in older patients. Over the first three months after an intervention, carotid artery stenting has a number needed to harm of 32 for stroke or death compared with carotid endarterectomy. This increased risk is attributed to the risks of stenting an unstable plaque.^{21,22} In patients 70 years and younger, these three-month event rates are nearly identical with stenting and endarterectomy. After three months, carotid artery stenting and carotid endarterectomy are equivalent.²³

Carotid endarterectomy within two weeks of symptom onset in patients with carotid artery stenosis greater than 50% reduces the risk of stroke with a number needed to treat of 5 over five years.¹³ After 12 weeks from the onset of symptoms or a stroke, the number needed to treat to prevent a stroke increases to 125. Carotid endarterectomy has a high short-term complication rate, with 7% of patients experiencing stroke or death within 30 days; 15% of patients experience stroke or death within five years of the procedure.¹³ Stroke within 30 days of carotid endarterectomy dramatically increases mortality.²⁴

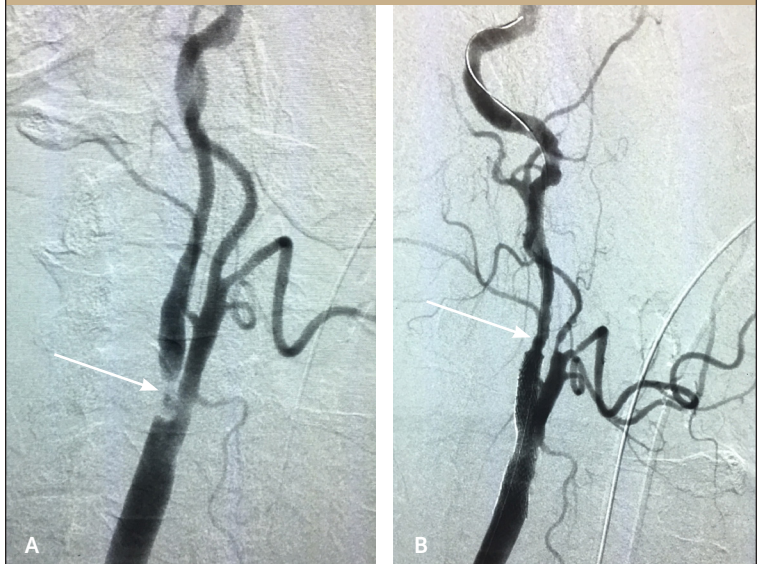
Transcarotid artery revascularization is a newer surgical approach for carotid stenosis. In transcarotid artery revascularization, carotid artery stents are placed by incising the affected artery. During the procedure, the carotid artery is clamped proximal to the stenosis, and the

FIGURE 3



Extensive internal carotid atherosclerotic plaque (arrow) before removal during carotid endarterectomy.

FIGURE 4



Carotid angiogram (A) demonstrating > 80% internal carotid stenosis (arrow) and follow-up angiogram (B) after internal carotid artery stent placement with minimal residual stenosis (arrow).

distal carotid flow is reversed using an extracorporeal circuit to the femoral vein. This protects the cerebral arteries while the backflow removes atherosclerotic debris released from the surgery (Figure 5). In a single-arm study of transcatheter artery revascularization in patients at high risk of complications from endarterectomy, only 2.3% of patients experienced stroke or death within 30 days of surgery.²⁵

Peripheral Artery Disease

Peripheral artery disease (PAD), or atherosclerotic lower extremity artery occlusive disease, affects up to 20% of people in the United States 60 years and older and nearly one-half of those 85 years and older.²⁶ PAD affects more than 200 million people worldwide, and that number is increasing.²⁷

The ankle-brachial index (ABI) is an inexpensive and reproducible initial test for patients with PAD symptoms (e.g., intermittent claudication, diminished peripheral pulses). The ABI is calculated by dividing the systolic pressure of an artery of the ankle by systolic pressure in the arm and is typically greater than 0.90. ABI has a sensitivity of at least 94% for detecting angiographically significant stenoses.²⁸ ABI is less sensitive in patients with small vessel disease from atherosclerosis associated with hypertension, diabetes, or chronic kidney disease. The USPSTF and AAFP conclude that current evidence is insufficient to assess the balance of benefits and harms of screening for PAD with ABI in adults who are asymptomatic.^{29,30}

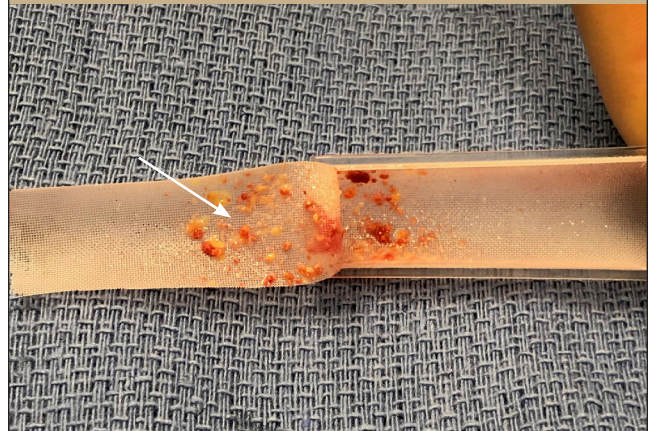
Two manifestations of PAD have the strongest indications for revascularization. Critical limb ischemia (CLI) is manifested by ischemic rest pain for more than two weeks, ischemic wounds or tissue loss, or gangrene in one or both legs (Figure 6). Up to 21% of patients with intermittent claudication eventually progress to CLI. Patients with CLI have an annual mortality rate approaching 25%, primarily from cardiovascular causes.³¹ Revascularization is indicated in CLI for limb preservation but has minimal effect on mortality.

Acute limb ischemia is a surgical emergency due to abrupt interruption of arterial blood flow to an extremity. Acute limb ischemia may present with a cold, painful, or pale extremity, diminished or absent pulses, motor weakness, or sensory impairment. Urgent revascularization is

required in acute limb ischemia to preserve limb integrity.

CLI and acute limb ischemia are the strongest indications for revascularization. Revascularization is a treatment option for patients

FIGURE 5



Atherosclerotic plaque debris (arrow) collected by extracorporeal filter during transcatheter artery revascularization.

FIGURE 6



Critical limb ischemia manifesting as dry gangrene of toes and distal forefoot.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
Men 65 to 75 years of age who have smoked more than 100 cigarettes in their lifetime should be offered a one-time screening for AAA with ultrasonography. ²	B	USPSTF grade B recommendation based on four large RCTs showing a 35% reduction in AAA-related mortality
Men 65 to 75 years of age who have never smoked can be offered one-time screening for AAA with ultrasonography; consider not screening patients with a reduced life expectancy or those who are not good candidates for surgical intervention. ²	B	USPSTF grade C recommendation based on four large RCTs, with only one reporting outcomes by smoking status in the screened group
AAA screening should not be offered to women who have never smoked and do not have a family history of AAA. ²	B	USPSTF grade D recommendation based on one trial demonstrating no benefit from screening in women who have never smoked and do not have a family history of AAA; evidence of benefit in women who have ever smoked or who have a family history of AAA is too limited to make a recommendation
Patients with an AAA ≥ 5.5 cm (2.2 in) in diameter should be referred for surgical repair. ^{2,8}	B	AAA repair for aneurysms ≥ 5.5 cm (2.2 in) decreases mortality, but there is no evidence of benefit for AAA repair of aneurysms < 5.5 cm; most available data are from RCTs conducted in men
Do not screen adults who are asymptomatic for carotid artery stenosis. ¹⁵	B	USPSTF D recommendation based on multiple trials demonstrating the harms of treatment of asymptomatic carotid stenosis outweigh the benefits
Symptomatic patients with $> 50\%$ internal carotid artery stenosis should be referred for consideration of carotid revascularization. ¹³	A	Moderate- or high-quality evidence from three nonblinded trials demonstrating significant reduction in five-year risk of stroke or operative death with carotid revascularization Carotid artery revascularization is most beneficial for patients with $\geq 70\%$ stenosis
Patients with signs of critical and acute limb ischemia should be referred for revascularization to preserve limb integrity with acute ischemia being an emergent indication. ³	C	American Heart Association/American College of Cardiology clinical practice guideline

AAA = abdominal aortic aneurysm; RCTs = randomized controlled trials; USPSTF = U.S. Preventive Services Task Force.

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

with lifestyle-limiting claudication who do not respond to other guideline-directed therapies. Revascularization is not beneficial in patients with incidentally discovered PAD.³

Surgical interventions, including bypass grafting, endarterectomy, and angioplasty with or without stenting, have similar outcomes based on limited evidence. Endovascular revascularization (angioplasty) is associated with fewer complications than bypass grafting; therefore, it

may be more appropriate for patients with significant comorbidity and associated increased surgical risk.³²

Renal Artery Disease

Atherosclerotic renal artery stenosis (RAS) commonly coexists with atherosclerotic conditions such as coronary artery disease and PAD. Up to 5% of patients with isolated hypertension have RAS, increasing to 40% in patients with clinically

evident atherosclerotic diseases. By disrupting intrarenal hemodynamics, RAS can accelerate the progression of hypertension and chronic kidney disease.³³

RAS is difficult to accurately diagnose by non-invasive methods. Vascular duplex ultrasonography is an accurate screening tool but does not often correlate well with computed tomography and magnetic resonance angiography, which may overestimate RAS. Angiography, the diagnostic standard, is also subject to interobserver variability and does not always correlate with ultrasonography, computed tomography, or magnetic resonance angiography.³³

Renal artery stenting does not improve outcomes compared with optimal medical therapy³⁴ (Table 1³). Despite the lack of prospective evidence, some vascular surgeons recommend considering renal artery revascularization in patients with significant clinical effects from stenosis. Patients with unilateral stenosis, normal renal function, and abrupt onset or worsening of severe hypertension despite more than three antihypertensive medications are typically considered for intervention. Other possible indications for renal artery stenting include patients with bilateral stenosis and rapidly declining renal function and younger patients with fibromuscular dysplasia affecting the renal artery.

This article updates a previous article on this topic by Lee, et al.³⁵

Data Sources: A search of PubMed was completed using the key words carotid artery disease, carotid artery stenosis, abdominal aortic aneurysm, peripheral artery disease, and renal artery stenosis. The search included systematic reviews, meta-analyses, randomized controlled trials, and review articles. Also searched were Essential Evidence Plus, Cochrane Library, and U.S. Preventive Services Task Force. References within these resources were also searched. Search dates: August 2020, March 2021, and August 14, 2021.

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References

- Herrington W, Lacey B, Sherliker P, et al. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. *Circ Res*. 2016;118(4):535-546.
- Owens DK, Davidson KW, Krist AH, et al.; US Preventive Services Task Force. Screening for abdominal aortic aneurysm: US Preventive Services Task Force recommendation statement. *JAMA*. 2019;322(22):2211-2218.
- Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Circulation*. 2017;135(12):e791-e792]. *Circulation*. 2017;135(12):e726-e779.
- Robertson L, Nandhra S. Laparoscopic surgery for elective abdominal aortic aneurysm repair. *Cochrane Database Syst Rev*. 2017;(5):CD012302.
- American Academy of Family Physicians. Clinical preventive service recommendation. Abdominal aortic aneurysm. Accessed August 10, 2021. <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/aaa.html>
- Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. *Cochrane Database Syst Rev*. 2007;(2):CD002945.
- Guirguis-Blake JM, Beil TL, Senger CA, et al. Primary care screening for abdominal aortic aneurysm: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2019;322(22):2219-2238.
- Ulug P, Powell JT, Martinez MA, et al. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev*. 2020;(7):CD001835.
- Paravastu SCV, Jayarajasingam R, Cottam R, et al. Endovascular repair of abdominal aortic aneurysm. *Cochrane Database Syst Rev*. 2014;(1):CD004178.
- Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med*. 2015;373(4):328-338.
- Lederle FA, Freischlag JA, Kyriakides TC, et al.; OVER Veterans Affairs Cooperative Study Group. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med*. 2012;367(21):1988-1997.
- Kim AS, Johnston SC. Temporal and geographic trends in the global stroke epidemic. *Stroke*. 2013;44(6 suppl 1):S123-S125.
- Rerkasem A, Orrapin S, Howard DP, et al. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database Syst Rev*. 2020;(9):CD001081.
- Bonati LH, Dobson J, Featherstone RL, et al.; International Carotid Stenting Study investigators. Long-term outcomes after stenting versus endarterectomy for treatment of

- symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet*. 2015; 385(9967):529-538.
15. LeFevre ML; U.S. Preventive Services Task Force. Screening for asymptomatic carotid artery stenosis: U.S. Preventive Services Task Force recommendation statement [published correction appears in *Ann Intern Med*. 2015;162(4):323]. *Ann Intern Med*. 2014;161(5):356-362.
 16. American Academy of Family Physicians. Clinical preventive service recommendation. Carotid artery stenosis. Accessed August 10, 2021. <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/carotid-artery-stenosis.html>
 17. Moresoli P, Habib B, Reynier P, et al. Carotid stenting versus endarterectomy for asymptomatic carotid artery stenosis: a systematic review and meta-analysis. *Stroke*. 2017; 48(8):2150-2157.
 18. Lal BK, Roubin GS, Rosenfield K, et al. Quality assurance for carotid stenting in the CREST-2 registry. *J Am Coll Cardiol*. 2019;74(25):3071-3079.
 19. Cohen ME, Liu Y, Ko CY, et al. An examination of American College of Surgeons NSQIP Surgical Risk Calculator Accuracy. *J Am Coll Surg*. 2017;224(5):787-795.e1.
 20. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association [published correction appears in *Stroke*. 2021;52(7):e483-e484]. *Stroke*. 2021;52(7):e364-e467.
 21. Müller MD, Lyrer P, Brown MM, et al. Carotid artery stenting versus endarterectomy for treatment of carotid artery stenosis. *Cochrane Database Syst Rev*. 2020;(2):CD000515.
 22. Rantner B, Goebel G, Bonati LH, et al.; Carotid Stenting Trialists' Collaboration. The risk of carotid artery stenting compared with carotid endarterectomy is greatest in patients treated within 7 days of symptoms. *J Vasc Surg*. 2013;57(3):619-626.e2, discussion 625-626.
 23. Bonati LH, Fraedrich G; Carotid Stenting Trialists' Collaboration. Age modifies the relative risk of stenting versus endarterectomy for symptomatic carotid stenosis – a pooled analysis of EVA-3S, SPACE and ICSS. *Eur J Vasc Endovasc Surg*. 2011;41(2):153-158.
 24. Reddy RP, Karnati T, Massa RE, et al. Association between perioperative stroke and 30-day mortality in carotid endarterectomy: a meta-analysis. *Clin Neurol Neurosurg*. 2019;181:44-51.
 25. Kashyap VS, Schneider PA, Foteh M, et al.; ROADSTER 2 Investigators. Early outcomes in the ROADSTER 2 study of transcatheter artery revascularization in patients with significant carotid artery disease. *Stroke*. 2020;51(9):2620-2629.
 26. Benjamin EJ, Virani SS, Callaway CW, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2018 update: a report from the American Heart Association [published correction appears in *Circulation*. 2018;137(12):e493]. *Circulation*. 2018;137(12):e67-e492.
 27. Fowkes FGR, Murray GD, Butcher I, et al.; Ankle Brachial Index Collaboration. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA*. 2008;300(2):197-208.
 28. Foley TR, Armstrong EJ, Waldo SW. Contemporary evaluation and management of lower extremity peripheral artery disease. *Heart*. 2016;102(18):1436-1441.
 29. Curry SJ, Krist AH, Owens DK, et al.; US Preventive Services Task Force. Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index: US Preventive Services Task Force recommendation statement. *JAMA*. 2018;320(2):177-183.
 30. American Academy of Family Physicians. Clinical preventive service recommendation. Peripheral arterial disease. Accessed August 10, 2021. <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/pad.html>
 31. Sigvant B, Lundin F, Wahlberg E. The risk of disease progression in peripheral arterial disease is higher than expected: a meta-analysis of mortality and disease progression in peripheral arterial disease. *Eur J Vasc Endovasc Surg*. 2016;51(3):395-403.
 32. Antoniou GA, Georgiadis GS, Antoniou SA, et al. Bypass surgery for chronic lower limb ischaemia. *Cochrane Database Syst Rev*. 2017;(4):CD002000.
 33. Gupta R, Assiri S, Cooper CJ. Renal artery stenosis: new findings from the CORAL Trial. *Curr Cardiol Rep*. 2017; 19(9):75.
 34. Cooper CJ, Murphy TP, Cutlip DE, et al.; CORAL Investigators. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med*. 2014;370(1):13-22.
 35. Lee ES, Dawson DL, Pevec WC. Vascular surgery: an update. *Am Fam Physician*. 2007;75(1):85-90. Accessed July 23, 2021. <https://www.aafp.org/afp/2007/0101/p85.html>