



A PHYSICIAN'S GUIDE TO THE

Diagnosis AND Management of Peripheral Arterial Disease (PAD)



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 **Bristol-Myers Squibb**

DEFINITION OF PERIPHERAL ARTERIAL DISEASE (PAD)

What is PAD?

Peripheral arterial disease (or PAD) is the term used for vascular diseases that alter the normal structure and function, or that block the aorta or some of its branches. These include arteries of the lower abdomen, the renal arteries and arteries of the lower extremities.^{1,2}

What causes PAD?

The major cause of lower extremity PAD is atherosclerosis.¹ Atherosclerosis is a degenerative disease characterized by a buildup of plaque and fatty substances within the arterial walls.³

Prevalence of PAD:

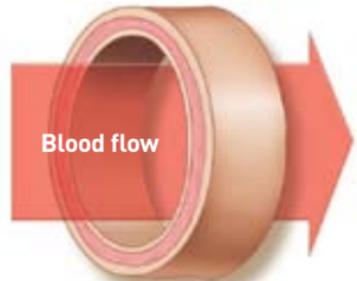
Peripheral arterial disease affects a large portion of the adult population worldwide.¹ As many as 27 million people are estimated to have PAD in North America and Europe alone.³ In a 2006 Canadian telephone survey of adults ≥ 50 years of age ($n=501$), only 36% of respondents reported familiarity with PAD, although approximately 800,000 Canadians are affected by PAD.^{4-6*} Peripheral arterial disease likely affects about 4% of Canadians over the age of 40* and 20% over 75.^{5-7**}

* Based on a results from the U.S. National Health and Nutrition Examination Survey, 1999–2000 ($n=2174$) and Statistics Canada.

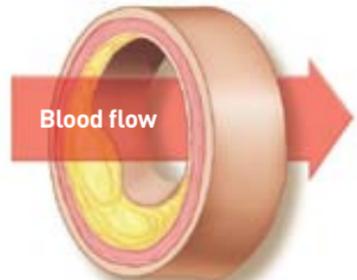
** Based on Statistics Canada data, and a study of 613 men and women (average age 66) from California assessed for large vessel PAD.



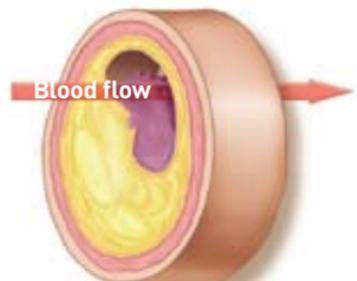
Artery cross-section



Healthy artery



Mild atherosclerosis



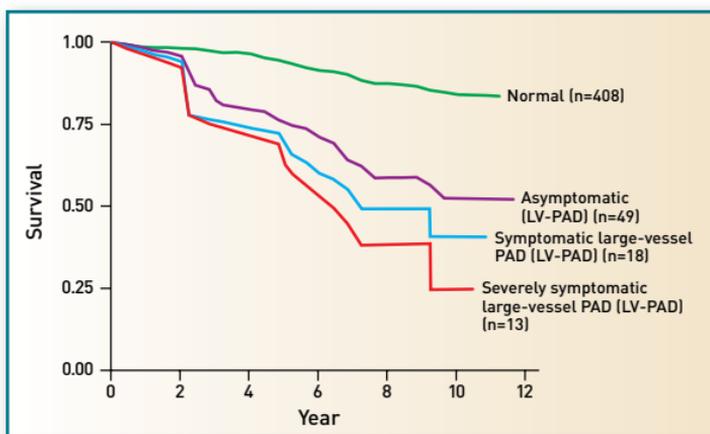
Severe atherosclerosis

RISK FACTORS

The leading cause of PAD in the lower extremities is atherosclerosis. Risk factors for atherosclerosis include^{1,3}:

- Age
- Family history
- Smoking
- Diabetes
- Dyslipidemia
- Hypertension
- Hyperhomocysteinemia
- Obesity
- Sedentary lifestyle

10-year survival for PAD vs. non-PAD patients*†



Adapted from Criqui, et al.⁸

* A study of 565 patients followed for 10 years identified 67 with large-vessel PAD. Forty-nine patients were asymptomatic.

† Kaplan-Meier survival curves based on mortality from all causes among normal subjects and subjects with symptomatic or asymptomatic large-vessel peripheral arterial disease (LV-PAD).

PRESENTATION OF PERIPHERAL ARTERIAL DISEASE (PAD)

Asymptomatic PAD

More than 60% of patients with PAD may present with no symptoms.³

Claudication

The most common manifestation of PAD is intermittent claudication, defined as leg pain induced by exercise and relieved by rest.³

Claudication may be intermittent or chronic, with symptoms varying from mild to severe. These include¹:

- Cramping
- Fatigue
- Frank pain
- Aching
- Weakness

These symptoms typically occur in the buttock, thigh, or calf muscles, and rarely, the foot.¹

Critical limb ischemia

Critical limb ischemia may present with pain in the foot at rest, or with non-healing foot wounds. The discomfort is often worse when the patient is supine (e.g., in bed) and may lessen when the limb is maintained in the dependent position.¹

Narcotics are usually required for analgesia.¹

REACH REGISTRY: A REAL-WORLD DATABASE ON ATHEROTHROMBOSIS

Study design⁹

An international, prospective cohort of patients with either:

- Established atherosclerotic arterial disease (coronary artery disease [CAD], PAD, cardiovascular disease [CVD]); n=55,814, or
- At least 3 risk factors for atherothrombosis; n=12,422
- 1 year follow-up (baseline, to follow-up at 12±3 months)

Baseline characteristics in REACH¹⁰

- Data from 5,473 physician practices in 44 countries
 - 44% of physicians were from general practice
- A total of 67,888 patients aged 45 years or older (recruited in 2003–2004)
 - Roughly 42% of patients were from general practice
 - 1,976 patients from Canada

Patients with established atherothrombotic disease¹⁰

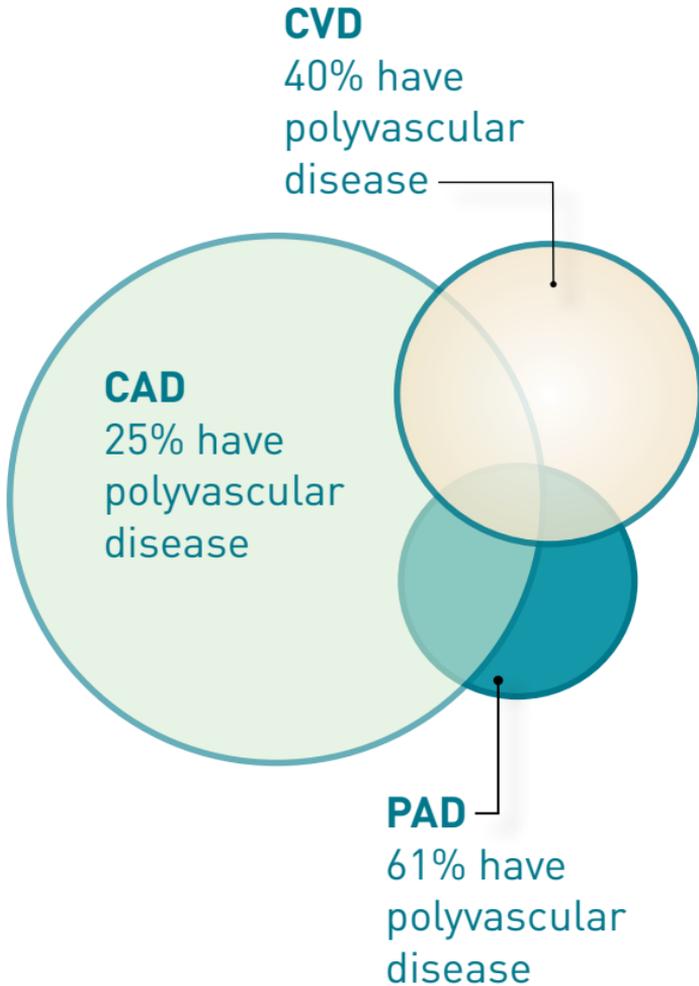
Coronary artery disease (CAD)	n= 40,258 (59.3%)
Cerebrovascular disease (CVD)	n= 18,843 (27.8%)
Peripheral arterial disease (PAD)	n= 8,273 (12.2%)

1-year Objectives⁹

To determine one-year cardiovascular (CV) event rates in the global population for outpatients with established arterial disease or with multiple risk factors or atherothrombosis.

REACH POLYVASCULAR PATIENT DISTRIBUTION

Prevalence of polyvascular disease in PAD⁹



What is polyvascular disease?^{9,10}

In some patients, arterial disease can exist in more than one vascular bed (CAD, PAD, CVD). This is called polyvascular disease.

KEY FINDINGS OF THE REACH REGISTRY

Total population

Peripheral arterial disease patients (n=8581) experienced higher rates of CV death and major CV events due to an atherothrombotic event compared with CAD (n=38602) and CVD (n=18013) patients (21.14% [20.17–22.09] vs. 15.20% [14.67–15.73] vs. 14.53% [13.89–15.16] respectively, 95% CI).⁹

More than 10% of patients with PAD underwent a lower extremity revascularization procedure or amputation.⁹

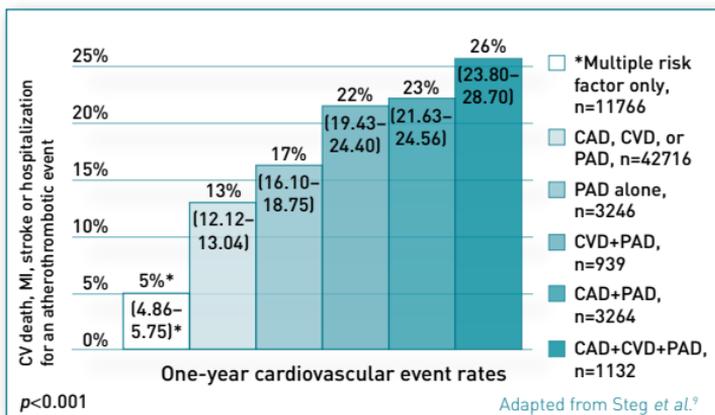
Approximately 1 in 5 (21.1%) patients with PAD suffered a major event (myocardial infarction [MI], stroke, or CV death) or hospitalization for an atherothrombotic event within 1 year as shown in the REACH Registry.⁹

KEY FINDINGS OF THE REACH REGISTRY

Patients with established atherosclerotic disease

1-year event rates in patients with PAD alone were lower than those for PAD in combination with any other arterial disease location.⁹

To further explore the relative risk for ischemic events, event rates were therefore also reported for single vs. multiple arterial beds. Overall major CV event rates increased in a stepwise fashion with the number of symptomatic vascular beds.



DIAGNOSING PERIPHERAL ARTERIAL DISEASE (PAD)

The Canadian Cardiovascular Society Consensus Guidelines indicate that PAD, because it is often asymptomatic, is under-diagnosed, under-recognized, and under-treated.³

Screening for PAD is recommended for³:

- Men over 40 and women who are postmenopausal or over 50 (Recommendation level 1A)
 - Screening efforts should target patients with a recognized CV risk factor, i.e., those who
 - ◊ Smoke
 - ◊ Have diabetes
 - ◊ Have a family history of PAD, CAD or stroke, or have dyslipidemia, or systolic and diastolic hypertension

Basic screening for PAD will include a directed history with key questions specific to claudication.³

The **Edinburgh Claudication Questionnaire** is a validated questionnaire that can help diagnose arterial claudication in patients suspected of suffering from PAD.³

A **complete physical examination** will focus on the following³:

- **Identifying femoral bruits**
- Grading pedal pulses
- Looking for trophic changes in hair or skin
- Inspection of the skin temperature, pallor, or rubor
- Palpation to exclude aneurysms (e.g., an aortic abdominal aneurysm)

The most common diagnostic tool is the **ankle-brachial index (ABI)**, which is used in conjunction with Doppler ultrasound to compare blood pressure measurements at the upper arm and ankle.³



THE ANKLE-BRACHIAL INDEX (ABI)

The ABI is a simple, non-invasive test that is performed using a regular blood pressure (BP) cuff and a Doppler (ultrasound probe).³

ABI ≤ 0.9 IS DIAGNOSTIC FOR PAD¹¹

ABI interpretation chart^{3,11}

>1.3*	Noncompressible calcified vessels
0.91–1.3	Normal
0.41–0.9	Mild to moderate PAD
0.4 or less	Severe PAD

* ABI >1.3 is abnormal but cannot be used to diagnose occlusive PAD. However, it is associated with increased vascular morbidity and mortality.³

Measurement of the ABI³

$$\text{Right ABI} = \frac{\text{Higher right-ankle pressure}}{\text{Higher arm pressure}}$$

$$\text{Left ABI} = \frac{\text{Higher left-ankle pressure}}{\text{Higher arm pressure}}$$

DP = dorsalis pedis artery

PT = posterior tibial artery

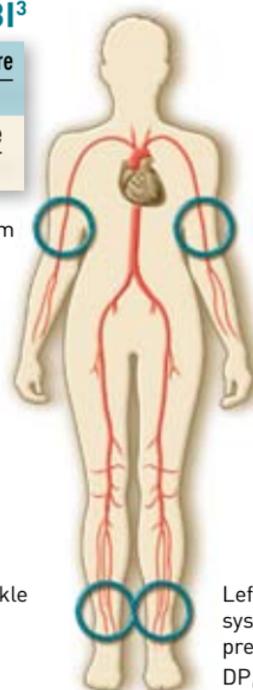
○ = indicates where the BP cuffs should be placed

Right-arm
systolic
pressure

Left-arm
systolic
pressure

Right-ankle
systolic
pressure
DP, PT

Left-ankle
systolic
pressure
DP, PT



Please refer to the tear sheet at the back of this booklet for a copy of the *Edinburgh Claudication Questionnaire*.

MANAGEMENT OF PERIPHERAL ARTERIAL DISEASE (PAD)

Patients with asymptomatic or symptomatic PAD suffer a three- to six-fold greater likelihood of MI, stroke and CV death compared to a non-PAD population.¹¹

Risk factor modification, and proven medical treatment, therefore, should be actively encouraged.¹¹

Risk factor management¹¹

- Assess all patients with PAD for modifiable risk factors.
- Manage risk factors to reduce risk of adverse cardiovascular events and progression of PAD.
- Recommend that patients with PAD quit smoking and have a regular walking program to reduce overall cardiovascular risk and improve symptoms.

Lifestyle changes (nonmedical)

Lifestyle changes which include smoking cessation and a supervised exercise program play an important role in PAD management.¹⁻³

MANAGEMENT OF PERIPHERAL ARTERIAL DISEASE (PAD)

Lifestyle changes

The importance of smoking cessation cannot be overemphasized for people with PAD.²

“Individuals with lower extremity PAD . . . should be offered comprehensive smoking cessation interventions, including behavior modification therapy, nicotine replacement therapy, or bupropion.”

ACC/AHA Guidelines¹

An exercise program is recommended for all patients with intermittent claudication.²

Supervised exercise training for a minimum of 30 to 45 minutes, in sessions performed at least 3 times per week for a minimum of 12 weeks, can significantly improve the limitation of walking.¹⁻³

Supportive measures²

Other non-medical therapies include:

- Keeping feet clean and well-moisturized
- Wearing well-fitting shoes
- Avoiding shoes made of synthetic materials that don't “breathe”

MANAGEMENT OF PERIPHERAL ARTERIAL DISEASE (PAD)

Pharmacological management

The basic components of medical management of PAD include¹:

- Lipid-lowering drugs
- Antihypertensive drugs
- Diabetes therapies
- Antiplatelet therapy

Medical therapies shown to reduce CV events in PAD patients³

Evidence supporting medical therapies to reduce CV events in PAD

Class of agents	Grade*
Statins	IA
Angiotensin-converting enzyme inhibitors	IA
Oral hypoglycemics or insulin	IIB
Antiplatelet agents	IA

* Quality of evidence

- I – Evidence obtained from at least one properly randomized controlled trial or one large epidemiological study.
- II – Evidence based on at least one non-randomized cohort comparison or multi-centre study, chronological series or extra ordinarily results from large non-randomized studies.

Classification and recommendations

- A – Evidence sufficient for universal use (usually based on randomized clinical trials).
- B – Evidence acceptable for widespread use, evidence less robust, but based on randomized clinical trials.

Adapted from the Canadian Cardiovascular Society.³

Please see respective Product Monographs for approved indications.

ANTITHROMBOTIC THERAPIES FOR PERIPHERAL ARTERIAL DISEASE (PAD)³

Agent	Recommendation	Grade*
Acetylsalicylic acid (ASA) or clopidogrel	Lifelong antiplatelet therapy with ASA (75 mg to 325 mg/day) or clopidogrel (75 mg/day) in patients with or without clinically manifest coronary or cerebrovascular disease is recommended.	IA
Ticlopidine [†]	ASA or clopidogrel is recommended over ticlopidine.	IB
Pentoxifyline [‡]	Pentoxifyline is not recommended.	IIB
Vitamin K antagonists [†]	Anticoagulant therapy with vitamin K antagonists is not recommended.	IIB

* Quality of evidence

- I – Evidence obtained from at least one properly randomized controlled trial or one large epidemiological study.
- II – Evidence based on at least one non-randomized cohort comparison or multi-centre study, chronological series or extra ordinarily results from large non-randomized studies.

Classification and recommendations

- A** – Evidence sufficient for universal use (usually based on randomized clinical trials).
- B** – Evidence acceptable for widespread use, evidence less robust, but based on randomized clinical trials.

[†] Not currently indicated for peripheral arterial disease.

[‡] Not currently indicated as antithrombotic therapy in peripheral arterial disease.

PATIENT EDUCATION

What is PAD?

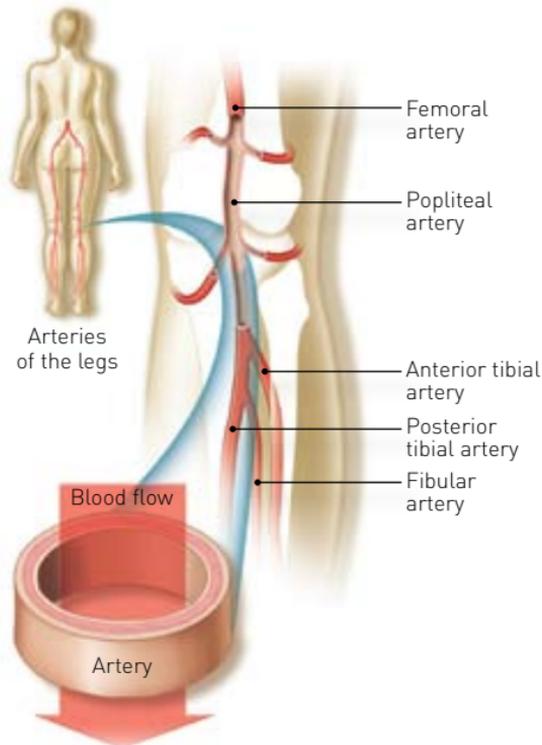
Peripheral arterial disease is a common circulatory problem in which narrowed arteries reduce the blood flow to your limbs/extremities.^{1,2}

When these arteries are healthy, blood flows through them easily.

With PAD, the narrowing of the arteries (atherosclerosis) is caused by a buildup of plaque and cholesterol (fatty deposits), and your limbs – usually your legs – can't get enough blood. **Peripheral arterial disease is usually a sign of widespread atherosclerosis.**^{1,3}

Patients with PAD have a greater risk of heart attacks and strokes from atherosclerosis because fat deposits can also build up in arteries that supply blood to the heart and the brain.³

Healthy arteries



PERIPHERAL ARTERIAL DISEASE (PAD)

Atherosclerosis is the leading cause of PAD.¹

Over 60% of people with PAD don't show any symptoms at all.³

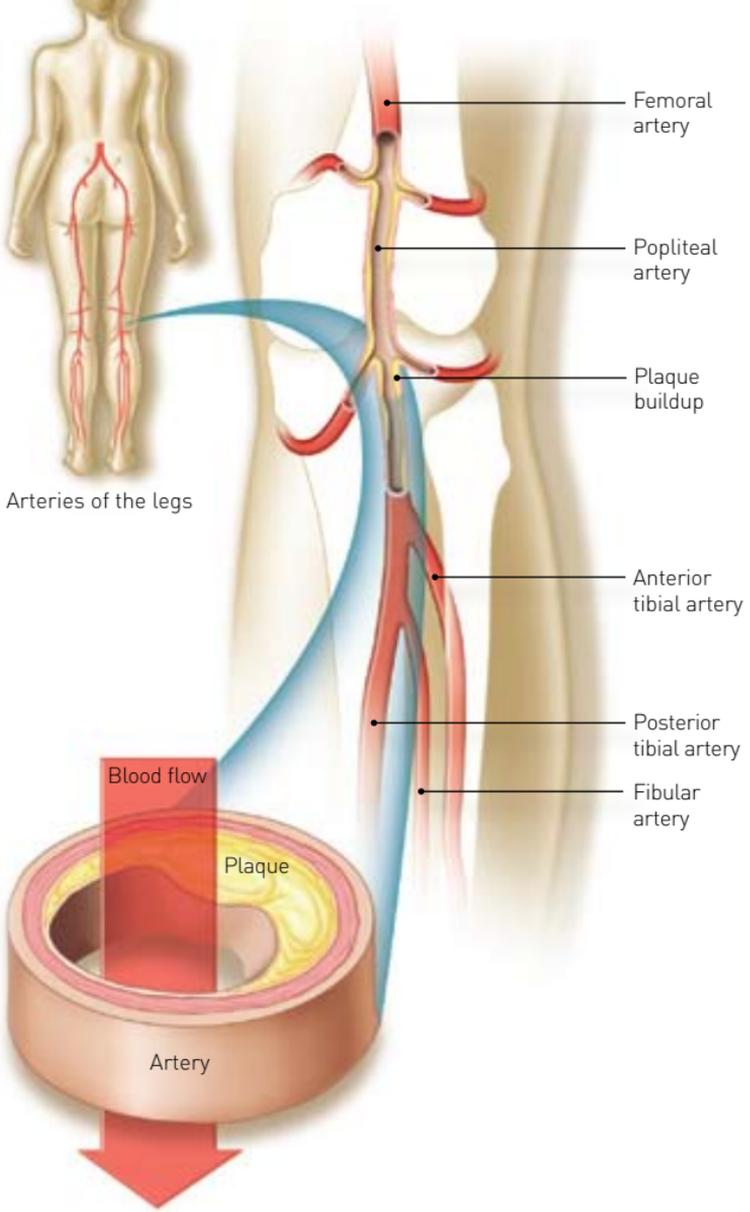
Some will feel pain or heaviness in the legs and have trouble walking. This pain often goes away when resting.

Signs and symptoms of mild PAD include leg pain when walking – a condition called intermittent claudication.³

MILD PERIPHERAL ARTERIAL DISEASE (PAD)



Arteries of the legs



Femoral artery

Popliteal artery

Plaque buildup

Anterior tibial artery

Posterior tibial artery

Fibular artery

Blood flow

Plaque

Artery

SEVERE PERIPHERAL ARTERIAL DISEASE (PAD)^{1,3}

As PAD progresses, it can lead to potentially serious problems with legs and feet such as open sores that don't heal, injury, or infection. There is even greater risk of developing these problems if you also have diabetes.

In extreme cases these problems can lead to gangrene and/or amputation.

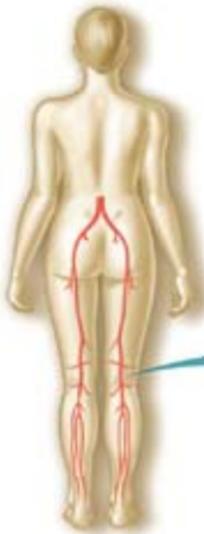
Stroke and heart attack are also common and serious problems that occur with PAD.^{3,9,11}

If atherosclerosis causes symptoms of PAD, it is likely that other blood vessels in your body are being affected, such as the arteries supplying your heart and brain. This in turn increases your risk of developing coronary artery disease (angina & heart attack) and stroke.¹¹

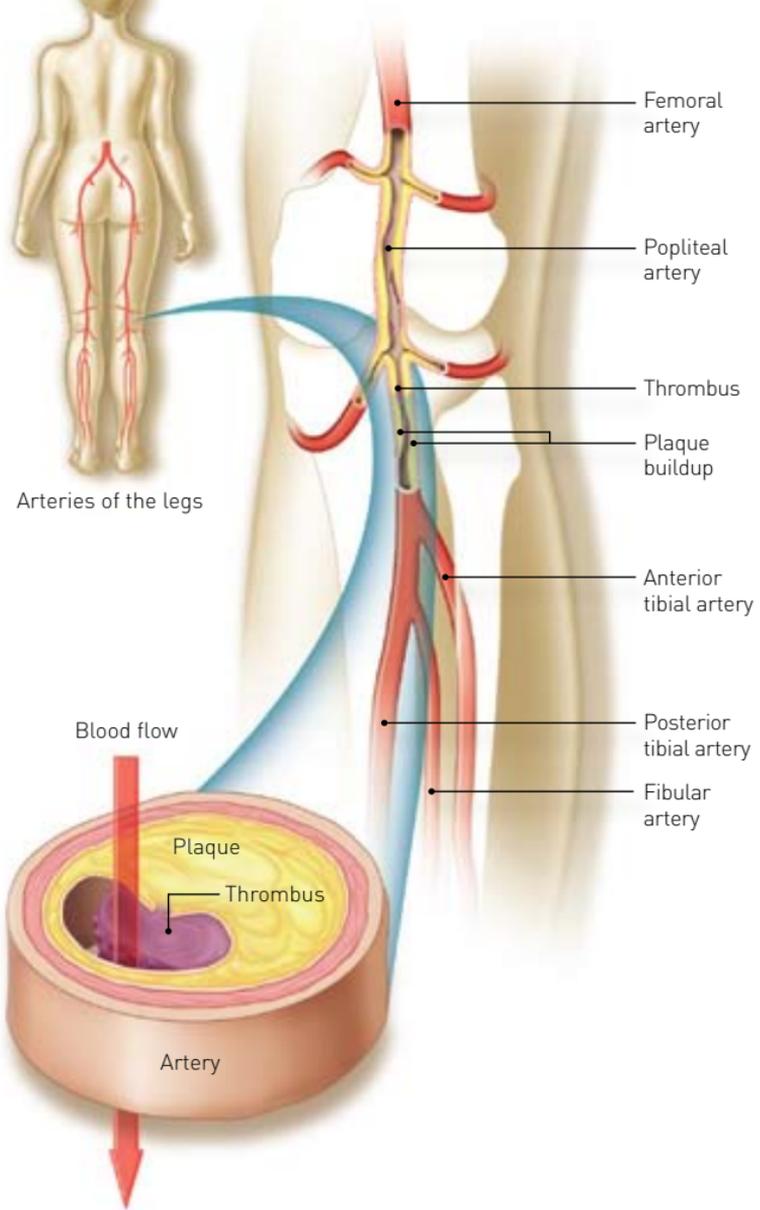
Signs and symptoms of severe PAD may include^{1,3}:

- Cramping
- Aching
- Fatigue
- Weakness
- Pain
- Pain in the foot at rest that is relieved by putting your foot down

SEVERE PERIPHERAL ARTERIAL DISEASE (PAD)



Arteries of the legs





References:

1. Hirsch AT, Haskal ZJ, Hertzler NR, et al. ACC/AHA Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic). *J Am Coll Cardiol*. 2006;47:1–192.
2. Creager MA, Dzau VJ. Vascular Diseases of the Extremities. In: Harrison's Online. Available at: <http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4>. Accessed November 12, 2007.
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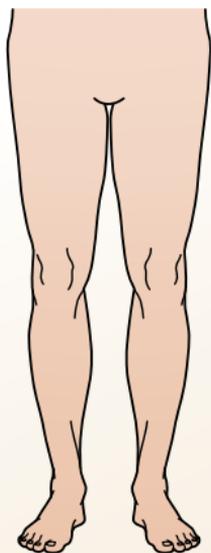
The Edinburgh Claudication Questionnaire¹

1. Do you get pain or discomfort in your leg(s) when you walk? YES NO Unable to walk

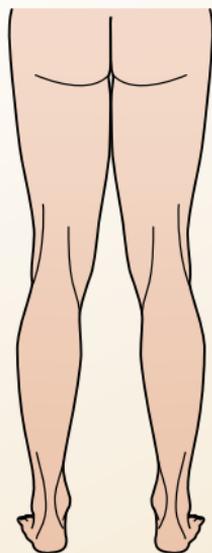
If you answered yes to question 1, please answer the following questions:

2. Does this pain ever begin when you are standing still or sitting? NO
3. Do you get it when you walk uphill or hurry? YES
4. Do you get it when you walk at an ordinary pace on the level? YES NO
5. What happens to it if you stand still?
- Usually continues more than 10 minutes? NO
 - Usually disappears in 10 minutes or less? YES
6. Where do you get this pain or discomfort? (see diagram)

Front



Back



Please share your completed questionnaire with your health care professional to determine if you have PAD.

A positive questionnaire diagnosis of claudication is made only if the “correct” answer is given to all questions.

What can I do about PAD?^{1,2}



- **Stop smoking.**



- **Take your medications as directed by your doctor to reduce your risk of heart attack and stroke.**



- **Exercise regularly, especially walking.**



- **Lower your blood pressure.**



- **Lower your cholesterol.**



- **Care for your feet and legs by:**
 - Keeping feet clean and well-moisturized
 - Wearing well-fitting shoes
 - Avoiding shoes made of synthetic materials that don't "breathe"

If you have questions or need more information, please speak with your health care professional.

References:

1. Abramson BL and Huckell V. Canadian Cardiovascular Consensus Conference. Available at: http://www.ccs.ca/download/consensus_conference/consensus_conference_archives/CCFinalPre_CJC_Pub.pdf. Accessed November 9, 2007.
2. Creager MA, Dzau VJ. Vascular Diseases of the Extremities. In: Harrison's Online. Available at: <http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4>. Accessed November 12, 2007.

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