A PHYSICIAN’S GUIDE TO THE

Diagnosis
AND
Management
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.\textsuperscript{1,2}

What causes PAD?
The major cause of lower extremity PAD is atherosclerosis.\textsuperscript{1} Atherosclerosis is a degenerative disease characterized by a buildup of plaque and fatty substances within the arterial walls.\textsuperscript{3}

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

* Based on 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.
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).
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 include\(^1\):

- Cramping
- Aching
- Fatigue
- Weakness
- Frank pain

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.\(^1\)
**Study design**

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 REACH**

- 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 disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease (CAD)</td>
<td>40,258</td>
<td>59.3%</td>
</tr>
<tr>
<td>Cerebrovascular disease (CVD)</td>
<td>18,843</td>
<td>27.8%</td>
</tr>
<tr>
<td>Peripheral arterial disease (PAD)</td>
<td>8,273</td>
<td>12.2%</td>
</tr>
</tbody>
</table>

**1-year Objectives**

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.
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.
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
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.
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 for\(^3\):

- 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 PAD[^11]**

<table>
<thead>
<tr>
<th>ABI interpretation chart[^3,11]</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.3*</td>
<td>Noncompressible calcified vessels</td>
</tr>
<tr>
<td>0.91–1.3</td>
<td>Normal</td>
</tr>
<tr>
<td>0.41–0.9</td>
<td>Mild to moderate PAD</td>
</tr>
<tr>
<td>0.4 or less</td>
<td>Severe PAD</td>
</tr>
</tbody>
</table>

[^*]: 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 ABI[^3]**

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

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

[^DP]: dorsalis pedis artery
[^PT]: posterior tibial artery
[^=]: indicates where the BP cuffs should be placed

Please refer to the tear sheet at the back of this booklet for a copy of the Edinburgh Claudication Questionnaire.
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.\textsuperscript{11}

Risk factor modification, and proven medical treatment, therefore, should be actively encouraged.\textsuperscript{11}

**Risk factor management\textsuperscript{11}**

- 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.\textsuperscript{1-3}
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”
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

<table>
<thead>
<tr>
<th>Class of agents</th>
<th>Grade*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>IA</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>IA</td>
</tr>
<tr>
<td>Oral hypoglycemics or insulin</td>
<td>IIB</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>IA</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendation</th>
<th>Grade*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylsalicylic acid (ASA) or clopidogrel</td>
<td>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.</td>
<td>IA</td>
</tr>
<tr>
<td>Ticlopidine†</td>
<td>ASA or clopidogrel is recommended over ticlopidine.</td>
<td>IB</td>
</tr>
<tr>
<td>Pentoxyfiline‡</td>
<td>Pentoxyfiline is not recommended.</td>
<td>IIB</td>
</tr>
<tr>
<td>Vitamin K antagonists†</td>
<td>Anticoagulant therapy with vitamin K antagonists is not recommended.</td>
<td>IIB</td>
</tr>
</tbody>
</table>

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**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 indicted for peripheral arterial disease.

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

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Adapted from the Canadian Cardiovascular Society.³
What is PAD?
Peripheral arterial disease is a common circulatory problem in which narrowed arteries reduce the blood flow to your limbs/extremities.\textsuperscript{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.**\textsuperscript{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.\textsuperscript{3}
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
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.\textsuperscript{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.\textsuperscript{11}

Signs and symptoms of severe PAD may include\textsuperscript{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

- Femoral artery
- Popliteal artery
- Thrombus
- Plaque buildup
- Anterior tibial artery
- Posterior tibial artery
- Fibular artery

Blood flow

Artery

Plaque

Thrombus
References:


These materials were developed by sanofi-aventis and Bristol-Myers Squibb in partnership with the P.A.D. Coalition.
The Edinburgh Claudication Questionnaire

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:


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