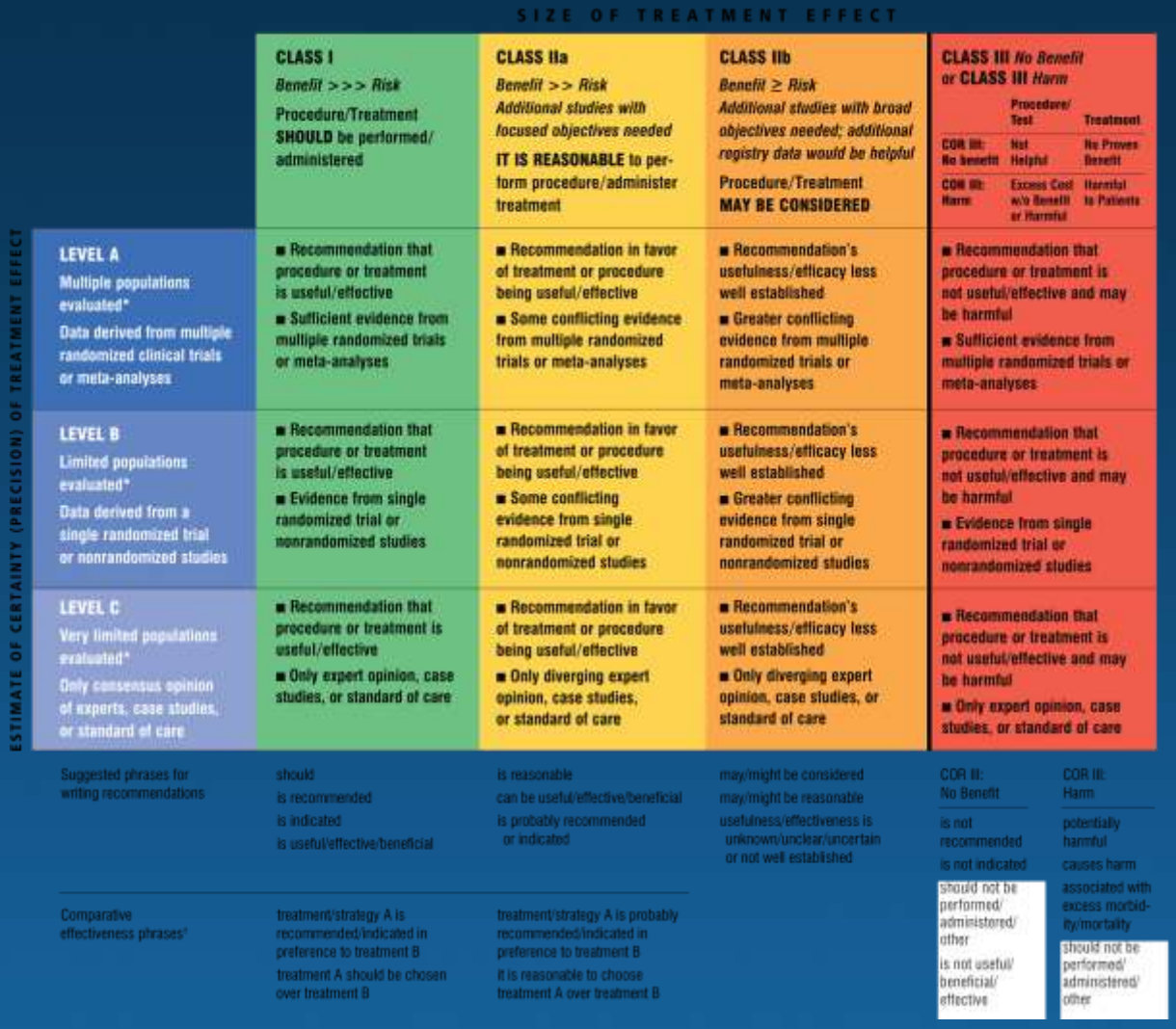
PAD
Clinical Presentations

Classification of Recommendations and Levels of Evidence



SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/ Test / Treatment COR III: No Benefit: Not Helpful / No Proven Benefit COR III: Harm: Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B It is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

****Data available from clinical trials or registries about the usefulness/ efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.***

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

This guideline recognizes that:

Individuals With PAD Present in Clinical Practice With Distinct Syndromes

Asymptomatic: Without obvious symptomatic complaint (but usually with a functional impairment).

Classic claudication: Lower extremity symptoms confined to the muscles with a consistent (reproducible) onset with exercise and relief with rest.

"Atypical" leg pain: Lower extremity discomfort that is exertional but that does not consistently resolve with rest, consistently limit exercise at a reproducible distance, or meet all "Rose questionnaire" criteria.

This guideline recognizes that:

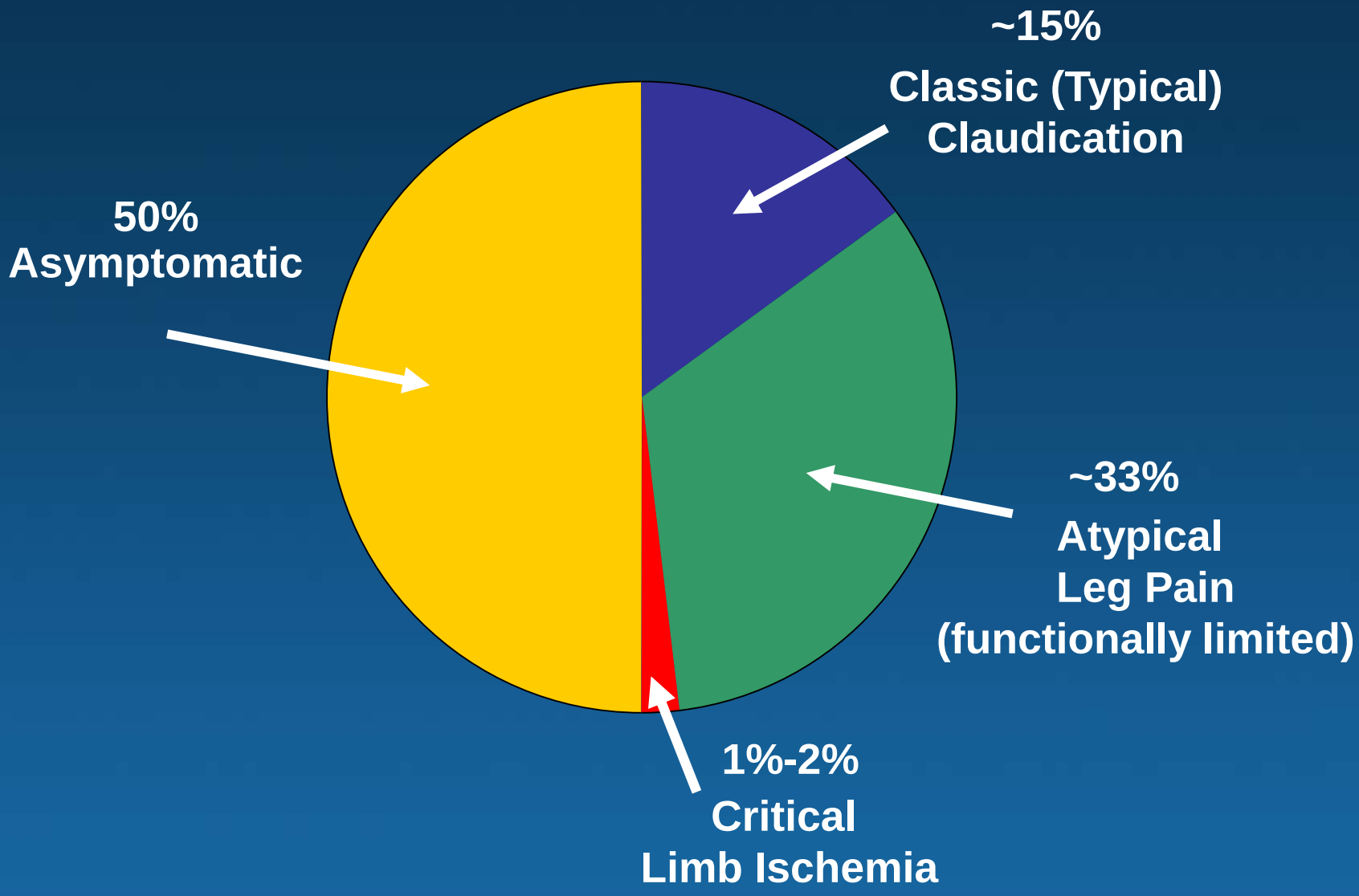
Individuals With PAD Present in Clinical Practice With Distinct Syndromes

Critical limb Ischemia: Ischemic rest pain, nonhealing wound, or gangrene/

Acute limb ischemia: The five "P"s, defined by the clinical symptoms and signs that suggest potential limb jeopardy:

- Pain
- Pulselessness
- Pallor
- Paresthesias
- Paralysis (& polar, as a sixth "P").

Clinical Presentations of PAD



Claudication vs. Pseudoclaudication

	Claudication	Pseudoclaudication
Characteristic of discomfort	Cramping, tightness, aching, fatigue	Same as claudication plus tingling, burning, numbness
Location of discomfort	Buttock, hip, thigh, calf, foot	Same as claudication
Exercise-induced	Yes	Variable
Distance	Consistent	Variable
Occurs with standing	No	Yes
Action for relief	Stand	Sit, change position
Time to relief	<5 minutes	≤30 minutes

Also see Table 4 of Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

Leg Pain Has a Differential Diagnosis

- Spinal canal stenosis
- Peripheral neuropathy
- Peripheral nerve pain
  - Herniated disc impinging on sciatic nerve
- Osteoarthritis of the hip or knee
- Venous claudication
- Symptomatic Baker's cyst
- Chronic compartment syndrome
- Muscle spasms or cramps
- Restless leg syndrome

Also see Table 3 of Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

Factors That Increase Risk of Limb Loss in Patients With Critical Limb Ischemia

- Factors that reduce blood flow to the microvascular bed
  - Diabetes
  - Severe renal failure
  - Severely decreased cardiac output (severe heart failure or shock)
  - Vasospastic diseases or concomitant conditions (e.g., Raynaud's phenomenon, prolonged cold exposure)
  - Smoking and tobacco use
- Factors that increase demand for blood flow to the microvascular bed
  - Infection (e.g., cellulitis, osteomyelitis)
  - Skin breakdown or traumatic injury

Also see Table 5 of Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

Differential Diagnosis of Common Foot Ulcers

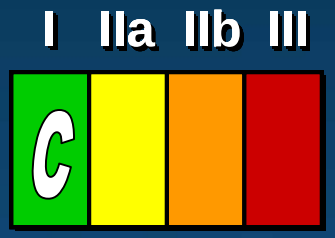
Neuropathic Ulcer	Neuroischemic Ulcer
Painless	Painful
Normal pulses	Absent pulses
Typically punches-out appearance	Irregular margins
Often located on sole or edge of foot or metatarsal head	Commonly located on toes
Presence of calluses	Calluses absent or infrequent
Loss of sensation, reflexes, and vibration sense	Variable sensory findings
Increase in blood flow (arteriovenous shunting)	Decrease in blood flow
Dilated veins	Collapsed veins
Dry, warm foot	Cold foot
Bone deformities	No bony deformities
Red appearance	Pale, cyanotic

Etiologic Classification of Foot and Leg Ulcers

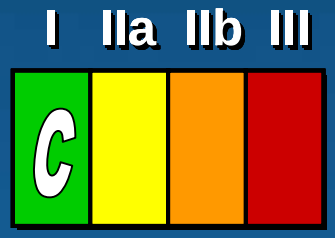
- Venous obstruction and insufficiency
- Arterial etiologies
  - Larger arteries
  - Atherosclerotic lower extremity PAD
  - Thromboemboli, atheroemboli
  - Thromboangiitis obliterans
- Microcirculatory
  - Diabetic microangiopathy
  - Vasculitis
  - Collagen vascular diseases
- Neuropathic
  - Diabetes mellitus
- Infectious
  - Leprosy
  - Mycotic
- Hematologic
  - Sickle cell anemia
  - Polycythemia
  - Thrombocytosis
- Malignancy
  - Squamous cell carcinoma
  - Kaposi's sarcoma
- Artifactual or factitious

Also see Table 10 of Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

The Vascular History and Physical Examination

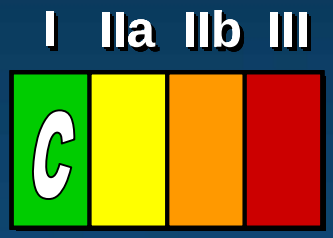


Individuals at risk for lower extremity PAD should undergo a vascular review of symptoms to assess walking impairment, claudication, ischemic rest pain, and/or the presence of nonhealing wounds.

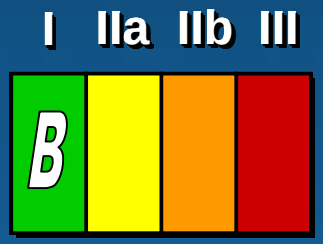


Individuals at risk for lower extremity PAD should undergo comprehensive pulse examination and inspection of the feet.

Identification of the Asymptomatic Patient With PAD

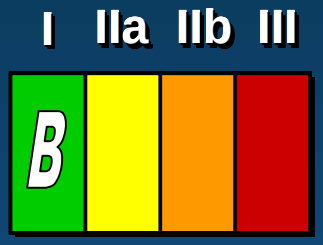


A history of walking impairment, claudication, and ischemic rest pain is recommended as a required component of a standard review of systems for adults ≥50 years who have atherosclerosis risk factors, or for adults ≥70 years.

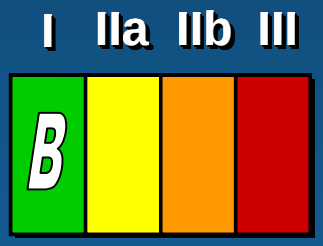


Individuals with asymptomatic PAD should be identified in order to offer therapeutic interventions known to diminish their increased risk of myocardial infarction, stroke, and death.

Identification of the Symptomatic Patient With Intermittent Claudication

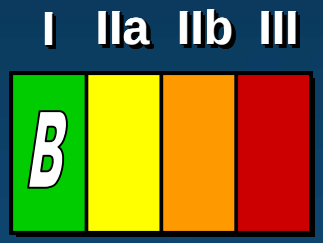


Patients with symptoms of intermittent claudication should undergo a vascular physical examination, including measurement of the ABI.

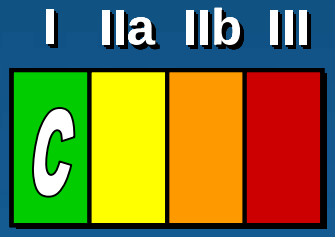


In patients with symptoms of intermittent claudication, the ABI should be measured after exercise if the resting index is normal.

Evaluation of the Patient With Critical Limb Ischemia



Patients at risk of CLI (ABI less than 0.4 in a nondiabetic individual, or any diabetic individual with known lower extremity PAD) should undergo regular inspection of the feet to detect objective signs of CLI.



The feet should be examined directly, with shoes and socks removed, at regular intervals after successful treatment of CLI.

Guideline for the Management of Patients with PAD

Smoking Cessation

Recommendations for Smoking Cessation

Patients who are smokers or former smokers should be asked about status of tobacco use at every visit.

Patients should be assisted with counseling and developing a plan for quitting that may include pharmacotherapy and/or referral to a smoking cessation program.

Recommendations for Smoking Cessation

Individuals with lower extremity PAD who smoke cigarettes or use other forms of tobacco should be advised by each of their clinicians to stop smoking and offered behavioral and pharmacological treatment.

In the absence of contraindication or other compelling clinical indication, 1 or more of the following pharmacological therapies should be offered: varenicline, bupropion, and nicotine replacement therapy.

The Clinical Approach to the Patient With, or at Risk for, PAD

Clinicians who care for individuals with PAD should be able to provide:

- A vascular review of symptoms
- A vascular-focused physical examination
- Use of the noninvasive vascular diagnostic laboratory (ABI and toe-brachial index [TBI], exercise ABI, Duplex ultrasound, magnetic resonance angiography [MRA], and computed tomographic angiography [CTA])
- When required, use of diagnostic catheter-based angiography

Comprehensive Vascular Examination

Key components of the vascular physical examination include:

- Bilateral arm blood pressure (BP)
- Cardiac examination
- Palpation of the abdomen for aneurysmal disease
- Auscultation for bruits
- Examination of legs and feet

- Pulse Examination
  - Carotid
  - Radial/ulnar
  - Femoral
  - Popliteal
  - Dorsalis pedis
  - Posterior tibial
- Scale:
  - 0=Absent
  - 1=Diminished
  - 2=Normal
  - 3=Bounding (aneurysm or AI)

The First Tool to Establish the PAD Diagnosis: *A Standardized Physical Examination*

Pulse intensity should be assessed and should be recorded numerically as follows:

- 0, absent
- 1, diminished
- 2, normal
- 3, bounding

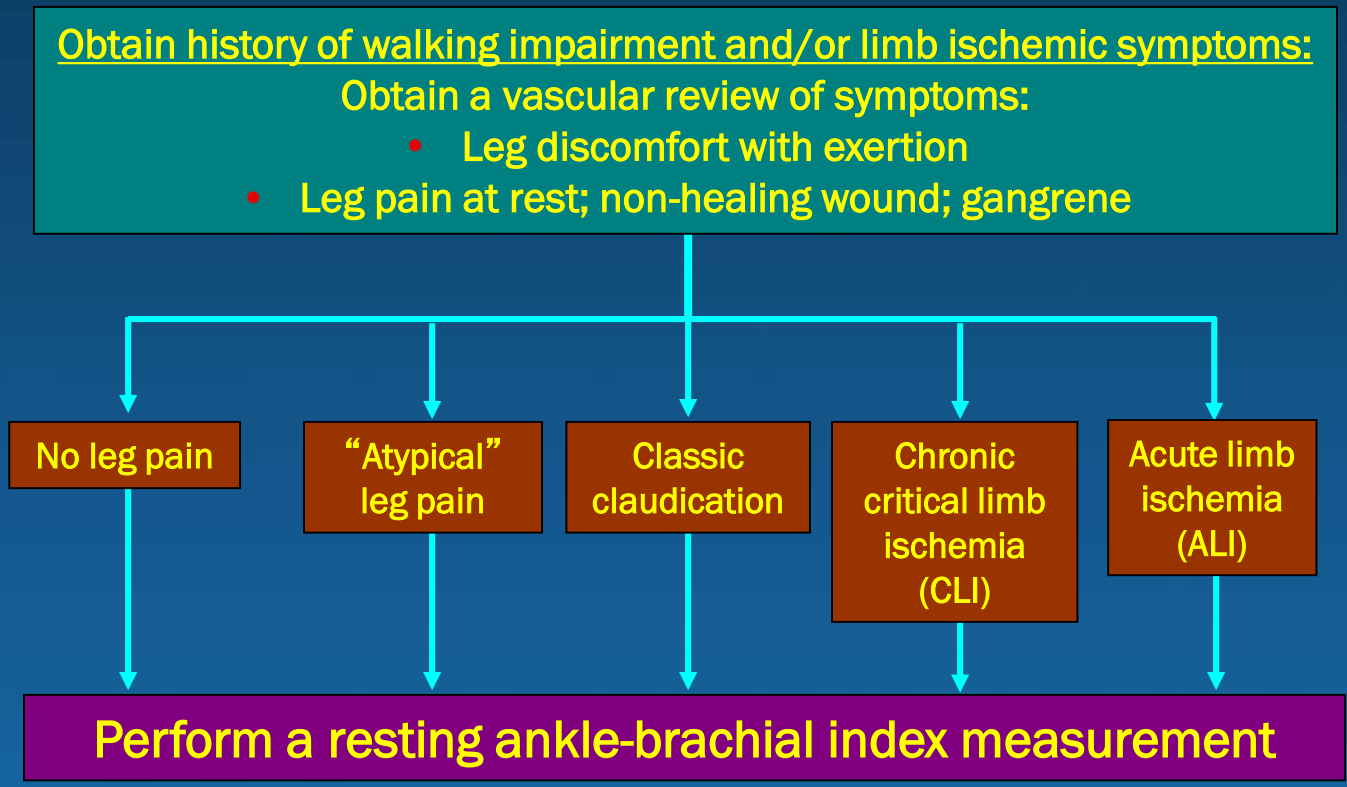
Use of a standard examination should facilitate clinical communication

Differential Diagnosis of PAD

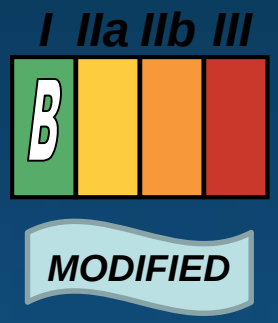
- Atherosclerosis
- Vasculitis
- Fibromuscular dysplasia
- Atheroembolic disease
- Thrombotic disorders
- Trauma
- Radiation
- Popliteal aneurysm
- Thromboangiitis obliterans (Buerger's disease)
- Popliteal entrapment
- Cystic adventitial disease
- Coarctation of aorta
- Vascular tumor
- Iliac syndrome of the cyclist
- Pseudoxanthoma elasticum
- Persistent sciatic artery (thrombosed)

ACC/AHA Guideline for the Management of PAD: Steps Toward the Diagnosis of PAD

Recognizing the "at risk" groups leads to recognition of the five main PAD clinical syndromes:



Recommendations for ABI, Toe-Brachial Index, and Segmental Pressure Examination



The resting ABI should be used to establish the lower extremity PAD diagnosis in patients with suspected lower extremity PAD, defined as individuals with 1 or more of the following: exertional leg symptoms, nonhealing wounds, age ≥65 years, or ≥50 years with a history of smoking or diabetes.

Recommendations for ABI, Toe-Brachial Index, and Segmental Pressure Examination

The ABI should be measured in both legs in all new patients with PAD of any severity to confirm the diagnosis of lower extremity PAD and establish a baseline.

Recommendations for ABI, Toe-Brachial Index, and Segmental Pressure Examination

The toe-brachial index should be used to establish the lower extremity PAD diagnosis in patients in whom lower extremity PAD is clinically suspected but in whom the ABI test is not reliable due to noncompressible vessels (usually patients with long-standing diabetes or advanced age).

Leg segmental pressure measurements are useful to establish the lower extremity PAD diagnosis when anatomic localization of lower extremity PAD is required to create a therapeutic plan.

Recommendations for ABI, Toe-Brachial Index, and Segmental Pressure Examination

ABI results should be uniformly reported with noncompressible values defined as >1.40, normal values 1.00 to 1.40, borderline 0.91 to 0.99, and abnormal ≤0.90.

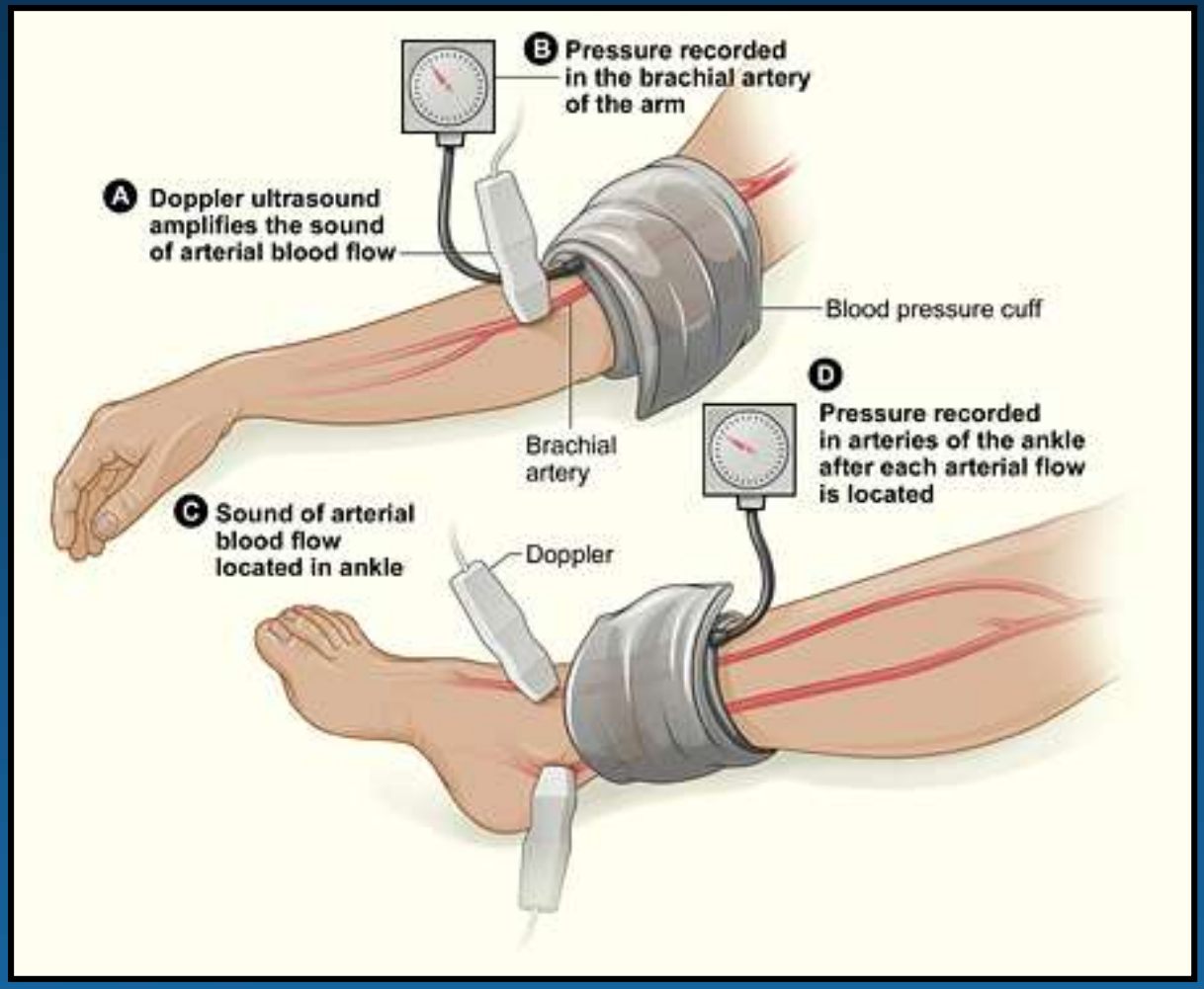
How to Perform an ABI Exam

- Performed with the patient resting in the supine position
- All pressures are measured with an arterial Doppler and appropriately sized blood pressure cuff (edge 1-2 inches above the pulse; cuff width should be 40% of limb circumference).
- Systolic pressures will be measured in the right and left brachial arteries followed by the right and left ankle arteries.

ABI Procedure

- Step 1: Apply the appropriately sized blood pressure cuff on the arm above the elbow (either arm).
- Step 2: Apply Doppler gel to skin surface.
- Step 3: Turn on the Doppler and place the probe in the area of the pulse at a 45-60˚ angle to the surface of the skin, pointing to the shoulder.
- Step 4: Move the probe around until the clearest arterial signal is heard.

ABI Procedure



http://www.nhlbi.nih.gov/health/dci/Diseases/pad/pad_diagnosis.html

ABI Procedure

- Step 5: Inflate the blood pressure cuff to approximately 20 mmHg above the point where systolic sounds are no longer heard.
- Step 6: Gradually deflate until the arterial signal returns. Record the pressure reading.
- Step 7: Repeat the procedure for the right and left posterior tibial and dorsalis pedis arteries. Place the probe on the pulse and angle the probe at 45^{o} toward the knee.
- Step 8: Record the systolic blood pressure of the contralateral arm.

Understanding the ABI

The ratio of the higher brachial systolic pressure and the higher ankle systolic pressure for each leg:

$$\text{ABI} = \frac{\text{Ankle systolic pressure}}{\text{Higher brachial artery systolic pressure}}$$

Calculate the ABI

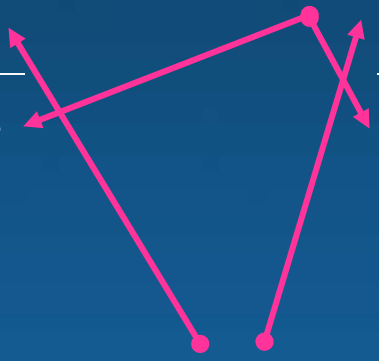
1. For the left side, divide the left ankle pressure by the highest brachial pressure and record the result.
2. Repeat the steps for the right side.
3. Record the ABIs and place the results in the medical record.

Right Leg ABI

$$\frac{\text{Right Ankle Pressure}}{\text{Highest Arm Pressure}}$$

Left Leg ABI

$$\frac{\text{Left Ankle Pressure}}{\text{Highest Arm Pressure}}$$



ABI Interpretation

≤ 0.90 is diagnostic of peripheral arterial disease

Hiatt WR. *N Engl J Med*. 2001;344:1608-1621; TASC Working Group. *J Vasc Surg.* 2000;31(1Suppl):S1-S296.

The Ankle-Brachial Index

$$\text{ABI} = \frac{\text{Lower extremity systolic pressure}}{\text{Brachial artery systolic pressure}}$$

- The ankle-brachial index is 95% sensitive and 99% specific for PAD
- Establishes the PAD diagnosis
- Identifies a population at high risk of CV ischemic events
- The "population at risk" can be clinically and epidemiologically defined:
  - *Age less than 50 years with diabetes, and one additional risk factor Age 50 to 69 years and history of smoking or diabetes*
  - *Age 70 years and older*
  - *Leg symptoms with exertion (suggestive of claudication) or ischemic rest pain*
  - *Abnormal lower extremity pulse examination*
  - *Known atherosclerotic coronary, carotid, or renal artery disease*
- Toe-brachial index (TBI) useful in individuals with non-compressible pedal pulses

Lijmer JG. *Ultrasound Med Biol* 1996;22:391-8; Feigelson HS. *Am J Epidemiol* 1994;140:526-34; Baker JD. *Surgery* 1981;89:134-7; Ouriel K. *Arch Surg* 1982;117:1297-13; Carter SA. *J Vasc Surg* 2001;33:708-14

Interpreting the Ankle-Brachial Index

ABI	Interpretation
1.00–1.29	Normal
0.91–0.99	Borderline
0.41–0.90	Mild-to-moderate disease
≤0.40	Severe disease
≥1.30	Noncompressible

Adapted from Hirsch AT, et al. *J Am Coll Cardiol*. 2006;47:e1-e192. Figure 6.

Using the ABI: An Example

Right ABI	Left ABI	ABI
80/160=0.50	120/160=0.75	(Normal >0.90)
Brachial SBP 150 mm Hg	**Brachial SBP 160 mm Hg**	Highest brachial SBP
PT SBP 40 mm Hg	**PT SBP 120 mm Hg**	Highest of PT or DP SBP
DP SBP 80 mm Hg	DP SBP 80 mm Hg	

ABI=ankle-brachial index; DP=dorsalis pedis; PT=posterior tibial; SBP=systolic blood pressure.

ABI Limitations

- Incompressible arteries (elderly patients, patients with diabetes, renal failure, etc.)
- Resting ABI may be insensitive for detecting mild aorto-iliac occlusive disease
- Not designed to define degree of functional limitation
- Normal resting values in symptomatic patients may become abnormal after exercise
- Note: "Non-compressible" pedal arteries is a physiologic term and such arteries need not be "calcified"

Toe-Brachial Index Measurement

- The toe-brachial index (TBI) is calculated by dividing the toe pressure by the higher of the two brachial pressures.
- TBI values remain accurate when ABI values are not possible due to non-compressible pedal pulses.
- TBI values ≤ 0.7 are usually considered diagnostic for lower extremity PAD.

Hemodynamic Noninvasive Tests

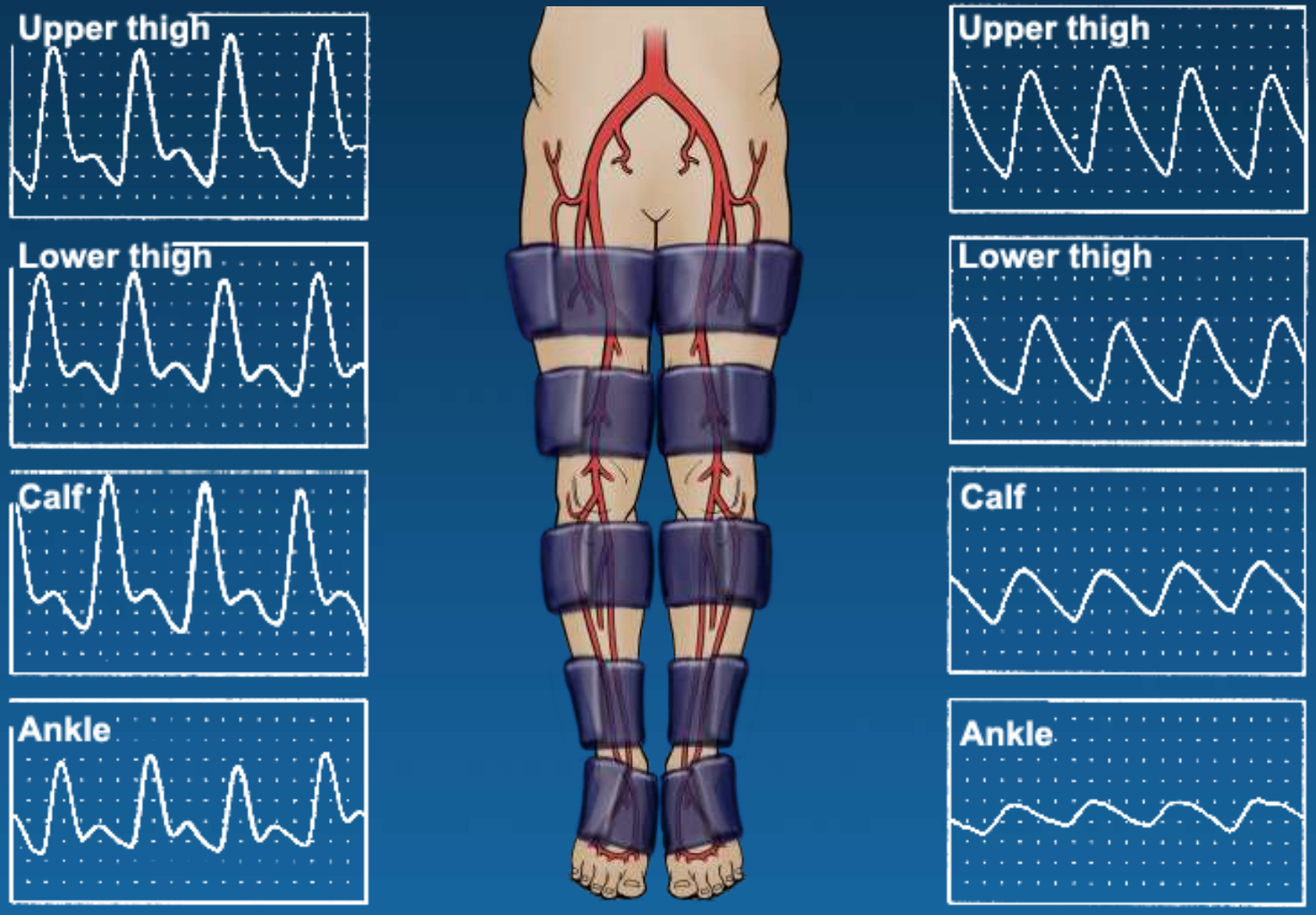
- Resting Ankle-Brachial Index (ABI)
- Exercise ABI
- Segmental pressure examination
- Pulse volume recordings

These traditional tests continue to provide a simple, risk-free, and cost-effective approach to establishing the PAD diagnosis as well as to follow PAD status after procedures.

Segmental Pressures (mm Hg)

150	Brachial	150
150		150
110		146
108		100
62		84
0.54	ABI	0.44

Pulse Volume Recordings



Exercise ABI Testing

- Confirms the PAD diagnosis
- Assesses the functional severity of claudication
- May “unmask” PAD when resting the ABI is normal
- Aids differentiation of intermittent claudication vs. pseudoclaudication diagnoses

Exercise ABI Testing: Treadmill

- Indicated when the ABI is normal or borderline but symptoms are consistent with claudication;
- An ABI fall post-exercise supports a PAD diagnosis;
- Assesses functional capacity (patient symptoms may be discordant with objective exercise capacity).

The Plantar Flexion Exercise ABI

Benefits:

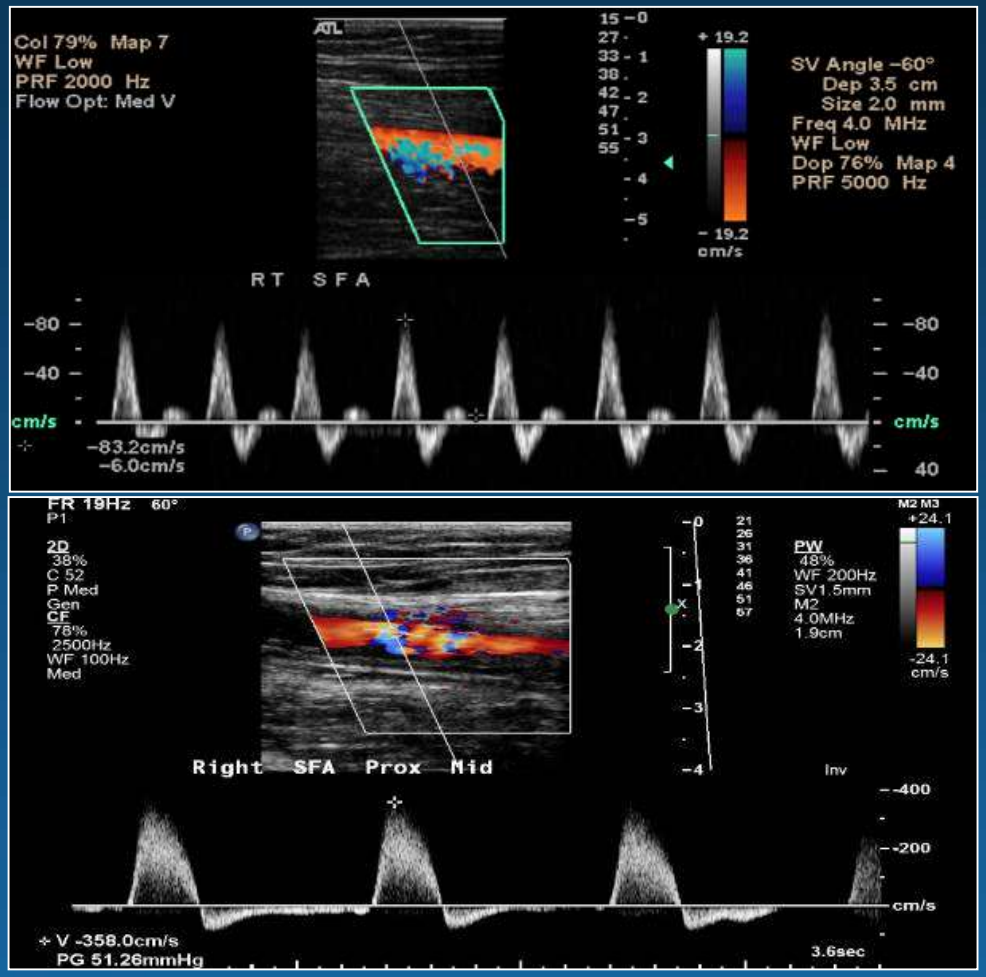
- Reproduces treadmill-derived fall in ABI
- Can be performed anywhere
- Inexpensive

Limitation:

- Does not measure functional capacity

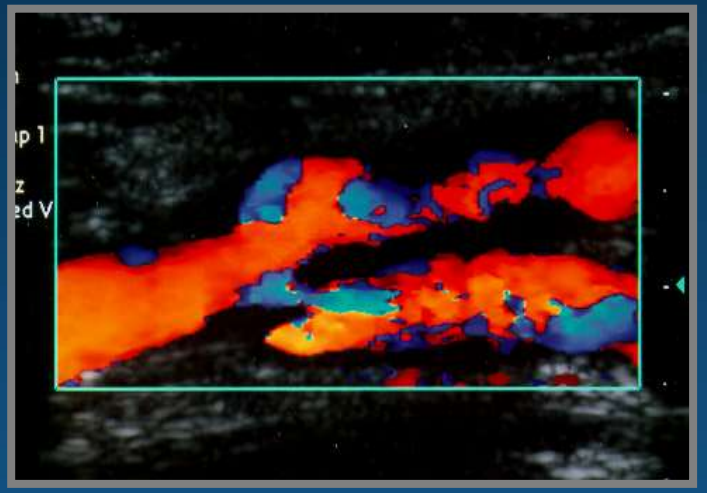
Reprinted with permission from McPhail, IR et al. *J Am Coll Cardiol.* 2001;37:1381.

Color Duplex Ultrasonography



Arterial Duplex Ultrasound Testing

- Duplex ultrasound of the extremities is useful to diagnose anatomic location and degree of stenosis of peripheral arterial disease.
- Duplex ultrasound is useful to provide surveillance following femoral-popliteal bypass using venous conduit (but not prosthetic grafts).
- Duplex ultrasound of the extremities can be used to select candidates for:
  (a) endovascular intervention
  (b) surgical bypass, and
  (c) to select the sites of surgical anastomosis.



However, the data that might support use of duplex ultrasound to assess long-term patency of PTA is not robust.

PTA=percutaneous transluminal angioplasty.

Noninvasive Imaging Tests

Duplex Ultrasound

I	IIa	IIb	III
A			

Duplex ultrasound of the extremities is useful to diagnose the anatomic location and degree of stenosis of PAD.

I	IIa	IIb	III
A			

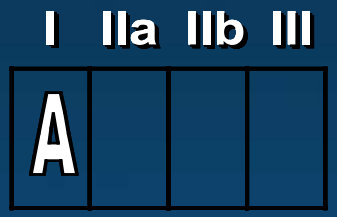
Duplex ultrasound is recommended for routine surveillance after femoral-popliteal or femoral-tibial-pedal bypass with a venous conduit. Minimum surveillance intervals are approximately 3, 6, and 12 months, and then yearly after graft placement.

Magnetic Resonance Angiography (MRA)

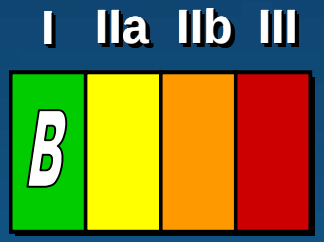
- MRA has virtually replaced contrast arteriography for PAD diagnosis
- Excellent arterial picture
- No ionizing radiation
- Noniodine–based intravenous contrast medium rarely causes renal insufficiency or allergic reaction
- ~10% of patients cannot utilize MRA because of:
  - Claustrophobia
  - Pacemaker/implantable cardioverter-defibrillator
  - Obesity
- Gadolinium use in individuals with an eGFR <60 mL/min has been associated with nephrogenic systemic fibrosis (NSF)/nephrogenic fibrosing dermopathy

Noninvasive Imaging Tests

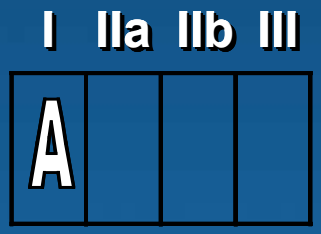
Magnetic Resonance Angiography (MRA)



MRA of the extremities is useful to diagnose anatomic location and degree of stenosis of PAD.

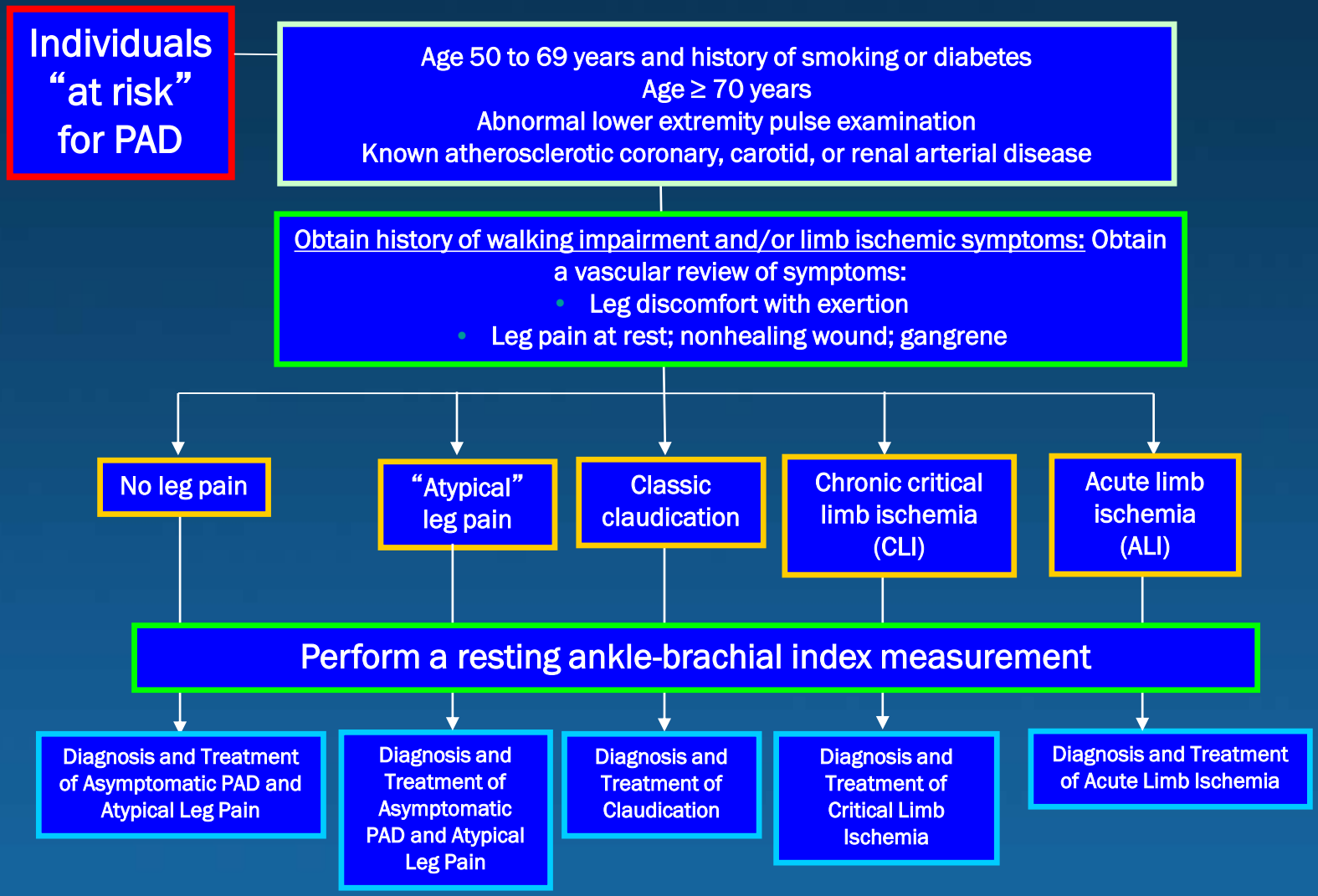


MRA of the extremities should be performed with gadolinium enhancement.



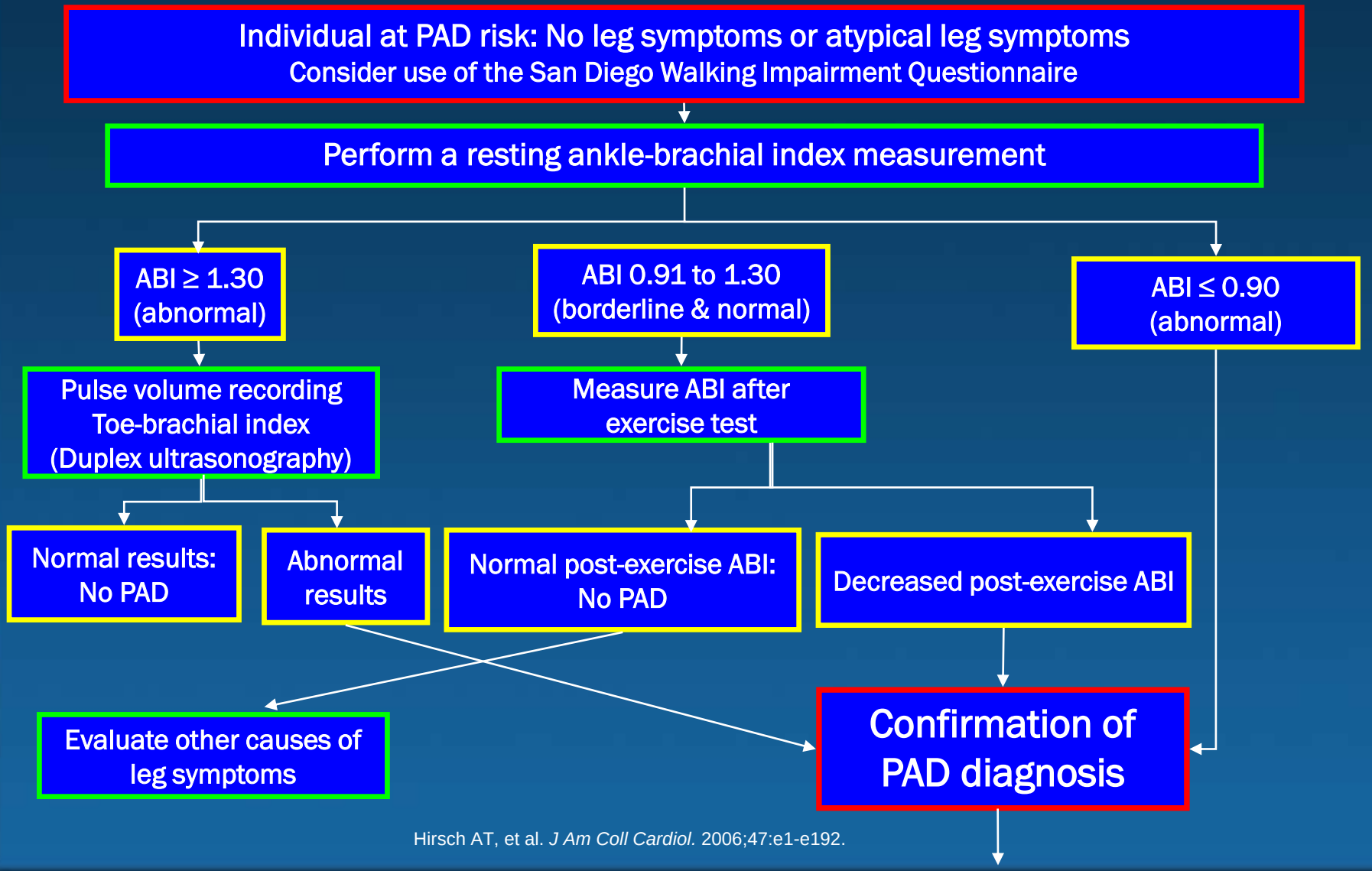
MRA of the extremities is useful in selecting patients with lower extremity PAD as candidates for endovascular intervention.

ACC/AHA Guideline for the Management of PAD:
Steps Toward the Diagnosis of PAD



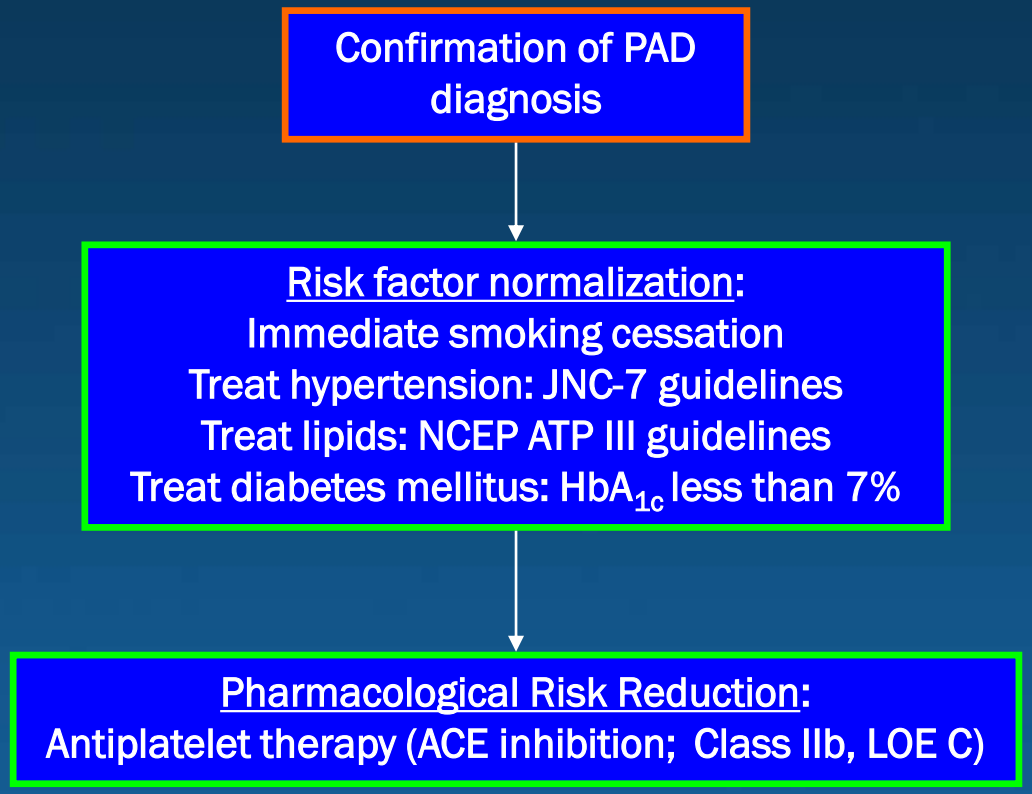
Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

ACC/AHA Guideline for the Management of PAD:
Diagnosis and Treatment of Asymptomatic PAD



Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

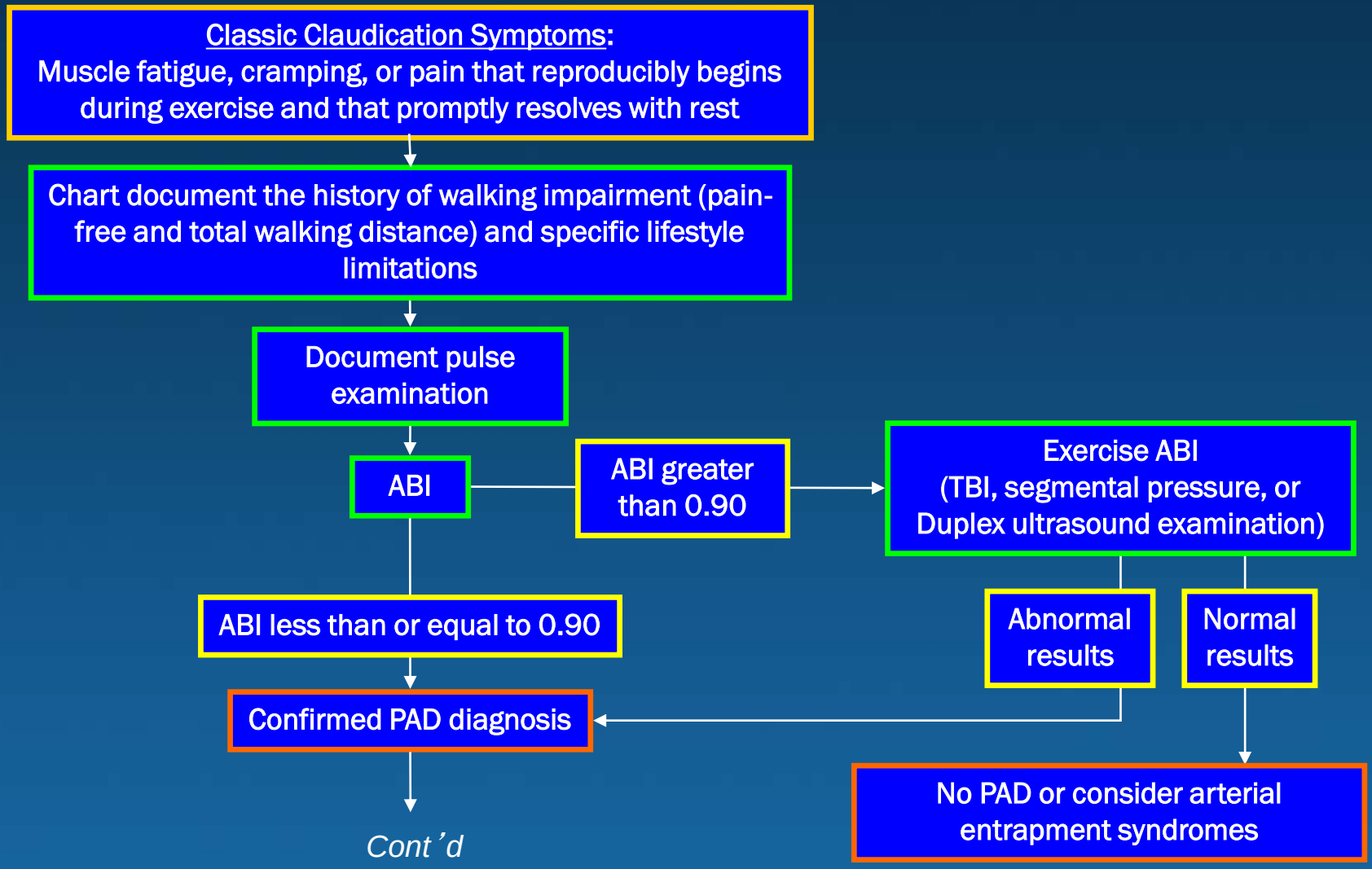
ACC/AHA Guideline for the Management of PAD:
Diagnosis and Treatment of Asymptomatic PAD



ACE=angiotensin-converting enzyme; JNC-7=Joint National Committee on Prevention ; NCEP=National Cholesterol Education Program – Adult Treatment Panel III.

Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

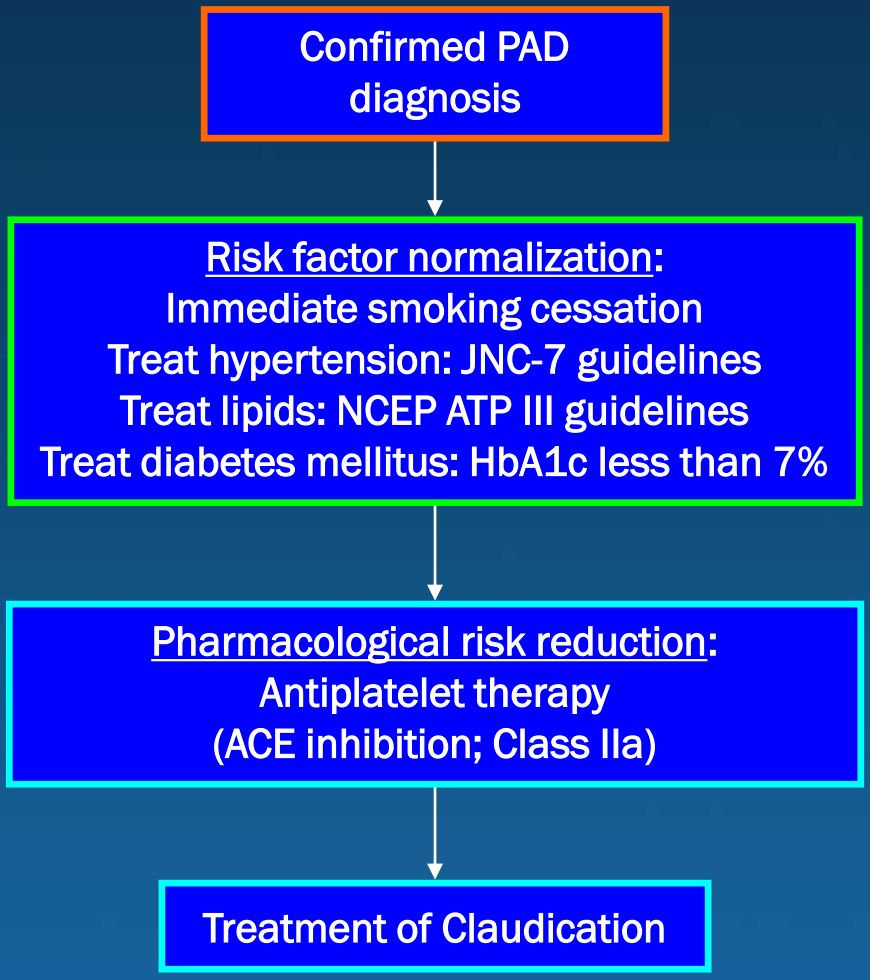
ACC/AHA Guideline for the Management of PAD:
Diagnosis of Claudication and Systemic Risk Treatment



ABI=ankle-brachial index; TBI=toe-brachial index.

Hirsch AT, et al. *J Am Coll Cardiol.* 2006;47:e1-e192.

ACC/AHA Guideline for the Management of PAD:
Diagnosis of Claudication and Systemic Risk Treatment



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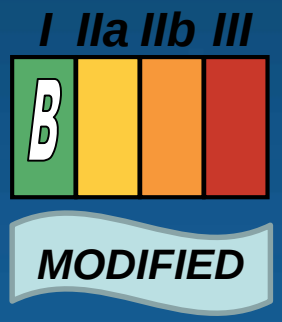
Guideline for the Management of Patients with PAD

Antiplatelet and Antithrombotic Drugs

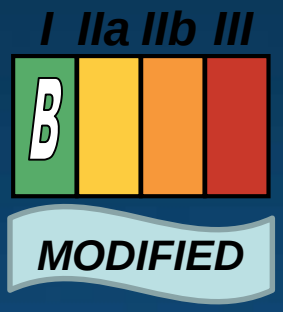
Recommendations for Antiplatelet and Antithrombotic Drugs

Antiplatelet therapy is indicated to reduce the risk of MI, stroke, and vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or CLI, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia.



Aspirin, typically in daily doses of 75 to 325 mg, is recommended as safe and effective antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or CLI, prior lower-extremity revascularization (endovascular or surgical), or prior amputation for lower-extremity ischemia.

Recommendations for Antiplatelet and Antithrombotic Drugs



Clopidogrel (75 mg per day) is recommended as a safe and effective alternative antiplatelet therapy to aspirin to reduce the risk of MI, ischemic stroke, or vascular death in individuals with symptomatic atherosclerotic lower-extremity PAD, including those with intermittent claudication or CLI, prior lower-extremity revascularization (endovascular or surgical), or prior amputation for lower-extremity ischemia.

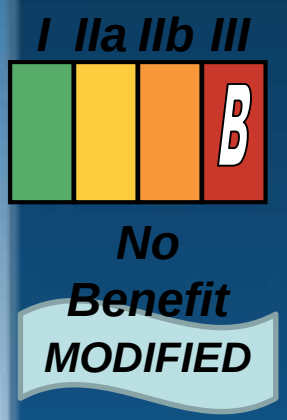
Antiplatelet therapy can be useful to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with an ABI ≤0.90.

Recommendations for Antiplatelet and Antithrombotic Drugs

The usefulness of antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with borderline abnormal ABI, defined as 0.91 to 0.99, is not well established.

The combination of aspirin and clopidogrel may be considered to reduce the risk of cardiovascular events in patients with symptomatic atherosclerotic lower-extremity PAD, including those with intermittent claudication or CLI, prior lower-extremity revascularization (endovascular or surgical), or prior amputation for lower-extremity ischemia and who are not at increased risk of bleeding and who are at high perceived cardiovascular risk.

Recommendations for Antiplatelet and Antithrombotic Drugs



In the absence of any other proven indication for warfarin, its addition to antiplatelet therapy to reduce the risk of adverse cardiovascular ischemic events in individuals with atherosclerotic lower extremity PAD is of no benefit and is potentially harmful due to increased risk of major bleeding.