

Guide to Lower Extremity Peripheral Arterial Disease (PAD)

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Disclosure

Consultant: AbbVie; Corcept; Novo Nordisk

Research Grant: Cleerly; Janssen; Massachusetts
General Hospital/PCORI; Novartis; Novo Nordisk



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Peripheral Vascular Disease

Group of diseases affecting blood vessels that includes atherosclerotic conditions, vasculitides, vasospasm, venous thrombosis, venous insufficiency, and lymphatic disorders



Braunwald's Heart Disease (15th ed). 2016

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Peripheral Arterial Disease

Disorder of blood flow to either the upper or lower extremities:

Atherosclerosis

Thrombosis/embolism

Vasculitis

Fibromuscular dysplasia

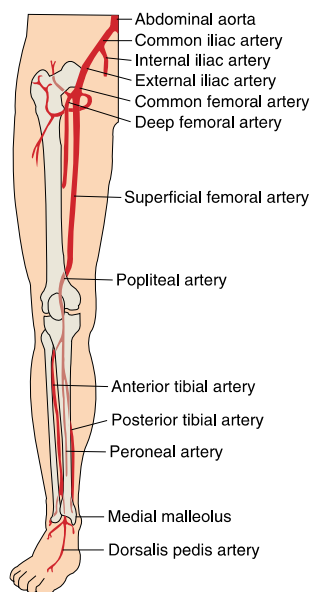
Entrapment



Braunwald's Heart Disease (15th ed). 2016

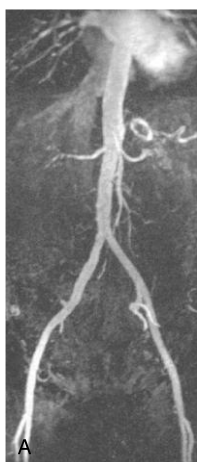
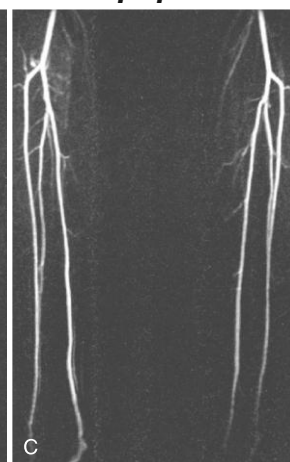
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Vascular Anatomy of the Lower Extremity



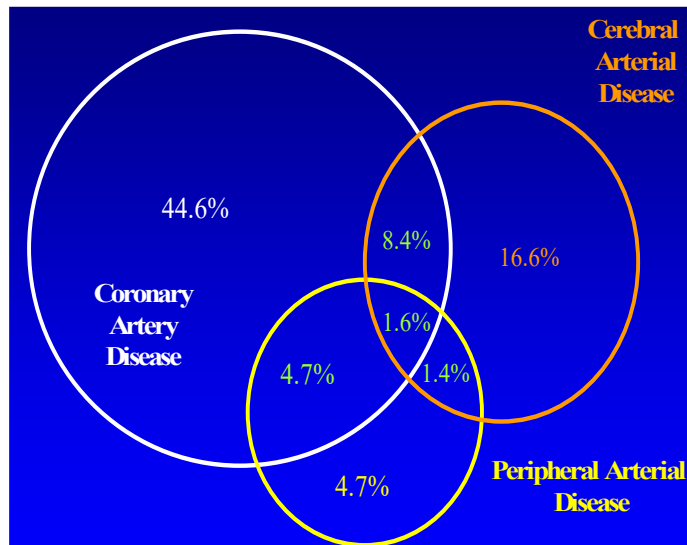
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Lower Extremity Vascular Anatomy

Aorto-Iliac**Femoropopliteal****Infrapopliteal**

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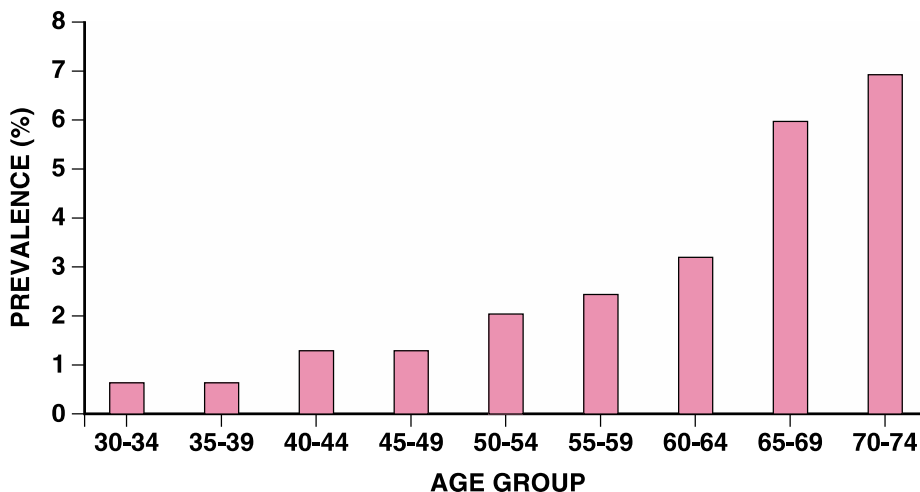
Epidemiology of Peripheral Arterial Disease n=67,888 Pts in the REACH Registry



Bhatt et al. JAMA. 2006; 295: 180

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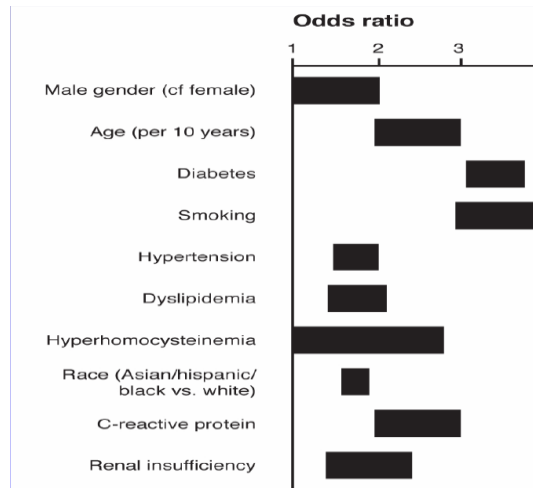
Epidemiology of Peripheral Arterial Disease



Eur J Vasc Endovasc Surg. 2007. 33: S1

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Risk Factors for Development of Peripheral Arterial Disease



Eur J Vasc Endovasc Surg. 2007. 33: S1

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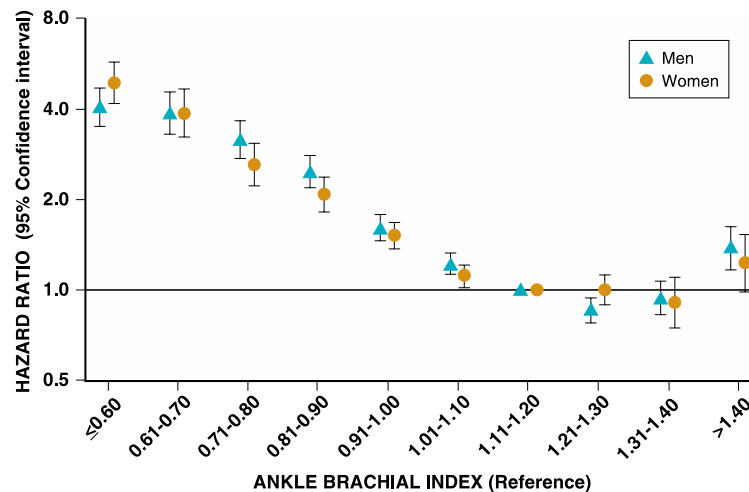
High Risk Populations for PAD

- Age ≥ 65 y
- Age 50–64 y, with risk factors for atherosclerosis (eg, diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD
- Age <50 y, with diabetes mellitus and 1 additional risk factor for atherosclerosis
- Individuals with known atherosclerotic disease in another vascular bed (eg, coronary, carotid, subclavian, renal, mesenteric artery stenosis, or AAA)



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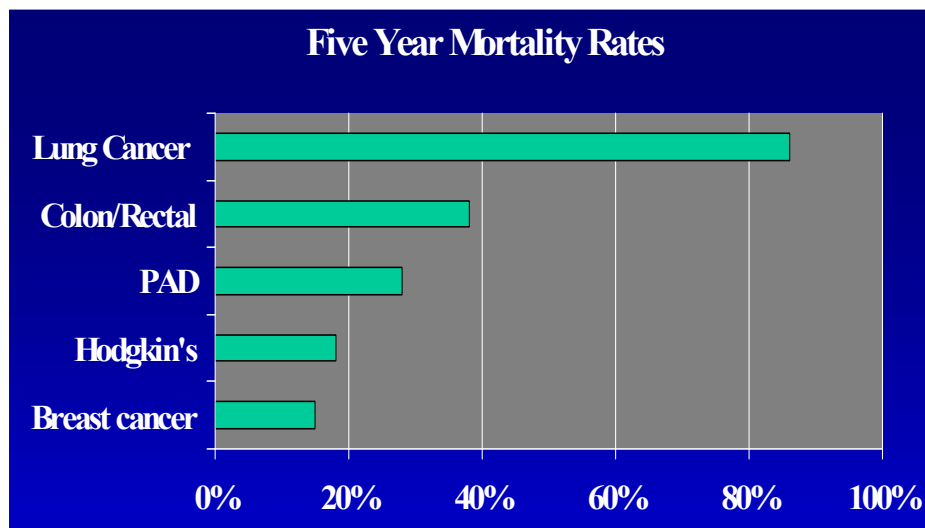
Risk of Death Associated w/ Peripheral Arterial Disease



Fowkes FG, et al: JAMA. 2008; 300: 197

11

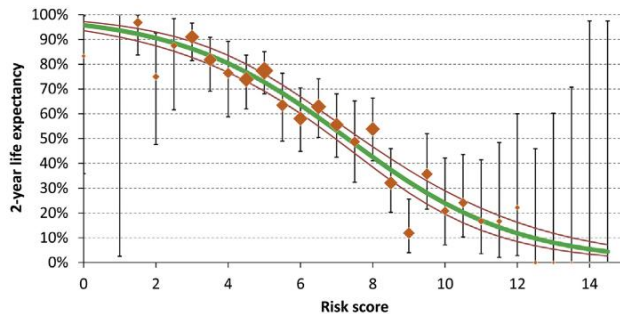
Risk Associated with Peripheral Arterial Disease



Eur J Vasc Endovasc Surg. 2007. 33: S1

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Risk Associated with Critical Limb Ischemia



Cause of Death

Cardiac - 29%
 Vascular - 10%
 SCD - 8%
 Non-CV 46%
 Unknown 7%

Variables	Score*
Nonambulatory status	2.0
Rutherford class	
5	1.5
6	3.0
Cerebrovascular disease	1.0
Hemodialysis	2.0
BMI, kg/m ²	
18.0-19.9	1.0
<18.0	2.0
Age, yrs	
65-79	1.5
≥80	3.0
Ejection fraction, %	
40-49	1.5
<40	2.0

J Am Coll Cardiol Interv 2014; 7: 1444

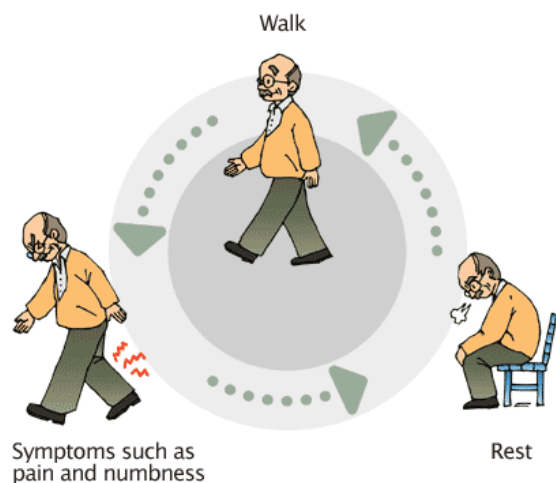


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Presentation of Peripheral Arterial Disease

Claudication

Fatigue, discomfort, cramping, or pain of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest (within 10 min)



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Differential Diagnosis of Exertional Extremity Pain

Vascular	Non-Vascular
Atherosclerosis	Radiculopathy (Spinal Stenosis, Herniated Disks)
Thrombosis/Embolism	Arthritis
Vasculitis (Thromboangiitis obliterans, Takayasu arteritis, Giant Cell)	Venous Insufficiency
Aortic Coarctation	Myositis
Fibromuscular Dysplasia	Glycogen Storage Disease (Type V) McArdle's Syndrome
Radiation	
Extravascular Entrapment (Endofibrosis of external iliac artery, Popliteal Entrapment, Thoracic Outlet)	

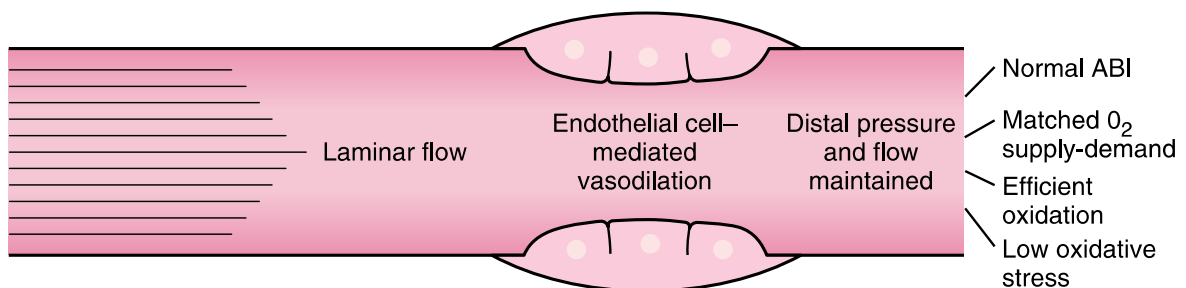


Braunwald's Heart Disease. 15th ed. 2016

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Pathophysiology of Peripheral Arterial Disease

Normal Peripheral Blood Flow



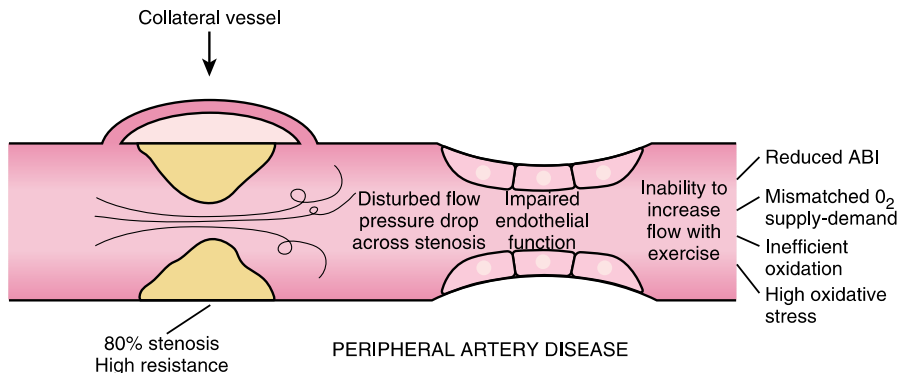
Vascular Medicine. A Companion to Braunwald's Heart Disease. 2nd ed. 2013

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Pathophysiology of Peripheral Arterial Disease

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Vascular Medicine. A Companion to Braunwald's Heart Disease. 2nd ed. 2013

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Pathophysiology of Peripheral Arterial Disease

Claudication

Fatigue, discomfort, cramping, or pain of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest (within 10 min)

Discomfort	Arterial Stenosis
Shoulder, Biceps, Forearm	Subclavian, Axillary
Buttock/Hip, Thigh	Aorta, Iliac, Common Femoral
Calf, Ankle	Superficial Femoral, Popliteal
Ankle, Foot	Tibial, Peroneal



Braunwald's Heart Disease. 15th ed. 2016

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Findings Suggestive of Peripheral Arterial Disease

History

Claudication
Other non–joint-related exertional lower extremity symptoms (not typical of claudication)
Impaired walking function
Ischemic rest pain

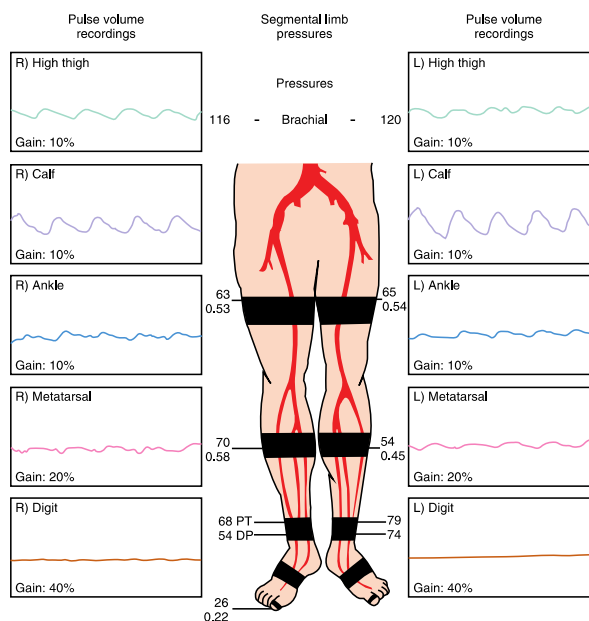
Physical Examination

Abnormal lower extremity pulses
Vascular bruit
Nonhealing lower extremity wound or gangrene
Other suggestive lower extremity physical findings (eg, elevation pallor/dependent rubor)



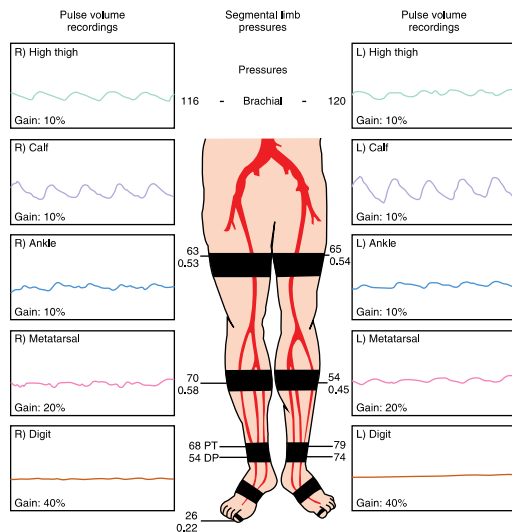
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Diagnostic Criteria for Peripheral Arterial Disease



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Diagnostic Criteria for Peripheral Arterial Disease



>1.40 – Noncompressible
 0.9-1.40 – Normal
 0.5- <0.9 – PAD
 <0.5 - Critical Limb Ischemia

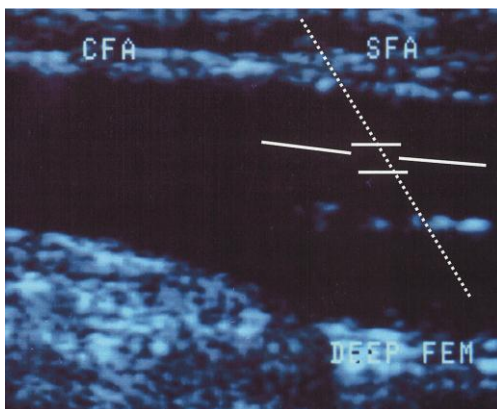
Decrease in the ABI >25%
 with Exercise is consistent
 with PAD



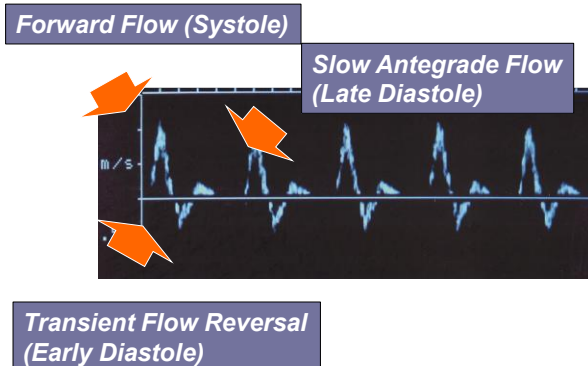
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Arterial Duplex

Grey Scale Doppler



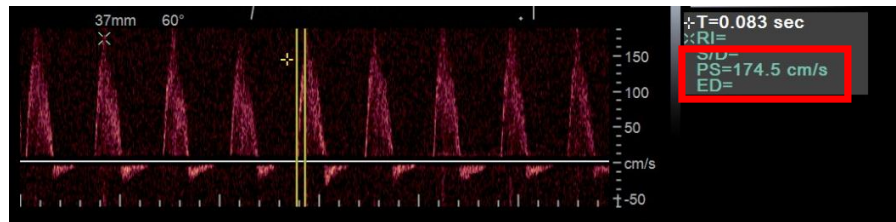
Pulse Doppler



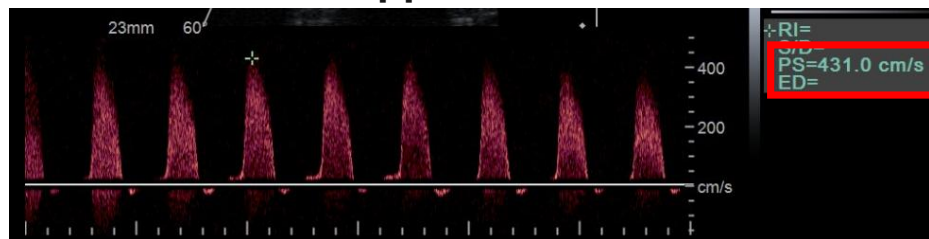
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Arterial Duplex

Normal Pulse Doppler – L CFA



Abnormal Pulse Doppler – R CFA



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Presentation of Peripheral Arterial Disease

Acute Limb Ischemia

Acute (<2 wk), severe hypoperfusion of the limb characterized by the 6 P's:

- Pain
- Pallor
- Pulselessness
- Poikilothermia (cold)
- Paresthesias
- Paralysis



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Presentation of Peripheral Arterial Disease

Critical Limb Ischemia

Chronic (≥ 2 wk) ischemic rest pain, nonhealing wound/ulcers, or gangrene in 1 or both legs attributable to objectively proven arterial occlusive disease.



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Guideline Recommendations for PAD

In pts at increased risk of PAD

Take a comprehensive history regarding exertional leg symptoms (claudication, ischemic rest pain, non-healing wounds)

Perform a vascular examination (assess pulses, listen for bruits, inspect feet)

Perform non-invasive BP in both arms at least once



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Guideline Recommendations for PAD

COR	LOE	Recommendations
I	B-NR	In patients with history or physical examination findings suggestive of PAD (Table 4), the resting ABI, with or without segmental pressures and waveforms, is recommended to establish the diagnosis.
I	C-LD	Resting ABI results should be reported as abnormal (ABI ≤ 0.90), borderline (ABI 0.91–0.99), normal (1.00–1.40), or noncompressible (ABI > 1.40).



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Guideline Recommendations for PAD

COR	LOE	Recommendations
I	B-NR	Duplex ultrasound, CTA, or MRA of the lower extremities is useful to diagnose anatomic location and severity of stenosis for patients with symptomatic PAD <u>in whom revascularization is considered</u> .
I	C-EO	Invasive angiography is useful for patients with CLI <u>in whom revascularization is considered</u> .
IIa	C-EO	Invasive angiography is reasonable for patients with lifestyle-limiting claudication with an inadequate response to GDMT <u>for whom revascularization is considered</u> .



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Guideline Recommendations for PAD

COR	LOE	Recommendation
Ila	B-NR	A screening duplex ultrasound for AAA is reasonable in patients with symptomatic PAD.

COR	LOE	Recommendations
I	A	Patients with PAD who smoke cigarettes or use other forms of tobacco should be advised at every visit to quit.



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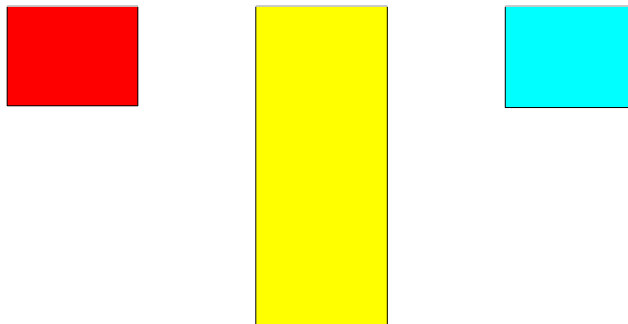
Guideline Recommendations for PAD

COR	LOE	Recommendations
I	A	Antiplatelet therapy with aspirin alone (range 75–325 mg per day) or clopidogrel alone (75 mg per day) is recommended to reduce MI, stroke, and vascular death in patients with <u>symptomatic</u> PAD.
Ila	C-EO	In <u>asymptomatic</u> patients with PAD (ABI ≤ 0.90), antiplatelet therapy is reasonable to reduce the risk of MI, stroke, or vascular death.



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CAPRIE trial: Risk reduction in specific subgroups



Lancet 1996; 348: 1329

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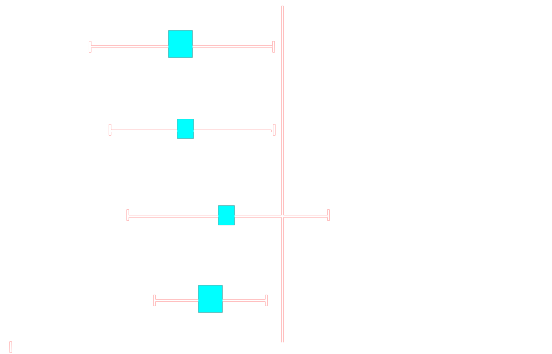
Guideline Recommendations for PAD

COR	LOE	Recommendations
IIb	C-LD	Dual-antiplatelet therapy (aspirin and clopidogrel) may be reasonable to reduce the risk of limb-related events in patients with symptomatic PAD after lower extremity revascularization.



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Aspirin + Clopidogrel for Peripheral Arterial Disease (CHARISMA)



Bhatt DL, *J Am Coll Cardiol* 2007; 49: 1982

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Guideline Recommendations for PAD

COR	LOE	Recommendations
I	A	Treatment with a statin medication is indicated for all patients with PAD.
I	A	Antihypertensive therapy should be administered to patients with hypertension and PAD to reduce the risk of MI, stroke, heart failure, and cardiovascular death.



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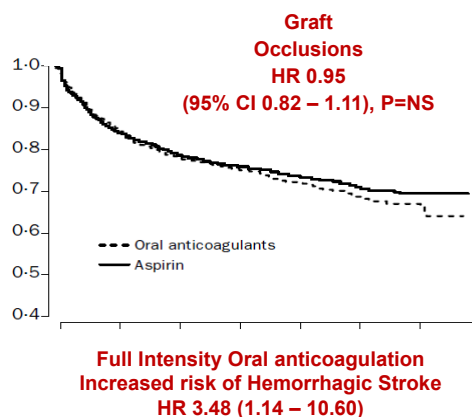
Guideline Recommendations for PAD

COR	LOE	Recommendations
III: Harm	A	Anticoagulation should not be used to reduce the risk of cardiovascular ischemic events in patients with PAD.



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Outcomes with DAPT and Anti-Coagulation Following Peripheral Revascularization



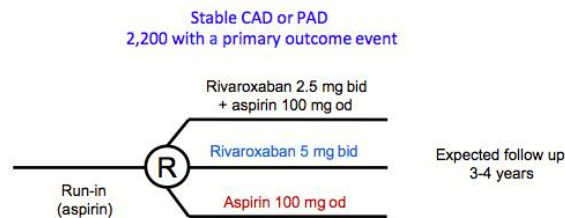
Dutch Bypass Oral anticoagulants or Aspirin (BOA) Study Group. Lancet. 2000

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Risk of CV Death, MI, Stroke in Pts with PAD

n=7,470 Pts with PAD

COMPASS design



Slides Courtesy of Sonia Anand
Presented at 2017 ESC (Barcelona, Spain)

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Risk of CV Death, MI, Stroke in Pts with PAD

n=7,470 pts with PAD



PAD Patients in COMPASS

PAD Groups	Number of patients
All Patients	7,470
Symptomatic PAD Limbs	4,129
Carotid Disease	1,919
CAD + Low ABI (<0.90) only	1,422

Mean Follow-up: 21 months



Slides Courtesy of Sonia Anand
Presented at 2017 ESC (Barcelona, Spain)

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Risk of CV Death, MI, Stroke in Pts with PAD

n=7,470 Pts with PAD

Outcome	R + A N=2,492	R N=2,474	A N=2,504	Riva + aspirin vs. aspirin		Riva vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	P	HR (95% CI)	P
MACE	126 (5.1)	149 (6.0)	174 (6.9)	0.72 (0.57-0.90)	0.005	0.86 (0.69-1.08)	0.19
MI	51 (2.0)	56 (2.3)	67 (2.7)	0.76 (0.53-1.09)	-	0.84 (0.59-1.20)	-
Stroke	25 (1.0)	43 (1.7)	47 (1.9)	0.54 (0.33-0.87)	-	0.93 (0.61-1.40)	-
CV Death	64 (2.6)	66 (2.7)	78 (3.1)	0.82 (0.59-1.14)	-	0.86 (0.62-1.19)	-



Slides Courtesy of Sonia Anand
Presented at 2017 ESC (Barcelona, Spain)

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Trial Design

NCT02504216

6,564 Patients with Symptomatic Lower Extremity PAD* Undergoing Peripheral Revascularization

*Ankle Brachial Index < 0.90 and Imaging Evidence of Occlusive Disease

ASA 100 daily for all Patients
Clopidogrel at Investigator's Discretion

Randomized 1:1 Double Blind

Rivaroxaban 2.5 mg twice daily

Stratified by
Revascularization Approach
(Surgical or Endovascular)
and Use of Clopidogrel

Placebo

Follow up Q6 Months, Event Driven, Median f/u 28 Months

Primary Efficacy Endpoint: Acute limb ischemia, major amputation of vascular etiology, myocardial infarction, ischemic stroke or cardiovascular death

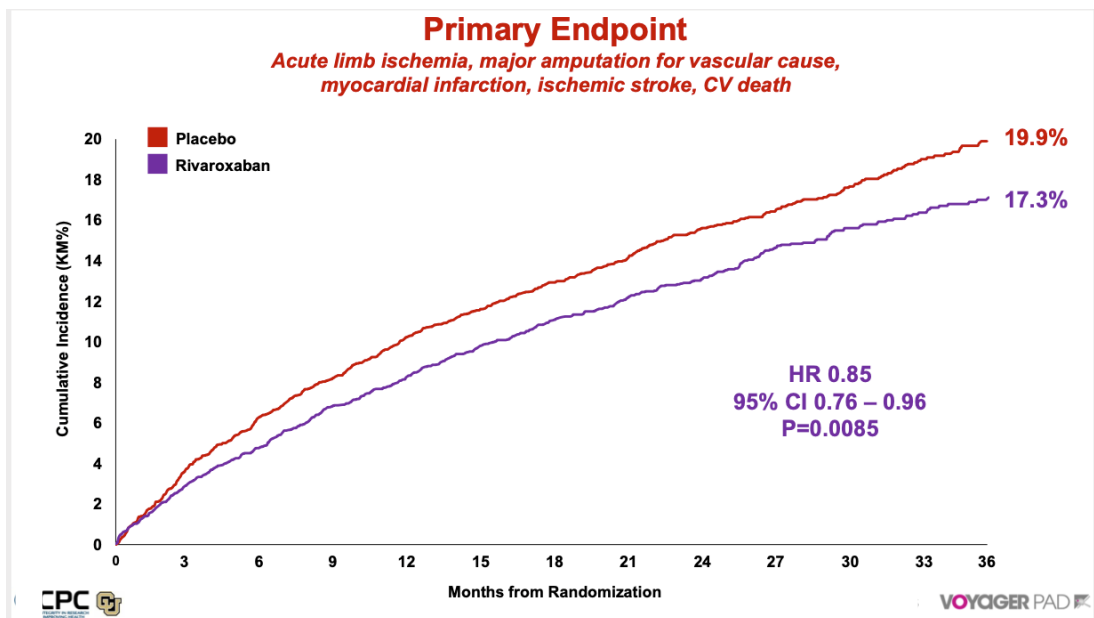
Principal Safety Outcome: TIMI Major Bleeding



Capell WH, Bonaca MP, Nehler MR...Hiatt WR. AHJ 2018



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Guideline Recommendations for PAD

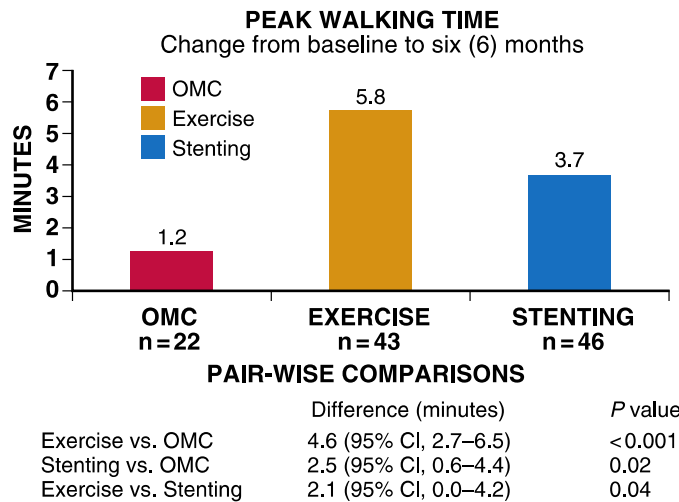
COR	LOE	Recommendations
I	A	In patients with claudication, a supervised exercise program is recommended to improve functional status and QoL and to reduce leg symptoms.
I	B-R	A supervised exercise program should be discussed as a treatment option for claudication before possible revascularization.



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Exercise Therapy Increases Walking Time

n=111 Pts in the CLEVER Trial



Murphy TP et al. *Circulation*; 2012. 125: 130

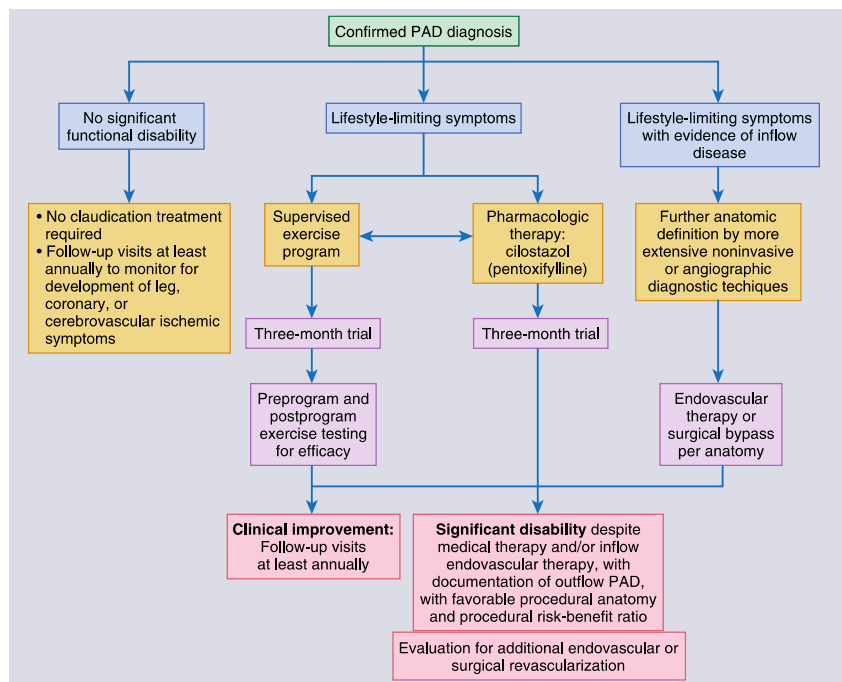
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Guideline Recommendations for PAD

COR	LOE	Recommendation
Ila	A	Revascularization is a reasonable treatment option for the patient with lifestyle-limiting claudication with an inadequate response to GDMT.



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Guideline Recommendations for PAD

COR	LOE	Recommendations
I	A	Endovascular procedures are effective as a revascularization option for patients with lifestyle-limiting claudication and hemodynamically significant aortoiliac occlusive disease.
Ila	B-R	Endovascular procedures are reasonable as a revascularization option for patients with lifestyle-limiting claudication and hemodynamically significant femoropopliteal disease.
Ilb	C-LD	The usefulness of endovascular procedures as a revascularization option for patients with claudication due to isolated infrapopliteal artery disease is unknown.



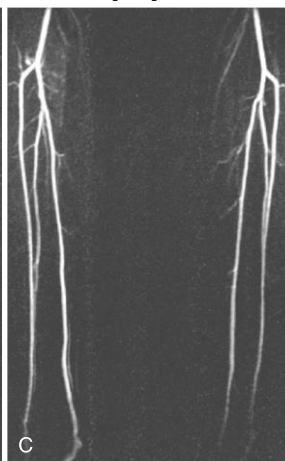
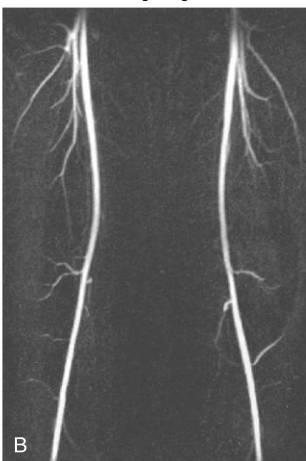
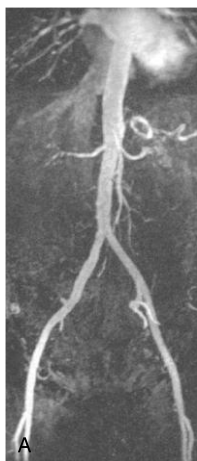
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Guidelines for Endovascular Revascularization in Pts Who Fail Medical Tx

Aorto-Iliac

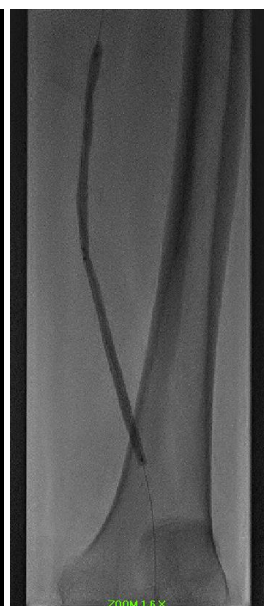
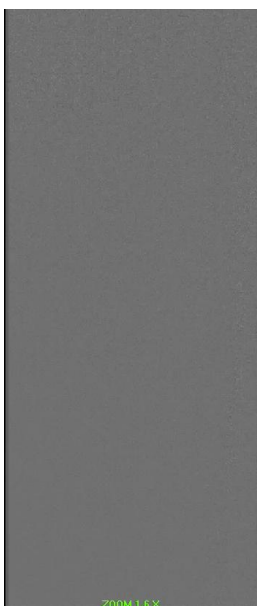
Femoropopliteal

Infrapopliteal



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Endovascular Revascularization in Pts Who Fail Medical Tx

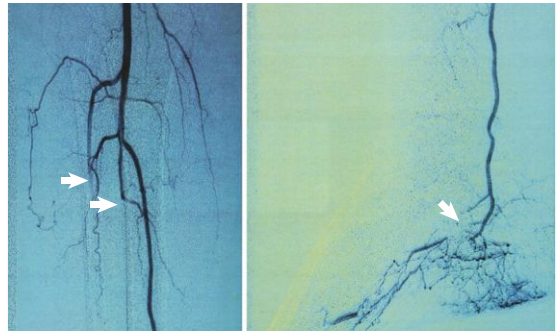


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Thromboangiitis Obliterans (Buerger's Disease)

Segmental vasculitis involving the distal arteries, veins, and nerves of young (~40) people who smoke

Treatment – tobacco cessation. Amputations occur in ~40% of pts who continue to smoke



Braunwald's Heart Disease (15th ed). 2016

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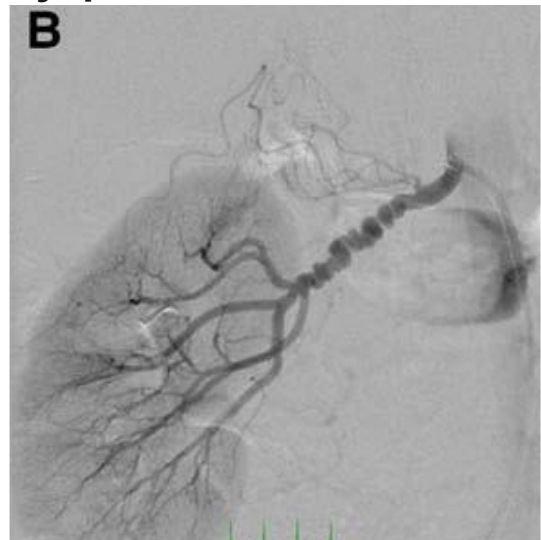
Fibromuscular Dysplasia

Affects medium-large artery (typically renal, carotid) in young, white women

Can present with poorly controlled HTN or tinnitus

Angiography shows a beaded appearance

Treatment is balloon angioplasty



Circulation. 2014; 129: 1048

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Fibromuscular Dysplasia

Effects medium-large artery (typically renal, carotid) in young, white women

Can present with poorly controlled HTN or tinnitus

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Circulation. 2014; 129: 1048



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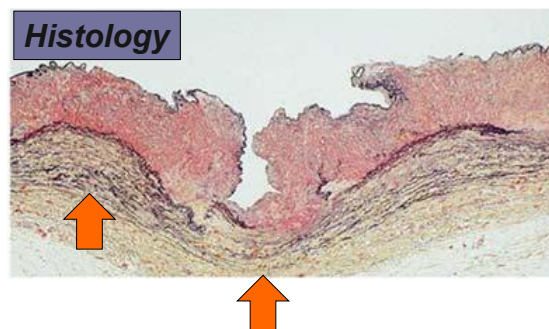
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Effects medium-large artery (typically renal, carotid) in young, white women

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Circulation. 2014; 129: 1048



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Top Ten Guidelines Based Recommendations for Patients with PAD

Evaluate pts at increased risk for PAD

Perform ABIs in those in whom PAD is suspected

Imaging (CTA, MRA) only needed for those in whom revascularization is being considered

Screen pts with PAD for AAA

Smoking cessation should be advised for all pts with PAD

Pharmacotherapy includes monotherapy with either aspirin or clopidogrel

All pts with PAD need aggressive statin therapy

Anti-HTN therapy (preferably ACEi/ARB) is indicated in pts with PAD

Pts w/ claudication benefit from supervised exercise program (Cardiac rehab now reimbursable from CMS)

Revascularization is indicated in pts with persistent claudication despite medical therapy and exercise, acute limb ischemia or critical limb ischemia.



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Interdisciplinary Approach to PAD

A team of professionals representing different disciplines to assist in the evaluation and management of the patient with PAD. For the care of patients with CLI, the interdisciplinary care team should include individuals who are skilled in

endovascular revascularization

surgical revascularization

wound healing therapies

foot surgery

medical evaluation/care

866-862-4327 (Referral)

984-843-5214 (Office)



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