



Editorial

Diagnosis and Treatment of Lower Extremity Peripheral Artery Disease

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ABSTRACT

Peripheral artery disease (PAD) is a chronic occlusive disease of arteries in the lower extremity due to atherosclerosis. PAD can lead to intermittent claudication, which is weakness or pain with walking alleviated with rest. Until now, the awareness of the public and medical personnel regarding PAD is still not as high as the alertness of coronary disorders. This editorial will focus on diagnosing and treating PAD focused on lower extremity artery disease (LEAD).

1. Definition

Peripheral artery disease (PAD) is defined as a chronic progressive disease due to stenosis and/or blockage of the moderate and large arteries except for the aorta and arteries in the heart or brain. PAD affects the lower limb more frequently than the upper limb vessels and can cause repeated fatigue, pain, a cramping sensation known as intermittent claudication.^{1,2} The term "PAD" is commonly used for LEAD.¹ LEAD includes claudication, chronic limb ischemia (CLI), and acute limb ischemia (ALI). ALI is defined as a sudden reduction in limb perfusion. It is a limb-threatening condition. The five "Ps," which include pain, paralysis, paresthesia, pulselessness, and pallor, suggest limb jeopardy. CLI is defined as resting limb pain because of chronic and severe blood flow blockage to the affected limb. It includes chronic ischemic rest pain, gangrene, or ulcers caused by arterial occlusion that objectively proven.^{1,2}

2. Epidemiology

Around the world, it is predicted that more than 200 million people suffer from PAD. The PAD prevalence rises with age. PAD is more common in the elderly population (> 20% of individuals > 80 years of age) than young or adult population. PAD is frequent in high cardiovascular (CVD) risk person (more than 70 years without any risk factors, or 50-69 years with smoking history or diabetes).² The 5-year nonfatal CVD incidence rate, including myocardial infarction (MI) and stroke among people with PAD symptoms, was 20%. The mortality rate ranges from 15-30% of those with CLI. As many as 25% of them eventually requiring amputation, and the annual mortality is reported as high as 25%.³

3. How to Diagnose

The data about the clinical history (personal and family) have to be obtained. Family history about cerebrovascular disease, CAD, LEAD, as well as aortic aneurysm should be gained. Clinical history involves the comprehensive assessment of CVD risk factors and comorbidities. The dietary pattern, lifestyle habits, physical activity, and walking performance have to be interrogated systematically.¹ Many questionnaires to identify Intermittent Claudication (IC) have been developed. Those questionnaires also can be used to distinguish IC from another type of limb pain. The Rose questionnaire is the first. While the San Diego Claudication Questionnaire is a modification of the Rose questionnaire.⁵ Classic Rose claudication can be found only in a small number of LEAD patients. About 70-90% of them are asymptomatic or reveal atypical symptoms.³

Persons who are at risk for LEAD include: (1) age below 50 years old with diabetes and another CVD risk factor (hypertension, hyperhomocysteinemia, dyslipidemia, or smoking); (2) age 50 to 69 years old and a history of diabetes and smoking; (3) age more than 70 years old; (4) leg symptoms during walking (suggestive for claudication); (4) ischemic rest pain; (5) abnormalities in limb pulse palpation; (6) known atherosclerotic carotid, renal, or coronary artery diseases.

The physical examination for the vascular system includes: (1) blood pressure measurement in both arms; (2) carotid pulses palpation and carotid bruit auscultation; (3) auscultation for bruits in the flank and abdomen area; (4) inspection for the aortic pulsation and palpation for abdominal aortic aneurysm (AAA); (5) auscultation for

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Table 2. San Diego Claudication Questionnaire, Brief Version.

Circle Answers	Clinical Indicators	Clinical Indicators
1. Do you get pain or discomfort in either leg on walking? (if no, stop)	Right leg Left leg	Yes NoYes No
2. Does this pain ever begin when you are standing still or sitting?	Right leg Left leg	Yes NoYes No
3. Does this pain include your calf/calves?	Right leg Left leg	Yes NoYes No
4. Do you get it when you walk at an ordinary pace on the level?	Right leg Left leg	Yes NoYes No
5. What do you do if you get it when you are walking?	Right leg Left leg	Stop or slow down Continue onStop or slow down Continue on
6. What happens to it if you stand still?	Right leg Left leg	Lessened or relieved UnchangedLessened or relieved Unchanged

Note, Determine pain category separately for each leg as follows: (1) no pain: 1=no; (2) pain at rest: 1=yes and 2=yes; (3) noncalf: 1=yes, 2=no, and 3=no; (4) classic: 1=yes, 2=no, 3=yes, 4=yes, 5=stop or slow down, and 6=lessened or relieved; and (5) atypical calf: 1=yes, 2=no, and 3=yes and not classic.

bruits in both femoral arteries; and (6) peripheral pulse palpation of the femoral, popliteal, dorsal pedis, posterior tibial, brachial, radial, and ulnar arteries.⁴

A non-invasive diagnostic test to assess blood flow in lower-extremity arteries involves: (1) ankle and brachial artery systolic blood pressure measurement, (2) velocity waveform characterization, and (3) duplex ultrasonography (DUS). An ankle-brachial index (ABI) below 0.90 is 95% sensitive and 99% specific for establishing the PAD diagnosis.⁴ Resting ABI results have to be classified as: normal (1.00–1.40), borderline (0.91–0.99), abnormal (≤ 0.90), and non-compressible (> 1.40).² An ABI of more than 1.40 represents medial arterial calcification or arterial stiffening. It is also correlated with higher cardiovascular events and mortality rates. The toe-brachial index (TBI) can confirm a PAD diagnosis in persons in whom LEAD is clinically suspected but the ABI is not appropriate (ABI more than 1.40 because of non-compressible arteries). Patients with non-joint-related leg symptoms during exercise and normal or borderline resting ABI (0.91–1.40) should have an exercise treadmill ABI test. It is beneficial in distinguishing arterial cause from non-arterial causes of limb pain.²

For screening and diagnosis purposes, DUS is often used as the first step. DUS involves B-mode echography, color Doppler, continuous-wave Doppler, pulsed-wave Doppler, and power Doppler. Computed tomography angiography (CTA) displays a 'vascularization roadmap.' CTA is very crucial for deciding interventional strategies. Magnetic resonance angiography (MRA) using contrast (gadolinium) and non-contrast techniques (phase contrast and time-off light sequences) can be performed for peripheral artery visualization. The latter approaches have several limitations include low resolution and are artifacts susceptibility.¹

4. Management

All PAD patients have to be asked to stop all kinds of tobacco use. A combination of behavioral changes and pharmacological treatment is likely to gain higher quit rates than either one alone.⁷ The guideline from the American Heart Association (AHA)/American College of Cardiology (ACC) gives a recommendation for lipid-lowering therapy using statin for PAD patients to achieve an LDL-cholesterol

level of < 100 mg/dL. The guideline suggests that an LDL-cholesterol level of < 70 mg/dL may be beneficial for high-risk patients. The blood pressure target for PAD patients has to be less than 140/90 mmHg. For PAD patients with specific indications such as CAD, β -blockers can be safely used.⁷ Monotherapy with aspirin or clopidogrel is beneficial for symptomatic patients with an ABI of ≤ 0.85 . However, in 2011, The AHA/ACC updated guideline for PAD stated that antiplatelet therapy, including clopidogrel or aspirin, is recommended to decrease the risk of vascular mortality, stroke, and myocardial infarction (MI) in symptomatic lower extremity PAD patients. It also can be beneficial in asymptomatic PAD patients with an ABI less than 0.90.⁷

The ALI patients with a salvageable limb should receive a rapid assessment to define the anatomical level of arterial occlusion and. They need urgent revascularization using an endovascular or surgical approach. Catheter-based thrombolysis is beneficial and is recommended for patients with ALI with an onset of fewer than 14 days. Balloon angioplasty is the first step strategy to restore blood flow in CLI patients with an estimated life expectancy of fewer than two years or CLI patients in whom an autogenous vein conduit is not available. For Trans-Atlantic Inter-Society Consensus (TASC) type A iliac and femoropopliteal arterial lesions, the preferred revascularization strategy is endovascular intervention. To assess the signification of endovascular intervention of iliac artery stenoses of 50% to 75%, the transactional pressure gradients with and without vasodilation should be conducted before the procedure.⁶

Long-term antiplatelet monotherapy is recommended in all LEAD patients who have revascularized. Clopidogrel may be preferred over aspirin. Due to a lack of clinical evidence, antiplatelet treatment is not generally recommended in isolated asymptomatic LEAD patients. For PAD patients with atrial fibrillation (AF) with a CHA2DS2-VASc score of 2 or more, oral anticoagulant (OAC) is recommended. In LEAD patients with a specific indication for OAC treatment (mechanical prosthetic heart valve or AF), the single OAC treatment should be considered. If the risk of bleeding is low, following an endovascular revascularization procedure, clopidogrel or aspirin should be given in addition to OAC for at least one month. However, OAC alone should be considered for the high risk of bleeding patients. OAC and antiplatelet monotherapy may be given for more than a month in high ischemic risk

patients or patients with another strong indication.¹

The aspirin 75 to 325 mg daily and Clopidogrel 75 mg daily is strongly recommended as a beneficial and safe antiplatelet treatment to decrease the risk of vascular death, MI, and stroke for symptomatic atherosclerotic LEAD patients, involving patients with IC or CLI, prior surgical or endovascular revascularization, or prior lower-extremity amputation due to ischemia. Cilostazol 100 mg 2 times/day is recommended as a beneficial pharmacological treatment to reduce claudication and improve walking distance in LEAD patients without the existence of heart failure.⁶

5. Conflict of interest

There is no conflict of interest

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