

CLINICAL EVIDENCE REVIEW

LE Peripheral Artery Disease

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Next Review to Begin June 2024

LE APAD Clinical Evidence Review Team

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List of Abbreviations

ABI ankle-brachial index

ACEI angiotensin-converting enzyme inhibitor

ARB angiotensin receptor blocker

ASCVD atherosclerotic cardiovascular disease

CCB calcium channel blocker

CDE Certified Diabetes Educator

CLI critical limb ischemia

CLTI chronic limb-threatening ischemia

DAPT dual antiplatelet therapy

DBP diastolic blood pressure

DM diabetes mellitus

EOL end of life

GDMT guideline-directed medical therapy

HRQOL health-related quality of life

IC intermittent claudication

LE APAD lower extremity atherosclerotic peripheral artery disease

MACE major adverse cardiovascular limb events

MALE major adverse limb events

RDN registered dietician/nutritionist

SBP systolic blood pressure

SDOH social determinants of health

SET supervised exercise therapy

TBI toe-brachial index

Care Pathway Purpose Statement

The purpose of the Care Pathway project is to reduce the major adverse limb events (MALE), including acute limb ischemia and major or minor lower extremity amputation, and the major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and death that are associated with Lower Extremity Atherosclerotic Peripheral Artery Disease (LE APAD). This is to be accomplished through consistent application of evidenced-based medicine and guideline-directed medical therapy. Keep in mind that LE APAD is caused by atherosclerosis and many of the goals of this pathway will be directed at improving guideline directed medical care for atherosclerosis.

Patients with LE APAD fall into two distinct categories. These categories are: 1. lower extremity claudication which limits the patient's lifestyle and places them at higher risk of a major adverse cardiovascular event. 2. Chronic limb-threatening ischemia (CLTI) which is the newer term for critical limb ischemia (CLI) which is an indicator of advanced LE APAD and systemic atherosclerosis. These patients are at high risk of suffering MALE and MACE.

This pathway adopts the best practices described by the Society for Vascular Surgery, American Heart Association/American College of Cardiology and the European Society of Vascular Surgery. The Lower Extremity Atherosclerotic Peripheral Artery Disease Care Pathway represents the best currently available information and will be updated periodically to reflect new findings. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5477786/

The goals of the LE APAD Care Pathway are as follows:

- Prevention of LE APAD to the greatest degree possible by instituting primary prevention measures in the at risk population.
- Delay or prevent costly, invasive interventions, i.e. stents or surgery, in LE APAD patients with claudication symptoms, because studies show an increased occurrence of a Major Adverse Limb Events in patients with claudication who are treated with an invasive intervention.
- Allow earlier identification and referral of patients with chronic limb threatening ischemia, i.e. those with ischemic rest pain, gangrene or tissue loss.
- Provide framework for LE APAD evidenced-based care delivery in the most effective, efficient manner possible.
- Raise awareness and education about LE APAD in the medical and layperson community so that guideline directed medical care can be initiated in order to decrease both MALE and MACE.

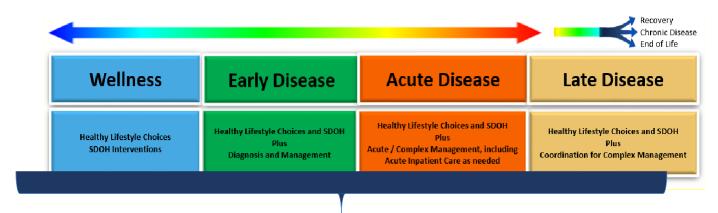
This Care Pathway should be used to facilitate conversations with patients and families to make optimal care decisions with respect to available resources, special circumstances, and the preferences and needs of each individual patient. This Care Pathway is not intended to replace sound clinical judgement.

The LE APAD Care Pathway Metric adopts a continuum of care approach:

- Extension of time from diagnosis to MALE or MACE for the LE APAD patient
- Delay and perhaps prevent costly, risky invasive arterial interventions like stents or surgery
- Increase enrollment of LE APAD patients into supervised exercise therapy (SET) provided by cardiovascular and pulmonary rehabilitation programs
- Reduce annual cost of care for LE APAD patients
- Reduce the rate and extent of amputation associated with LE APAD
- Increase provider knowledge related to appropriate patient referral to a LE APAD specialist
- Increased utilization/enrollment of patients in services such as support groups, depression screenings, nutrition services, etc.
- Increase the number of patients receiving guideline directed medical care for their LE APAD

CARE PATHWAY MODEL

The Full Continuum of Care



In Every Phase of Care:

- 1. Educate / Support Healthy Lifestyle Choices
- 2. Seek to Understand and Refer to Social Resources as needed
- 3. Assess and Manage Underlying Causes and Co-Morbidities

Rutherford Classification of LE APAD

Grade	Category	Clinical description	Objective criteria
0	0	Asymptomatic—no hemodynamically significant occlusive disease	Normal treadmill or reactive hyperemia test
	1	Mild claudication	Completes treadmill exercise; AP after exercise > 50 mm Hg but at least 20 mm Hg lower than resting value
1	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete standard treadmill exercise, and AP after exercise < 50 mm Hg
II	4	Ischemic rest pain	Resting AP < 40 mm Hg, flat or barely pulsatile ankle or metatarsal PVR; TP < 30 mm Hg
III	5	Minor tissue loss—nonhealing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP $<$ 60 mm Hg, ankle or metatarsal PVR flat or barely pulsatile; TP $<$ 40 mm Hg
	6	Major tissue loss—extending above TM level, functional foot no longer salvageable	Same as category 5

Executive Summary

<u>Wellness</u> [Rutherford category 0; patients without confirmed disease and those at high risk for developing LE APAD]:

Prevention

- Teach, advocate and support Healthy Lifestyle choices as a means to prevent cardiovascular disease
- Assess Social Determinants of Health (SDOH) needs and make referrals as needed
- Prevent / manage emerging comorbidities Screening/Treatment
- Ensure accurate cardiovascular disease risk factor identification
- Engage patients at high risk pre-disease and emphasize the importance of healthy lifestyle choices and medication as a means to prevent / delay cardiovascular disease and LE APAD
- Risk factor modification; guideline directed medical management for known atherosclerosis/risk
- ABI screening as indicated by the guidelines.^[50]

<u>Early Disease/Established Stable Disease</u> [Rutherford categories 1 thru 3; i.e. patients with subclinical PAD, presence of PAD with no symptoms, or with LE claudication symptoms)]:

Medical Evaluation and Diagnosis: Include all of the Wellness Prevention strategies PLUS

- Reassess SDOH needs to ensure care coordination is addressed as needed
- Vascular work up
 - Physical assessment including check for ulcers, gangrene, sores, infection, foot complications
 - Assessment of limb pain
 - Pulses in feet/ankles
 - ABI/TBI with waveform
 - o Coronary artery disease (CAD) evaluation for those with elevated cardiac risk
- Exercise prescription and if appropriate, referral to cardiac rehab center for Supervised Exercise Therapy
- For patients with LE pain/discomfort who have no evidence of LE APAD based on pulse exam, ABI at rest and/or with exercise, and then must consider orthopedic or neurogenic causes of LE pain/discomfort.

Treatment

- Engage each patient in the development of a Lifestyle Plan
- First line of treatment is healthy lifestyle management and pharmacotherapy

- o Follow AHA Life's Simple 7 as a guide to medical and lifestyle management
- o Referral to supervised exercise training at a local cardiac rehab facility
- o Tobacco cessation both through counseling and pharmacotherapy, if indicated
- o Follow guideline-directed medical therapy for treatment of atherosclerosis
- Referral to vascular surgery if first line therapy fails to relieve patient symptoms or if progression to CLTI

<u>Chronic Critical Limb Threatening Disease or Critical Limb Ischemia</u> [Rutherford categories 4 thru 6]:

Treatment and Referrals: Include all of the Wellness Prevention strategies PLUS

- Referral to vascular surgery for work-up/evaluation
- Referral to wound care and/or podiatry
- Referral to endocrinology for blood glucose management

Emergent and Urgent Treatment

- Manage urgent and emergent CLTI/CLI situations or Major Adverse Limb event (MALE)
- Post event, re-employ all of the Wellness strategies and ensure communication/hand off backto primary care team

Follow up: All of the Wellness Prevention strategies as appropriate for the situation, PLUS

- Develop effective system for care coordination for complex communication and care delivery
- Initiate goals of care discussions timely for participatory decision making with patient and family in cases of severe patient infirmity or non-salvageable LE ischemia or gangrene

CALL TO ACTION

- LE APAD is a common, chronic disease in the US population, with higher prevalence in communities like those of eastern North Carolina where there are high rates of obesity, diabetes and smoking.
- LE APAD is believed to be under-diagnosed & under-treated due primarily to screening difficulties, asymptomatic presentation of patients, and lack of awareness among patients and providers.
- It is estimated that at least 20% of Americans over 70 years old have LE APAD. Older individuals believe that pain while walking is normal when this may be claudication.
- LE APAD is a costly disease for patients and the health care system due to medical care costs over the life of the patient, including high rates of amputation in the CLTI/CLI subset of the LE APAD population.
- While atherosclerosis is the cause of CLTI/CLI it is not per se a curable condition. However, LE APAD onset and progression can be managed through early identification, proper guideline directed medical therapy and lifestyle interventions, reducing the need for invasive intervention.
- Significant gaps in care coordination exist across the patient journey and many patients who present with claudication and CLTI/CLI are poorly managed.
- Like other chronic diseases, the LE APAD patient's needs change over time and must be managed in the right place, at the right time, by the right provider(s).

- LE APAD tends to be progressive over time, with patient quality of life further impacted by the burdens of living with various comorbidities, as well as the emotional, social and economic burdens associated with the disease.
- LE APAD is a marker for system atherosclerosis, therefore secondary prevention measures used in treating the LE APAD patient can result in the reduction of MACE.

WELLNESS

Rutherford category 0; patients without disease and those at high risk for developing LE APAD

HEALTHY LIFESTYLE: Adoption of a healthy lifestyle is critical for prevention of atherosclerotic cardiovascular disease (ASCVD) and more specifically LE APAD.^[1] Healthy lifestyle prevention strategies include:

Prevention Strategy	Recommendation
Weight reduction ^[1]	Maintain normal body weight (body mass
	index of 18.5 – 24.9 kg/m ²).
Healthy nutrition ^[1]	A diet emphasizing intake of vegetables,
	fruits, legumes, nuts, whole grains, and fish
	is recommended to decrease
	ASCVD risk factors.
Regular physical	Adults should engage in at least 150
activity ^[1,13]	minutes per week of accumulated
	moderate-intensity physical activity or
	75 minutes per week of vigorous-
	intensity physical activity.
Cholesterol	After improvements in or in addition to
management [1,14,17]	nutrition and physical activity, statin
	therapy is first-line treatment for primary
	prevention of ASCVD in patients with
	elevated low-density lipoprotein
	cholesterol levels (≥190mg/dL), those with
	diabetes mellitus, who are 40 to 75 years of
	age, and those determined to be at
	sufficient ASCVD risk after a clinician—
B'-b	patient risk discussion.
Diabetes	The risks of LE APAD increase with the
management ^[1,16-17]	severity of diabetes: for every 1% increase
	in hemoglobin A1c level, the risk of LE
Blood pressure	APAD increases by 26%. Nonpharmacologic interventions are
management ^[1,15-16]	recommended for all adults with
management.	elevated blood pressure or hypertension.
	For those requiring pharmacological
	therapy, the target blood pressure
	should generally be <140/90 mm Hg (See
	Hypertension pathway for more info).
Smoking cessation	Smoking is the most harmful risk factor for
[15,46,68]	the development of LE APAD and at least
	doubles the risk compared with that of a
	nonsmoker.
Adequate sleep[1]	Adults need at least 7 hours of sleep per
	night to maintain good health.

RECOMMENDATIONS:

- Each patient should receive counseling and participate in the development of a lifestyle plan with the provider, a health coach, dietician, exercise specialist and/or the appropriate specialist
- The plan should be documented and follow up updated with each office visit

RESOURCES:

https://www.ruralhealthinfo. org/toolkits/sdoh/4/assessm ent-tools

https://www.aafp.org/dam/A
AFP/documents/patient care
/everyone project/teambased-approach.pdf

https://nccare360.org/

https://innovation.cms.gov/fi les/worksheets/ahcmscreeningtool.pdf

Additional resources located below under "Screening and Treatment for ASCVD Risk Factors"

Maintain good mental health [44,80-81]	Develop and maintain mental health resilience through stress management, connectivity, and
	purposeful living.
Assess social determinants of health (SDOH) and	One of the fundamental strategies to control risk
support patient with identified issues [19-21,43]	factors of ischemic heart disease and LE APAD in
	populations is by addressing social determinants of
	health and socioeconomic status.

Lifestyle factors such as smoking, high calorie diets, high intake of saturated fats, low intake of fruits and vegetables, being sedentary, and psychological factors are associated with the development of atherosclerotic disease. Lifestyle interventions such as those listed below play an important role in prevention of cardiovascular disease outcomes and its promotion has been emphasized in many prevention guidelines.

Research has also shown that despite the decline in CVD mortality over the past several decades many disadvantaged groups are disproportionally burdened with poor cardiovascular health.^[20] A potential reason for this burden maybe the influence of social factors on the incidence, treatment and outcomes of atherosclerotic disease and the potential behavioral, biological and psychological pathways linking them. We must now broaden the focus of disease management to incorporate another arm of risk, the social determinants of health. Examples of upstream social determinants of health that affect treatment adherence and ASCVD health outcomes include comorbid mental illness, lack of health literacy, exposure to adversity (e.g., home/community violence, trauma exposures, safety concerns), financial strain, inadequate housing conditions, lack of food security (i.e., access to affordable and nutritious food), and inadequate social support.^[1]

Wellness Resources: Wellness activities can occur in many different venues, including clinics, health departments and through medical and non-medical resources. Some resources in eastern North Carolina that may be potential partners for ASCVD and LE APAD are:

- Hospital-sponsored programs
- Wellness centers
- Faith-based programs
- Nonprofit organizations
- Free websites
- Employers

- State-sponsored programs
- Insurance carriers
- Grants
- Mental health programs
- NC Cooperative extension offices

- Eat Smart, Move More NC
- Local health departments
- National Institute of Health

Social Determinants of Health [SDOH] resources: Low socioeconomic status and SDOH have been linked with higher prevalence of coronary artery disease, CHD mortality and with higher rates for CHD risk factors

such as diabetes, hypertension, smoking and physical inactivity. This connection also exists for PAD. Lower income and lower attained educational statuses correlate with a higher prevalence of PAD. The Centers for Medicare & Medicaid Services has developed a screening tool to assess 5 domains of non—health related measures that affect health outcomes: housing instability, food insecurity, transportation difficulties, utility assistance needs, and interpersonal safety. The North Carolina Department of Health and Human Services and the Foundation for Health Care Leadership and Innovation launched a robust, web-based Resource Directory including local and state resources. The program, called NCCARE360, includes:

- Real-time communication via a call center
- Capacity for electronic referrals
- Secure sharing of information [the patient must consent]
- Ability to track outcomes

SCREENING AND TREATMENT FOR ASCVD RISK FACTORS:

Assessment of ASCVD risk remains the foundation of primary and secondary prevention. After age 20 years, traditional risk factors should be measured at least every 4 to 6 years. [1] All individuals should be encouraged to follow a heart-healthy lifestyle and assessing an individual's 10-year absolute ASCVD risk enables providers to match prevention interventions to the patient's absolute risk. This is done in order to maximize anticipated benefit and minimize potential harm from overtreatment.

Nutrition, Physical Activity and Weight:

<u>Screening</u>: At each visit, a healthcare provider should have a discussion with the patient around their nutritional status, daily physical activity and weight. Counseling and comprehensive lifestyle interventions should be recommended for patients if the patient (nutritional resources can be found in the appendix)^[31]:

- is determined to be obese (BMI ≥30 kg/m2) or overweight (BMI=25 to 29.9 kg/m²)
- is achieving less than 150 minutes of activity per week
- is not consuming a diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish

<u>Treatment</u>: More than 80% of chronic conditions, including CVD, could be avoided through the adoption of healthy lifestyle recommendations. Several large studies have conclusively shown that diet and exercise modifications not only substantially improve long term survival but also result in a portrait more nearly approaching total health. At the very least treatment

RECOMMENDATIONS:

Each patient should have a documented SDOH assessment.

If SDOH resources are needed, a consent should be obtained and SDOH referrals initiated.

SDOH follow up should occur with each office visit with additional referrals as needed

- Use the tools provided within the EHR to assess and track SDOH
- Inpatient and Ambulatory settings of ECU Health have access to the SDOH via the histories section of the chart
- The SDOH wheel can found on the HP LPOC snapshot report.
 All SDOH needs are found under the Social History section of a patients chart.

RESOURCES:

Lifestyle Medicine

https://www.lifestylemedicine.org

https://www.ornish.com/prove nprogram/the-research/

Exercise

https://exerciseismedicine.org/

https://www.ornish.com/zine/the -best-exercise-for-peripheralartery-disease/ should include a referral to a health coach and/or exercise and nutrition professionals to guide their healthy lifestyle adoption. A more thorough response can include Lifestyle Medicine which further addresses principles that are the cornerstone of health and well-being. Research has shown us that intensive lifestyle programs: (10%-fat vegetarian diet, moderate aerobic exercise, stress management training, smoking cessation, and group psychosocial support) can not only have a positive impact on cardiac risk factors but in fact can delay, stop, or reverse the progression of CAD in ambulatory patients over prolonged periods. [86-88]

Tobacco:

<u>Screening</u>: All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit. See Appendix for additional resources on counseling/support for patients.

Treatment: Use the "5-A" framework for counseling:

- 1. Ask about tobacco use.
- 2. Advise to quit through clear personalized messages.
- 3. Assess willingness to quit.
- 4. Assist to quit.
- 5. Arrange follow-up and support.

Combination therapy with counseling and medications is more effective than either component alone. FDA-approved pharmacotherapy includes nicotine replacement therapy, sustained-release bupropion, and varenicline. [32]

Blood pressure:

<u>Screening</u>: Accurate measurement is necessary for proper assessment and management. Recommendations for this assessment can be found in the appendix.

<u>Treatment</u>: Providers should follow the ECU Health Hypertension pathway and JNC8 recommendations.

Cholesterol:

<u>Screening</u>: After age 20 years, it is reasonable to measure traditional risk factors at least every 4 to 6 years. For adults 20 to 39 years of age, limited data exist on the performance and utility of 10-year risk estimation tools. Because age is a major driver of risk, most in this age range (<40 years) are unlikely to have a sufficiently elevated 10-year risk to warrant pharmacological therapy with a statin. There are some with some exceptions, such as in familial hypercholesterolemia. Nevertheless, periodic assessment of risk factors (e.g., at least every 4 to 6 years in adults < 40 years of age) is important to guide discussions about intensity of lifestyle interventions, frequency of risk factor monitoring, and treatment of nonlipid risk factors. [1,28]

<u>Treatment</u>: For young adults (20 to 39 years of age), priority should be given to estimating lifetime risk and promoting a healthy lifestyle. Only in select patients with moderate high LDL-C (> 160mg/dL) or those with very high LDL-C (> 190 mg/dL) is drug therapy indicated along with healthy lifestyle promotion. In adults 40-75

RESOURCES:

Nutrition

https://medinsteadofmeds.com/

https://www.eatsmartmovemore nc.com/

https://www.nhlbi.nih.gov/educat ion/dash-eating-plan

Tobacco

https://quitlinenc.dph.ncdhhs.gov/

http://www.uptodate.com/conten ts/quitting-smoking-beyond-thebasics?topicRef=3866&source=see link

Blood pressure

https://www.nhlbi.nih.gov/files/docs/guidelines/phycard.pdf

https://jamanetwork.com/journal s/jama/fullarticle/1791497

Cholesterol

https://www.aafp.org/pubs/afp/issues/2009/1201/p1273.html

years of age, 10 year ASCVD risk should guide therapeutic considerations. The higher the estimated risk, the more likely the patient is to benefit from statin treatment along with healthy lifestyle choices and counseling. ^[1,31] It is recommended that providers consult ACC/AHA Guidelines for the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. ^[14]

Blood Glucose: Diabetes mellitus is strongly associated with an elevated risk of PAD. The presence of diabetes mellitus increases the risk of adverse outcomes among patients with PAD, including progression to CLI, amputation, and death.

<u>Screening</u>: Regular monitoring of blood glucose levels and A1C is recommended. The US Preventative Services Task Force recommends screening for abnormal blood glucose as a part of cardiovascular risk assessment in adults aged 40-70 who are overweight or obese. Clinicians should offer or refer patients with abnormal blood glucose to intensive behavioral counseling interventions to promote a healthful diet and physical activity^[29] as well as make a referral to a Certified Diabetes Educator (CDE) and endocrinology if necessary.

Criteria for the diagnosis of diabetes^[30]

Normoglycemia	Impaired fasting glucose or impaired glucose tolerance	Diabetes
FPG* <110 mg/dl	FPG ≥110 and <126 mg/dl (IFG)	FPG ≥126 mg/dl
2-h PG <140 mg/dl	2-h PG ≥140 and <200 mg/dl (IGT)	2-h PG ≥200 mg/dl

^{*}Fasting plasma glucose

Treatment: A comprehensive care plan for patients with PAD and diabetes mellitus (DM) is important and may include diet and weight management, pharmacotherapy for glycemic control and management of other cardiovascular risk factors, and foot care and ulcer prevention. For adults with DM) a tailored nutrition plan focused on a heart healthy dietary plan is recommended. In addition, adults with DM should perform at least 150 minutes per week of moderate- intensity or 75 minutes of vigorous-intensity physical activity. It is also recommended that all people with diabetes should participate in diabetes self-management education (DSME) and receive the support needed to facilitate the knowledge, decision-making, and skills mastery necessary for diabetes self-care. [33] For T2DM metformin should be considered as a first-line pharmacologic to improve glycemic control and reduce CVD risk. If HbA1c is still greater than 7.0% after lifestyle therapies and metformin, there are several classes of medications that can be considered by the patient's PCP or endocrinologist.

Adequate sleep: Research shows that sleep alters autonomic nervous system function and other physiologic events that influence blood pressure. In addition, sleep disorders such as sleep apnea alter the blood pressure response and increase hypertension risk.^[34] The American Academy of Sleep Medicine (AASM) and Sleep Research Society (SRS) recommend that adults should sleep 7 or more hours per night on a regular basis to promote optimal health.^[35]

<u>Treatment</u>: It is suggested that the provider discuss sleep quality with patients and work with them to improve sleep quality including but not limited to: practicing good sleep hygiene, cognitive behavioral therapy or relation techniques, pharmacotherapy, and evaluation and treatment for sleep apnea.

Maintain good mental health: The psychological state of a patient can influence physical health. People with mental illness, such as anxiety and depression, frequently have high rates of adverse health behaviors, including tobacco and other substance use, physical inactivity, and poor diet. [80] Screening for early detection and treatment of mental illness (or behavioral issues) and substance use disorders in primary care settings can improve quality of life, help contain health care costs, and reduce complications from co-occurring

behavioral health and medical comorbidities.^[81] In regards to CVD, it is known that depression is a major cause of morbidity and poor quality of life among patients with CVD and is also considered an independent risk factor for major adverse cardiovascular events. Depression can also complicate the optimal management of CVD by decreasing adherence to healthy lifestyles and evidence based medical therapies.^[79]

<u>Treatment</u>: Providers should be prepared to screen for and treat mental health issues. Referral to a behavioral health specialist should be offered for positive screens for mood-related signs and symptoms (anxiety, depression, HRQOL, stress) and/or behavioral health intervention for lifestyle-related concerns (smoking cessation, stress management/coping, weight management, treatment adherence, education-appropriate psychoeducation related to disease state).^[85]

Risk Stratification for Lower Extremity APAD

Although there is insufficient evidence to recommend screening for PAD in asymptomatic patients, patients at increased risk of PAD (see below) should undergo a comprehensive medical history and review of symptoms to assess for exertional leg symptoms.^[17] Patients at risk of LE APAD:

- 1. Age \geq 65 years of age
- 2. Age 50-64 years of age, with risk factors for atherosclerosis (e.g. diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD
- 3. Individuals with known atherosclerotic disease in another vascular bed (e.g. coronary, carotid, subclavian, renal, or mesenteric artery stenosis or abdominal aortic aneurysm).

RECOMMENDATIONS

- Develop EHR workflow that allows patients with PAD risk factors to be flagged for PAD screening questions and possible ABI.
- If patient has clinical symptoms of PAD, a referral to a cardiologist or vascular provider should be automatically generated.

Screening for LE APAD

If the patient is determined to be at elevated risk or has existing LE PAD the next step would be a vascular work up including physical assessment including checking for ulcers, gangrene, and sores; assessment of limb pain; and evaluation of lower extremity pulses, ankle-brachial index (ABI), or toe-brachial index (TBI). The ankle-brachial index (ABI) is recommended as the first line noninvasive test for assessing lower extremity hemodynamics and to establish a diagnosis of PAD.^[37-38] In patients with non-compressible lower extremity vessels (ABI greater than 1.3), the toe-brachial index can be used.^[38-39]

Diagnostic Criteria for LE APAD on ABI and TBI

Ankle-Brachial Index		
1.0 – 1.3	Normal	
0.9 – 1.0	Borderline	
0.7 – 0.9	Mild	
0.4 – 0.7	Moderate	
< 0.4	Severe	

Toe-Brachial Index (used when ABI is >1.3)		
> 0.7	Normal	
0.4 – 0.7	Abnormal	
< 0.4	Severe	

Classification of LE APAD

The Rutherford system classifies LE PAD into acute and chronic limb ischemia, emphasizing that each

presentation requires different treatment algorithms. Rutherford also associated patient clinical symptoms with objective findings.^[40]

Grade	Category	Clinical description	Objective criteria
0	0	Asymptomatic—no hemodynamically significant occlusive disease	Normal treadmill or reactive hyperemia test
	1	Mild claudication	Completes treadmill exercise; AP after exercise > 50 mm Hg but at least 20 mm Hg lower than resting value
I	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete standard treadmill exercise, and AP after exercise < 50 mm Hg
П	4	Ischemic rest pain	Resting AP $<$ 40 mm Hg, flat or barely pulsatile ankle or metatarsal PVR; TP $<$ 30 mm Hg
Ш	5	Minor tissue loss—nonhealing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP $<$ 60 mm Hg, ankle or metatarsal PVR flat or barely pulsatile; TP $<$ 40 mm Hg
	6	Major tissue loss—extending above TM level, functional foot no longer salvageable	Same as category 5

Patients who are at high risk of developing LE APAD or are classified as Rutherford 0 should be considered part of the Wellness category. Management of asymptomatic PAD should be directed at accepted risk factor modification for patients with atherosclerosis.^[37] High priority should be given to:

- Exercise prescription and training: It is recommended that exercise training should be performed for a minimum of 30-45 minutes, in sessions performed at least 3 times per week for a minimum of 12 weeks. [41]
- Patient education that focuses on their understanding of risk factors for atherosclerosis and action steps that can decrease their risk including but not limited to: tobacco cessation, exercise, medication compliance, stress management, etc.
- Assessment/reassessment of SDOH to determine barriers to patient's ability to engage in the prescribed care plan.
- Pharmacotherapy (as patient-appropriate) [17,38,40,71,74]
 - Antihypertensives

Cilostazol

Antiplatelets

Tobacco cessation

Statins

Note: when patients with LE pain/discomfort who have no evidence of LE APAD based on pulse exam, ABI at rest and/or with exercise, then provider must consider orthopedic or neurogenic causes of LE pain/discomfort.

EARLY DISEASE/ESTABLISHED STABLE DISEASE

Patients with subclinical LE APAD and Rutherford categories 1 through 3.

MEDICAL EVALUATION AND DIAGNOSIS

Intermittent claudication (IC) is the most common clinical manifestation of LE APAD. Patients often present with a wide range of symptoms and associated impact on daily function. The discomfort caused by LE APAD is more often atypical than typical. Descriptions such as "tired", "giving way", "sore", and "hurts" are offered more often than "cramp". Defining how the symptoms have an impact on vocation, activities of daily living and social activities should be done with each evaluation. [49] The appendix contains specific questions that can help the provider better understand the patient's symptoms.

Vascular work up should include:

- Physical assessment including checking for ulcers, gangrene, sores, infection, foot complications
- Assessment of limb pain
- Pulses in feet/ankles
- ABI/TBI with waveform
- Coronary artery disease (CAD) evaluation for those with elevated cardiac risk

TREATMENT

Patients with LE APAD should receive a comprehensive program of guideline-directed medical therapy, including structured exercise therapy and lifestyle modification to reduce major adverse cardiac events (MACE) and major adverse limb events and to improve functional status.

Once LE APAD has been identified, the provider should prescribe the following medical management care plan to the patient with a planned follow up in three months.

Exercise: Patients with claudication should be enrolled in a supervised exercise program to improve functional status, quality of life, and reduce leg symptoms. [73] Exercise programs combined with risk factor modification offers the possibility of altering the clinical trajectory of PAD. [51] Walking exercise programs for PAD should be tailored for the individual patient. Some patients with PAD may be able to accomplish only 10 min of walking exercise at the initial exercise sessions. The duration of exercise should be increased by 5 minutes each week, until the patient with LE APAD is walking at least 30 minutes per session. [51] This should be done most days of the week. [54] Participants able to walk > 30 minutes per session should be encouraged to increase their walking exercise duration up to 45 to 50 minutes per session. Effective exercise interventions for patients with PAD have advised the patient to walk to near maximal leg pain, [56-57] although evidence suggests that walking to the onset of ischemic leg pain is also beneficial. [55] Patients with PAD should be told that stopping to rest during walking exercise is acceptable and typical in LE APAD. Once leg pain subsides during a rest period, the patient with PAD should resume walking again. Alternative exercise modes such as cycling and upper arm ergometry may be useful when walking is not an option for patients, as these have been shown to be effective.

Mental Health: Blanket mental and behavioral health screening are recommended for patients with established diagnosis of PAD: anxiety, depression, HRQOL, stress, social support, and health-literacy.^[82] It is recommend that a referral be made to a behavioral health specialist for positive screens for mood-related signs and symptoms (anxiety, depression, HRQOL, stress, social support, and health literacy) and/or behavioral health intervention for lifestyle-related concerns (smoking cessation, stress management/coping, weight management, and treatment adherence). Behavioral health specialist may make recommendation or referral to psychiatry for concomitant pharmacological treatment of mood symptoms affecting patient's ability to participate and engage in their own healthcare.^[83-84]

Antidepressant treatments, including pharmacotherapy, psychotherapy, and/or exercise, may relieve depressive symptoms and improve quality of life in patients with CVD. Medications that can either be used alone (selective serotonin reuptake inhibitors [SSRIs], serotonin-norepinephrine reuptake inhibitors [SNRIs], or other antidepressants) or to augment other therapies (such as second-generation antipsychotics [SGAs]) excluding tricyclic antidepressants or monoamine-oxidase inhibitors due to their unfavorable cardiovascular safety profile.

Tobacco cessation: Tobacco cessation is a vital component of care for patients with LE APAD. Patients with PAD who smoke cigarettes should be assisted in developing a plan for quitting that includes pharmacotherapy (i.e., varenicline, bupropion, and/or nicotine replacement therapy) and/or referral to a smoking cessation program. [1,52-53,63,68,70]

Reassessment of SDOH and referral as needed: Identify health disparities preventing treatment of LE APAD in individuals with lower socioeconomic statuses. Explore access to health care and any potential disparities and/or barriers/limitations preventing individuals from seeking medical attention.^[45]

Glycemic control: Management of diabetes mellitus in the patient with LE APAD should be coordinated between members of the healthcare team. [37] A comprehensive care plan for patients with LE APAD and diabetes mellitus is important and may include diet, and weight management, pharmacotherapy for glycemic control, management of other CV risk factors and foot care and ulcer prevention. [17] Patients with LE APAD and diabetes mellitus should be counseled about self–foot examination and healthy foot behaviors. [63]

Pharmacotherapy:

Antiplatelet therapy – Antiplatelet therapy with aspirin alone (range 75-325 mg per day) or clopidogrel alone (75mg per day) is recommended to reduce MI, stroke, and vascular death in patients with symptomatic LE APAD. [17,37,58-59,74] DAPT should only be considered in patients at high risk of CV ischemic events who are not at high risk of bleeding. [75-76]

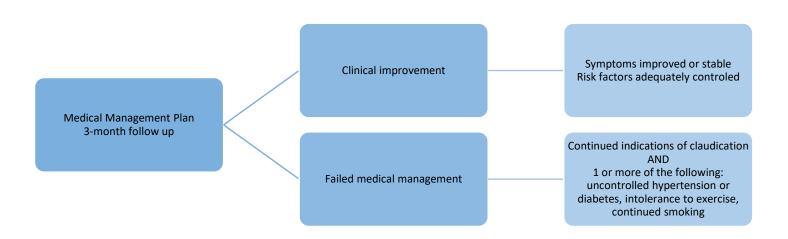
<u>Statin agents</u> – Statin therapy improves both cardiovascular and limb outcomes in patients with LE APAD. [17,37,60-61] Treatment of PAD should include statin therapy to achieve low-density lipoprotein level of 100mg per dL or less.[72]

<u>Cilostazol</u> – is a phosphodiesterase inhibitor that suppresses platelet aggregation and a direct vasodilator. Cilostazol therapy should be trialed in PAD without an incidence of heart failure. It has been shown to increase maximal and pain-free walking distance.^[17,37,63] However, in one study a treatment group reported higher incidence of headache, bowel complaints, and palpitations than

placebo group.[77]

<u>Antihypertensive agents</u> – There is a strong association between hypertension and CVD, including LE APAD. Antihypertensive therapy should be given to all patients with PAD and hypertension to reduce risk of MI, stroke, heart failure and CV death. Treatment of elevated high blood pressure is indicated to lower the risk of CV events.^[17,37,62,71]

The natural history of intermittent claudication (IC) is usually one of a slow progressive decline in the ability to walk a distance before the onset of pain. With intensive medical management, <5% of patients will develop symptoms of advanced ischemia, such as ischemic rest pain and tissue loss, or will ultimately require amputation. [37,65] A study by Madabhushi concluded that revascularization of IC patients is associated with an increased rate of progression to critical limb threatening ischemia (CLTI) and increased rate of amputation. Whereas further studies are required to identify which if any IC patients benefit from revascularization procedures, given the results of this study, it is recommended that IC patients should be treated with supervised exercise therapy (SET) and best medical therapy (BMT). [66]



If there are indicators of clinical improvement after 3 months of a medical management program, it is recommended that patients with IC be followed up annually to assess compliance with lifestyle measures (smoking cessation, exercise) and medical therapies as well as to determine if there is evidence of progression in symptoms or signs of PAD. Yearly ABI testing may be of value to provide objective evidence of disease progression.^[37]

If medical management fails or if there is a progression to CLI, a referral should be made to vascular surgery.

Care Management: Unfortunately for many patients the presence of multiple co- morbidities make it more difficult to manage treatment plans on their own. The primary care provider and medical home team oversees the care plan and overall direction of patient management. Collaboration with the health care team is needed to coordinate complex care needs across numerous disciplines and specialties.

RECOMMENDATIONS

- Follow a standardized process for Care coordination
- Initiate EOL discussions and participatory decision-making

The goal is to maximize wellbeing and comfort to the greatest degree possible, while providing effective and efficient care.

The primary care team should initiate goals of care discussions as well as End of Life (EOL) discussion early so the patient is able to understand, participate in decision-making and have an opportunity to communicate their wishes.

CHRONIC CRITICAL LIMB THREATENING DISEASE OR CRITICAL LIMB ISCHEMIA

Rutherford categories 4 through 6

Patients with Critical Limb Ischemia (CLI) are at increased risk of amputation and major CV ischemic events. Care of the patient with CLI includes:

- Evaluation for revascularization and wound healing therapies with the objective to minimize tissue loss, completely heal wounds, and preserve a functional foot
- Referral to vascular surgery for work-up/evaluation
- Referral to wound care and/or podiatry
- Continued medical management and secondary prevention
- At home or supervised exercise therapy
- Socks and footwear
- Orthotics/Prosthetics
- Feedback to referring providers/care team

MEDICAL EVALUATION

The 2016 AHA/ACC guidelines recognized critical evidence gaps to support the determination of optimal antiplatelet and statin therapy, role of dietary intervention and appropriate exercise programs. A study by Kadosh, et al. showed that lifestyle modification and guideline directed medical therapy (GDMT) use is suboptimal in patients with known CVD, particularly in those patients with PAD.^[67]

This is why, throughout the trajectory of the patient, risk factors and subsequent treatment should be assessed to ensure that GDMT is being utilized in the following areas:

- Exercise/Activity
- Tobacco cessation^[69-70]
- Glycemic control
- Lipids
- Blood pressure
- Socioeconomic risk factors

Other considerations would be an evaluation for aneurysmal disease (e.g., abdominal aortic, popliteal, or common femoral aneurysms),^[63] and regular inspection of the feet to detect objective signs of CLI.^[63]

TREATMENT

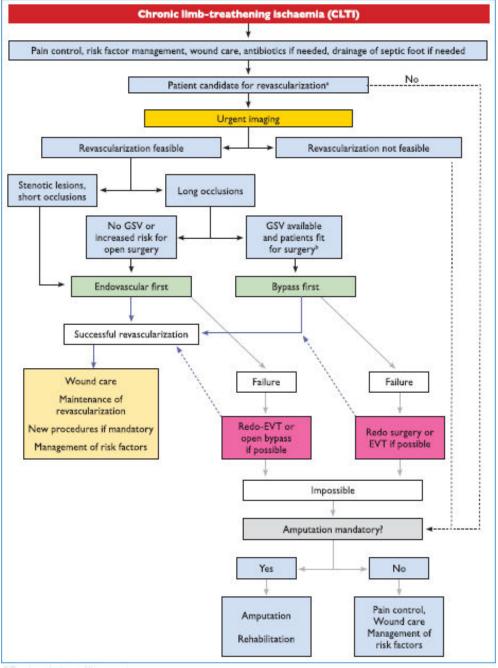
A team of professionals, representing different disciplines, is recommended to assist in the evaluation and management of the patient with PAD. For the care of patients with CLI, the interdisciplinary care team should 20

include individuals who are skilled in endovascular revascularization, surgical revascularization, wound healing foot surgery, and medical evaluation. [63]

Revascularization should only be considered in patients with critical limb ischemia or severely debilitating claudication symptoms that persist despite maximal medical treatment. [64] The decision to intervene should be individualized taking into consideration factors such as loss of ambulatory function on activities of daily living, occupation, quality of life, clinical response to noninterventional therapies and weighing the potential risks against the expected functional benefits for the patient. [37] Patient preference and goals of care are important

in the

considerations evaluation for



revascularization. If a strategy of revascularization for claudication is undertaken, the revascularization strategy should be evidence based and can include endovascular revascularization, surgery or both. The below algorithm from the European Society of Cardiology^[62] gives an illustration of the path that can be expected for a patient with CLI or CLTI.

FOLLOW UP

Follow up for a patient with LE APAD will vary significantly based on the individual patient but the provider should always start with the basics of care including treatment for the risk factors of atherosclerosis (hypertension, hypercholesterolemia, diabetes, etc.), supervised exercise therapy, a healthy eating plan or nutrition counseling from a Registered Dietitian / Nutritionist (RDN) evaluation and care plan development for identified issues (inclusive of SDOH) and tobacco cessation.

Other consideration would include:

- Physical/Occupational/Recreation therapy
- Wound healing
- Psychotherapy/Counseling
- Tobacco cessation counseling/assistance
- Referral to social worker/Care coordination
- Palliative care consultation
- Prosthetics
- Podiatry
- Support Groups/Community Support

References

- 1.Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 40:e596–e646.
- 2.Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med. 2018;378:e34.
- 3.Kim H, Caulfield LE, Rebholz CM. Healthy plant-based diets are associated with lower risk of all-cause mortality in US adults. J Nutr.2018;148:624–31.
- 4.Reedy J, Krebs-Smith SM, Miller PE, et al. Higher diet quality is associated with decreased risk of all-cause cardiovascular disease and cancer mortality among older adults. J Nutr. 2014;144:881–9.
- 5.Satija A, Bhupathiraju SN, Spiegelman D, et al. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in US adults. J Am Coll Cardiol. 2017;70:411–22.
- 6.Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Association of changes in diet quality with total and cause-specific mortality. N Engl J Med. 2017;377:143–53.
- 7. Whalen KA, Judd S, McCullough ML, et al. Paleolithic and Mediterranean diet pattern scores are inversely associated with allcause and cause-specific mortality in adults. J Nutr. 2017;147:612–20.
- 8.Bao Y, Han J, Hu FB, et al. Association of nut consumption with total and cause-specific mortality. N Engl J Med. 2013;369:2001–11.
- 9.Bernstein AM, Sun Q, Hu FB, et al. Major dietary protein sources and risk of coronary heart disease in women. Circulation. 2010;122:876–83.
- 10. Song M, Fung TT, Hu FB, et al. Association of animal and plant protein intake with all-cause and cause-specific mortality. JAMA Intern Med. 2016;176:1453–63.
- 11. Tharrey M, Mariotti F, Mashchak A, et al. Patterns of plant and animal protein intake are strongly associated with cardiovascular mortality: the Adventist Health Study-2 cohort. Int J Epidemiol.2018;47:1603–12.
- 12. Martinez-Gonzalez MA, Sanchez-Tainta A, Corella D, et al. A provegetarian food pattern and reduction in total mortality in the Prevencion con Dieta Mediterranea (PREDIMED) study. Am J Clin Nutr 100 suppl 1 2014:320S–28S.
- 13. Wolters Kluwer. (2018). ACSMs guidelines for exercise testing and prescription. Philadelphia.
- 14. Stone, N. J., Robinson, J. G., Lichtenstein, A. H., Merz, C. N. B., Blum, C. B., Eckel, R. H., ... Wilson, P. W. F. (2013). 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic

- Cardiovascular Risk in Adults. Circulation, 129(25 suppl 2). doi: 10.1161/01.cir.0000437738.63853.7a
- 15. Criqui, M. H., & Aboyans, V. (2015). Epidemiology of Peripheral Artery Disease. *Circulation Research*, 116(9), 1509–1526. doi: 10.1161/circresaha.116.303849
- 16. Fowkes, F. G. R., Aboyans, V., Fowkes, F. J. I., Mcdermott, M. M., Sampson, U. K. A., & Criqui, M. H. (2016). Peripheral artery disease: epidemiology and global perspectives. *Nature Reviews Cardiology*, 14(3), 156–170. doi: 10.1038/nrcardio.2016.179
- 17. Gerhard-Herman, M. D., et al. (2016) AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Retrieved from https://www.ahajournals.org/doi/10.1161/CIR.0000000000000471
- 18. Integrated Behavioral Health in Primary Care: Step-by-Step Guidance for Assessment and Intervention. Chapter 10 Cardiovascular Disease, 2016
- 19. Gupta, R., & Wood, D. A. (2019). Primary prevention of ischaemic heart disease: populations, individuals, and health professionals. *The Lancet*, *394*(10199), 685–696. doi: 10.1016/s0140-6736(19)31893-8
- 20. Havranek, EP., et al. (2015). Social Determinants of Risk and Outcomes for Cardiovascular Disease A Scientific Statement from the American Heart Association. *Circulation*, 132: 873-898.
- 21. Thornton, RL., et al (2016). Evaluating Strategies for Reducing Health Disparities by addressing the social determinants of health. *Health Affairs*, 35(8): 1416-1423.
- 22. Khanji, M., et al (2018). Lifestyle advice and interventions for cardiovascular risk reduction: A systematic review of guidelines. *International Journal of Cardiology*, 263: 142-151.
- 23. Canzanello VJ, Jensen PL, Schwartz GL. Are aneroid sphygmomanometers accurate in hospital and clinic settings? *Arch Intern Med* 2001;161:729-31.
- 24. Stergiou GS, Alpert B, Mieke S, Asmar R, Atkins N, Eckert S, et al. A universal standard for the validation of blood pressure measuring devices: Association for the Advancement of Medical Instrumentation/European Society of Hypertension/International Organization for Standardization (AAMI/ESH/ISO) Collaboration Statement. J Hypertens 2018; 36:472–478.
- 25. JNC 6. National High Blood Pressure Education Program. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997;157: 2413-46.
- 26. James, PA., Oparil, S., and Carter, BL. (2014). Evidence-Based Guideline for the Management of High Blood Pressure in AdultsReport From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 33(5): 507-520.
- 27. Jacobson, TA., et al. (2015). National lipid Association Recommendations for Patient-Centered

- Management of Dyslipidemia: Part 1 Full Report. Journal of Clinical Lipidology; 9: 129-169.
- 28. Grundy, SM., et al (2019). AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/AphA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*; 139: e1082-1143.
- 29. Siu, AL. (2015). Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*; 63(11): 861-869.
- 30. ADA Position Statement: Screening for Diabetes. (2002) Diabetes Care; s21-s24.
- 31. Eckel, RH., et al. (2014). 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk. *Circulation*; 129: s76-s99.
- 32. AHRQ The Guide to Clinical Preventative Services. (2014).
- 33. American Diabetes Association. (2020, January 01). Standards of Medical Care in Diabetes-2020 Abridged for Primary Care Providers. Retrieved May 27, 2020, from https://doi.org/10.2337/cd20-as01
- 34. Calhoun, DA and Harding, SM. (2010). Sleep and Hypertension. *Chest*: 2010; 138(2): 434 443.
- 35. Watson, NF., et al (2015). Recommended Amount of Sleep for a Healthy Adult: A Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society. *J Clin Sleep Med*; 11(6):591–592.
- 36. Alahdab, F., et al (2015). A systematic review for the screening for peripheral arterial disease in asymptomatic patients. *Journal of Vascular Surgery*; 61: 42S-53S.
- 37. Society for Vascular Surgery Lower Extremity Guidelines Writing Group, Conte MS, Pomposelli FB, et al. Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: management of asymptomatic disease and claudication [published correction appears in J Vasc Surg. 2015 May;61(5):1382]. *J Vasc Surg.* 2015;61(3 Suppl):2S-41S.
- 38. Firnhaber, JM & Powell, CS., Lower Extremity Peripheral Artery Disease: Diagnosis and Treatment. Am. Fam Physician; 99(6): 362-369.
- 39. Foley, TR., Armstrong, EJ., & Waldo, SW. (2016). Contemporary evaluation and management of lower extremity peripheral artery disease. Heart; 102(18): 1436-1441.
- 40. Hardman, RL., et al (2014). Overview of Classification Systems in Peripheral Artery Disease. Semin Intervent Radiol; 31:378–388
- 41. Olin, JW and Sealove BA. (2010) Peripheral Artery Disease: Current Insight Into the Disease and Its Diagnosis and Management. Mayo Clinic Proc; 85(7):678-692.
- 42. Treat-Jacobson, D., et al (2019). Implementation of Supervised Exercise Therapy for Patients With

- Symptomatic Peripheral Artery Disease: A Science Advisory From the American Heart Association. *Circulation*. 2019;140:e700–e710.
- 43. Pande, RL and Creager, MA. (2014) Socioeconomic Inequality and Peripheral Artery Disease Prevalence in US Adults. *Circ Cardiovasc Qual Outcomes*; 7(4):532-9
- 44. Aquaris, AE., et al (2006). Clinical Indicators and Psychosocial Aspects in Peripheral Arterial Disease. *Arch Surg*;141(2):161-6.
- 45. Vart, P., et al. (2017) Socioeconomic Status and Incidence of Hospitalization With Lower-Extremity Peripheral Artery Disease: Atherosclerosis Risk in Communities Study. *J Am Heart Assoc*. 2017;6:e004995.
- 46. Austin, et al. (2019) Outcomes After Peripheral Artery Disease Intervention Among Medicare-Medicaid Dual-Eligible Patients Compared With the General Medicare Population in the Vascular Quality Initiative Registry. *BMJ Surg Interv Health Technol*; 1(1): . doi:10.1136/bmjsit-2019-000018.
- 47. Arya, S., et al (2018) Race and Socioeconomic Status Independently Affect Risk of Major Amputation in Peripheral Artery Disease. *J Am Heart Assoc*;7:e007425
- 48. Conen, et al (2011) Smoking, Smoking Cessation and Risk of Symptomatic Peripheral Artery Disease in Women: A Prospective Study. *Ann Intern Med*; 154(11): 719–726
- 49. Wennberg, PW. (2013). Approach to the patient with peripheral arterial disease. *Circulation*; 128:2241-2250.
- 50. The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery. Aboyans, V., et al (2018). *Eur J Vasc Endovasc Surg*; 55, 305-368.
- 51. Hamburg, NM and Balady, GJ. (2011) Exercise Rehabilitation in Peripheral Artery Disease: Functional Impact and Mechanisms of Benefits. *Circulation*; 123(1):87-97.
- 52. Patnode CD, Henderson JT, Thompson JH, et al. (2015) Behavioral counseling and pharmacotherapy interventions for tobacco cessation in adults, including pregnant women: a review of reviews for the US Preventive Services Task Force. *Ann Intern Med*;163:608–21.
- 53. Stead LF, Koilpillai P, Fanshawe TR1, et al. (2016) Combined pharmacotherapy and behavioural interventions for smoking cessation. *Cochrane Database Syst Rev*;3:CD008286.
- 54. McDermott, MM. (2018) Exercise Rehabilitation for Peripheral Artery Disease. *Journal of Cardiopulmonary Rehabilitation and Prevention*; 38:63-69.
- 55. Fakhry F, van de Luijtgaarden KM, Bax L, et al. (2012) Supervised walking therapy in patients with intermittent claudication. *J Vasc Surg*; 56 (4): 1132 1142.
- 56. McDermott MM, Ades P, Guralnik JM, et al. (2009) Treadmill exercise and resistance training in

- patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial . *JAMA*; 301 (2): 165 174.
- 57. McDermott MM, Ferrucci L, Tian L, et al. (2017) Effect of granulocyte-macrophage colony-stimulating factor with or without supervised exercise on walking performance in patients with peripheral artery disease: the PROPEL Randomized Clinical Trial. *JAMA*; 318(21): 2089 2098.
- 58. Berger, JS. (2009). Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease; a meta-analysis of randomized trails. *JAMA*; 301: 1909-19.
- 59. Cacoub PP, Bhatt DL, Steg PG, et al. 92009) Patients with peripheral arterial disease in the CHARISMA trial. *Eur Heart J*;30:192–201.
- 60. Ramos R, García-Gil M, Comas-Cufí M, et al. (2016) Statins for prevention of cardiovascular events in a low-risk population with low ankle-brachial index. *J Am Coll Cardiol*;67:630–40.
- 61. Heart Protection Study Collaborative Group. (2007) Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg*;45: 645–54.
- 62. Aboyans, V., et al. (2017) 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Disease, in collaboration with the European Society for Vascular Surgery. *Eur J Vasc Endovasc Surg*; 55: 305-368.
- 63. Hirsh, AT., et al. (2005) ACC/AHA 2005 Practice Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic). Circulation; 113 (11): e463–e654.
- 64. O'Donnell, ME., et al. (2011) Optimal Management of Peripheral Arterial Disease for the Non-specialist. Ulster Med J; 80(1): 33-41.
- 65. Norgen, L., et al. (2007). Inter-Society Consensus for the Management of Peripheral arterial disease. *J Vasc Surgery*; 45: S5-S67.
- 66. Madabhushi, V. et al. (2020). Revascularization of Intermittent Claudicants Leads to Higher Rates of Chronic Limb- threatening Ischemia and Rates of Amputation. *Journal of Vascular Surgery*. 71. e15. 10.1016/j.jvs.2019.10.028.
- 67. Kadosh, B. et al. Risk factor control, lifestyle modification, and guideline-directed medical therapy in patients with cardiovascular disease. *J Am Coll Cardiol*. 2019 Mar, 73 (9) Supplement 1) 1854
- 68. Clair C, et al. (2013) Association of smoking cessation and weight change with cardiovascular disease among people with and without diabetes. *JAMA*; 309(10): 1014–102.
- 69. Armstrong, EJ., et al. Smoking Cessation Is Associated With Decreased Mortality and Improved Amputation-Free Survival Among Patients With Symptomatic Peripheral Artery Disease. *J Vasc Surg*;60(6):1565-71.

- 70. Girolami B., et al. (1999) Treatment of intermittent claudication with physical training, smoking cessation, pentoxifylline, or nafronyl: a meta-analysis. *Arch Intern Med*;159(4):337–345.
- 71. Yusuf S, et al. (2000) Effects of an angiotensin-converting enzyme inhibitor, Rampipril, on cardiovascular events in high risk patients. HOPE Trial. *N Engl J Med*. 2000 Jan 20; 342 (3).
- 72. Paraskevas KI, et al. (2012). Statins and noncardiac vascular disease. Curr Opin Cardiol;27(4):392–397.
- 73. Murphy TP, et al. Supervised Exercise, Stent Revascularization, or Medical Therapy for Claudication Due to Aortoiliac Peripheral Artery Disease: The CLEVER Study. *J Am Coll Cardiol*; 65(10): 999–1009.
- 74. CAPRIE Steering Committee. (1996). A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet*;348(9038):1329–1339.
- 75. Cacoub PP, et al. (2009) Patients with peripheral artery disease in the CHARISMA trial. *Eur Heart J*;30:192-201.
- 76. Bonaca MP., et al. (2016) Ticagrelor for prevention of ischemic events and myocardial infarction in patients with peripheral artery disease. *J Am Coll Cardiol*. 2016;67(23):2719-28.
- 77. Thompson PD., et al (2002) Meta-analysis of results from eight randomized, placebo-controlled trials on the effect of cilostazol on patients with intermittent claudication. *Am J Cardiol*;90(12):1314–1319.
- 78. Cohen, BE., Edmondson, D., and Kronish, IM. (2015). State of the art review: depression, stress, anxiety and cardiovascular disease. *Am J of Hypertension*; 28(11): 1295-1302.

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Social Determinants of Health (SDOH) tools

Multiple tools exist to assist providers in evaluating SDOH. This list is not intended to be comprehensive:

- https://www.chcs.org/resource/screening-social-determinants-health-populations-complex-needsimplementation-considerations/
- https://www.ruralhealthinfo.org/toolkits/sdoh/4/assessment-tools
- https://www.aafp.org/dam/AAFP/documents/patient_care/everyone_project/hops19-physicianguide-sdoh.pdf
- https://innovation.cms.gov/files/worksheets/ahcm-screeningtool.pdf

Psychological Screening

Primary care practices with multiple co-occurring behavioral health conditions in their patient population may wish to consider the screening tools derived from the PHQ. Practices can combine these tools to assess for the most common conditions. The PHQ-9 is one of the few tools endorsed by the National Quality Forum for behavioral health screening. Its administration is reimbursed by Medicare and Medicaid, and some commercial insurance, though practices must always emphasize the need for diagnostic follow-up. Practices that serve a high proportion of seriously ill patients on an outpatient basis might consider tools that were originally developed for patients with co-occurring physical health disorders (e.g., HADS). These are only suggestions there is a lack of evidence to recommend one screening instrument over another.

- PHQ9 or PHQ2: https://www.apa.org/pi/about/publications/caregivers/practice-settings/assessment/tools/patient-health
- HADS: https://eprovide.mapi-trust.org/instruments/hospital-anxiety-and-depression-scale
- Screening and Management of depression in patients with CVD:
 https://www.sciencedirect.com/science/article/pii/S0735109719305133

Exercise Resource

	Aerobic and/	or Resistance	Neuromotor**	Flexibility	The New ACSM FITT Exercise Recommendations
Frequency	≥2-3 sessions per week	≥2-3 sessions per week	≥2-3 session per week	≥2-3 sessions per week with daily being most effective	***On most, preferably all, days of the week
Intensity	*Moderate (i.e., 40% - 59% VO2R or HRR; RPE 12-13 on a 6–20 scale to Vigorous (i.e., 60% - 80% VO2R or HRR; RPE 14-16 on a 6–20 scale)	Moderate (i.e., 60% - 70% 1-RM; may progress to 80% 1-RM. For older adults and novice exercisers begin with 40-50% 1RM)	Low to Moderate	Stretch to the point of feeling tightness or slight discomfort	Low, Moderate, or Vigorous with an emphasis on Moderate
Time	≥20-30 min per session of continuous or accumulated exercise of any duration	2-4 sets of 8-12 repetitions of 8-10 resistance exercises of each of the major muscle groups per session to total >20 min per session with rest days interspersed depending on the muscle groups being exercised	≥20-30 min per session	Hold static stretch for 10-30 s with 2-4 repetitions of each exercise targeting the major muscle tendon units to total 60 s of total stretching time for each exercise; ≤10 min per session	≥20 to 30 min per day to total ≥90 to 150+ min per week of continuous or accumulated exercise of any duration
Type	Prolonged, rhythmic activities using large muscle groups (e.g., walking, cycling, swimming)	Resistance machines, free weights, resistance bands, and/ or functional body weight exercise	Exercise involving motor skills and/or functional body weight and flexibility exercise such as yoga, pilates, and tai chi	Static, dynamic, and/ or proprioceptive neuromuscular facilitation	An emphasis on aerobic or resistance exercise alone or combined in addition to neuromotor and flexibility depending on personal preference

VO,R=oxygen uptake reserve; HRR= heart rate reserve; RPE=rating of perceived exertion; 1-RM=one repetition maximum.



^{*} The magnitude of the BP reductions resulting from aerobic exercise are directly proportional to intensity such that the greatest BP reductions occur after vigorous intensity exercise if the patient/client is willing and able to perform vigorous intensity exercise (4).

^{**} Neuromotor functional body weight exercise can be substituted for resistance exercise, and depending on the amount of flexibility exercise integrated into a session, neuromotor flexibility exercise can be substituted for flexibility exercise depending on patient/client preference. The evidence is promising but limited for neuromotor exercise to be recommended alongside aerobic and resistance exercise as a primary exercise modality at this time (6).

^{***} The frequency recommendation is made due to the immediate blood pressure lowering effects of exercise, termed postexercise hypotension (4).

	Supervised Treadmill Exercise ^a	Home-Based Walking Exercise	Ergometry Exercise
Overview of exercise characteristics	Treadmill walking in an exercise facility delivered by personnel trained in exercise therapy for PAD	Unsupervised walking for exercise in or around home or in an exercise facility	Supervised arm or leg ergometry
Frequency	3 times per wk	3-5 times per wk	Twice per wk
Duration of each exercise session	Begin at 15 min per session increasing to 45-50 min per session	Begin at 10-15 min per session increasing gradually to 50 min per session	10 sets of 2 min of ergometry (total = 20 min per session)
Intensity	Walking to near-maximal or maximal leg pain ^b	Walking at self-selected pace or to near-maximal or maximal leg pain ^c	High intensity
Program duration	12 wk minimum	12 wk to 6 mo	12 wk to 6 mo
Benefit	180 m of treadmill walking 18 15-35 m in 6-min walk distance. 19,20,21,22	45-55 m in 6-min walk distance ^{22,23}	Improved shuttle corridor-walk test (walk) by about 30% ⁴⁰
Additional considerations	Medicare provides coverage as of 2017	Effective programs have incorporated behavioral change techniques	Effective ergometry interventions have been supervised
Class of recommendation; Level of evidence ¹¹	Class I; Level of evidence: A	Class IIa; Level of evidence: A	Class IIa; Level of evidence: A

Supervised Exercise Training for LE PAD^[54]

Supervised Exercise Therapy is now a covered service by the Centers for Medicare and Medicaid for beneficiaries with IC for the treatment of symptomatic PAD.

Elements that are required:

- Beneficiaries must have a face-to-face visit with the physician responsible for PAD treatment to obtain the referral for SET
- Consist of sessions lasting 30-60 minutes comprising a therapeutic exercise-training program for PAD in patients with claudication
- Prescribed exercise must consist of 12 weeks of exercise session that is typically three times weekly
- The exercise session must take place in a physician's office or outpatient hospital affiliated setting
- Be under the direct supervision of a physician, physician assistant, or nurse practitioner/clinical nurse specialist who must be trained in both basic and advanced life support techniques.

Hypertension Assessment and Management

Accurate measurement for blood pressure is necessary for proper assessment and management. Equipment should be regularly inspected and validated.^[23] Operators should be trained and regularly retrained in the standardized technique and the patient must be properly prepared and positioned.^[24] The measurement process should include^[25]:

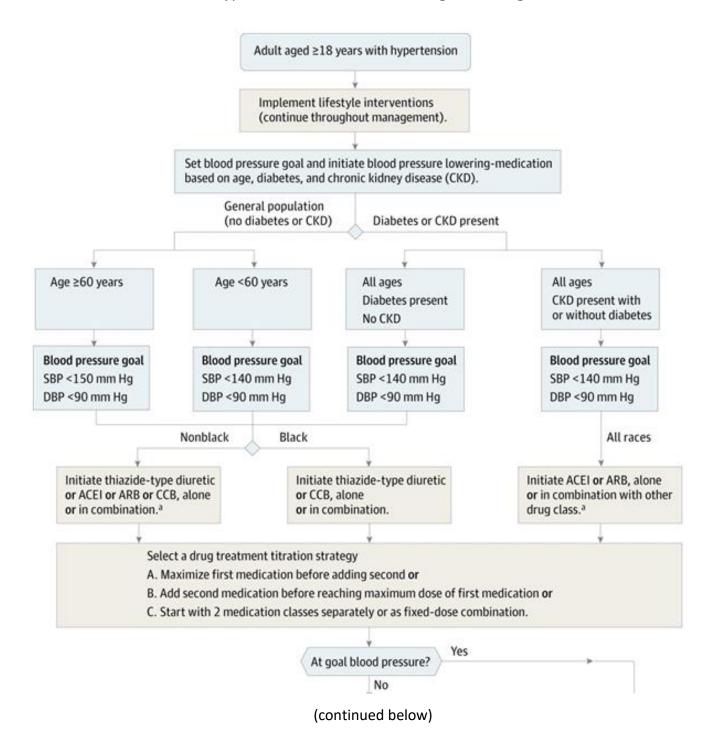
- Patient should avoid smoking, exercise, caffeine intake and weight measurements at least 30 minutes prior to the blood pressure measurement
- The patient should empty their bladder and be seated quietly for at least 5 minutes in a chair with feet on the floor, back against the chair and arm supported at heart level
- An appropriate sized cuff should be used (the cuff bladder should encircle at least 80% of the arm, usually 12-13 cm wide and 35 cm long, but larger cuffs may be needed for a larger patient arm circumference)
- The patient and the staff person should remain quiet during the measurement
- At least 2 measurements should be made with at least 1-2 minute intervals between measurements
- The average measurement should be recorded

Blood pressure should be measured in both arms at least on the initial office visit. A systolic BP difference of >15mm Hg is suggestive of atheromatous disease. [25]

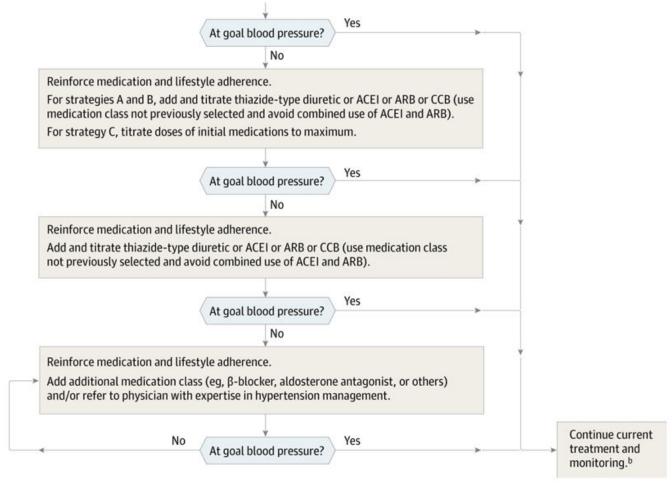
BP should be measured in standing position at 1 and 3 min after standing for older and diabetic patients or for suspected orthostatic hypotension (defined as a reduction in Systolic Blood Pressure of at least 20mm Hg and Diastolic Blood Pressure of at least 10mm Hg). This is associated with increased risk of mortality and cardiovascular events.

Algorithm for hypertension management – following the JNC8 guidelines

2014 Hypertension Guideline Management Algorithm



JNC8 hypertension management, continued



^aACEIs and ARBs should not be used in combination.

^bIf blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.

Tobacco Cessation Counseling and Support

Million Hearts change package

https://millionhearts.hhs.gov/files/Tobacco Cessation Change Pkg.pdf

Center for Disease Control and Prevention

Healthcare Provider tools and resources:

https://www.cdc.gov/tobacco/campaign/tips/partners/health/index.html

Patient resources:

- How to Quit Smoking (https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?scid=OSH tips D9755) This "How to Quit Smoking" page has a variety of resources, including apps that you can share with members to share with patients.
- Taking Care/Caregivers Resources
 (https://www.cdc.gov/tobacco/campaign/tips/groups/caregivers.html?scid=OSH email E210) Learn the real stories of people taking care of loved ones living with a smoking-related disease or disability.
- Quit Guide Handout (https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/guide/index.html)
 The Quit Guide has many helpful pieces of content, in English and Spanish, and can be embedded into provider's offices and clinic's websites, newsletters, and emails.
- E-Cigarette Information (https://www.cdc.gov%2Fecigarettes%2Findex.html)
 Here is the CDC's latest information on e-cigarettes, which is available in both English and Spanish and includes a Powerpoint presentation that providers can share with patients

NC Tobacco Prevention and Control

Tobacco treatment standards for healthcare providers: https://quitlinenc.dph.ncdhhs.gov/health-professionals/tobacco-treatment-standard-of-care.html

Patient Resources: https://quitlinenc.dph.ncdhhs.gov/ QuitlineNC provides free cessation services to any North Carolina resident who needs help quitting tobacco use. Quit Coaching is available in different forms, which can be used separately or together, to help any tobacco user give up tobacco.

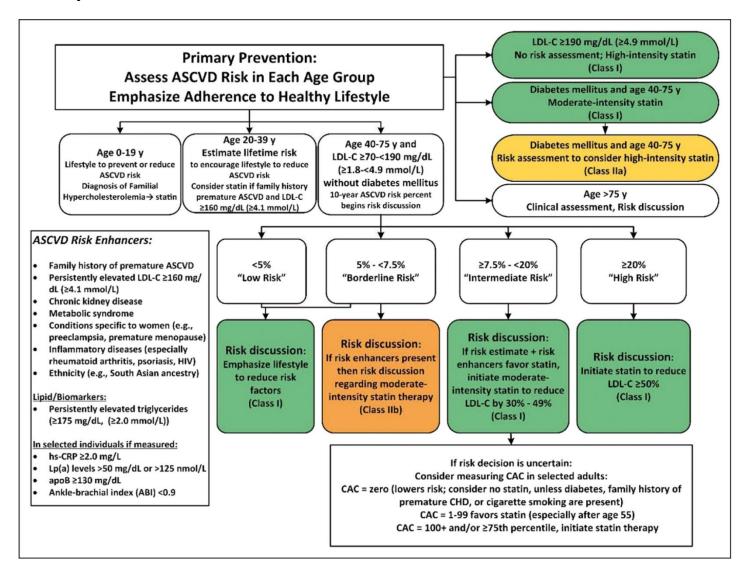
Agency for Healthcare Research and Quality

Quick Reference Guide for Clinicians: https://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/references/quickref/index.html This Quick Reference Guide for Clinicians presents summary points from the Clinical Practice Guideline, specifically the guideline strategies for providing appropriate treatments for every patient.

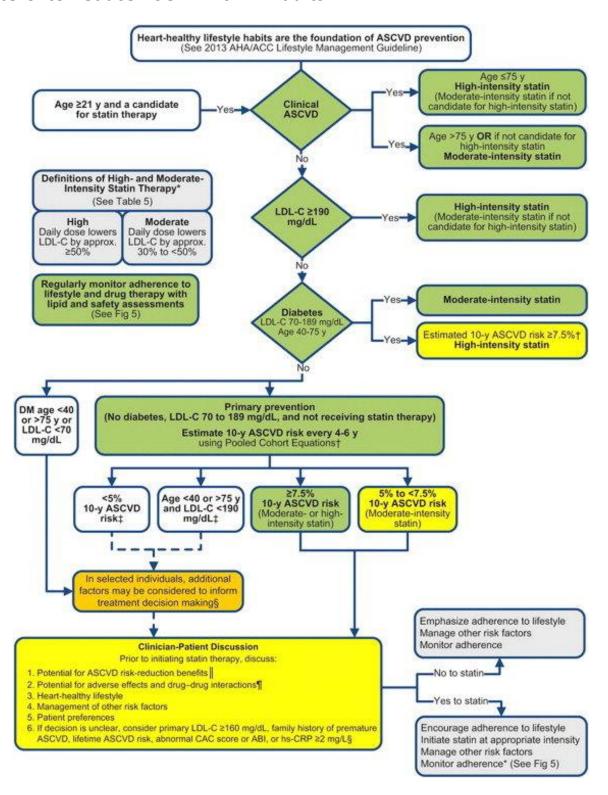
Helping Smokers Quit: A Guide for Clinicians:

https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/references/clinhlpsmkqt/clinhlpsmksqt.pdf This pocket guide outlines the 5 A's (Ask, Advise, Assess, Assist, Arrange) that clinicians can employ to encourage patients to quit tobacco use.

Primary Prevention²²



Summary of Statin Initiation Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults¹⁴



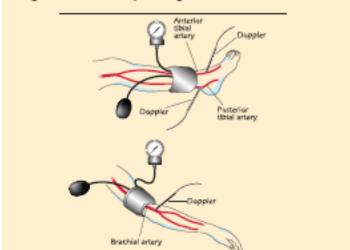
Physical Examination

Points of History for LE PAD

- Site
 - O Where is the pain?
 - o Is there more than one site? Does pain migrate?
- Quality
 - O What does the pain feel like?
 - o Is there more than one type of discomfort?
- Exacerbating factors: What makes it worse?
- Relieving factors: What makes it better?
- Timing
 - o When did it begin?
 - o Was onset sudden or gradual?
 - o Have you stopped or altered activities because of the pain?

How to measure ABI? [50]

In supine position, with cuff placed just above the ankle, avoiding wounded zones. After a 5—10 minute rest, the SBP is measured by a Doppler probe (5—10 MHz) on the posterior and the anterior tibial (or dorsal pedis) arteries of each foot and on the brachial artery of each arm. Automated BP cuffs are mostly not valid for ankle pressure and may display overestimated results in case of low ankle pressure. The ABI of each leg is calculated by dividing the highest ankle SBP by the highest arm SBP.



Interdisciplinary Care Team for LE APAD

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 and foot surgery, and medical evaluation and care.
Interdisciplinary care team members may include:
Vascular medical and surgical specialists (ie, vascular medicine, vascular surgery, interventional radiology, interventional cardiology)
Nurses
Orthopedic surgeons and podiatrists
Endocrinologists
Internal medicine specialists
Infectious disease specialists
Radiology and vascular imaging specialists
Physical medicine and rehabilitation clinicians
Orthotics and prosthetics specialists
Social workers
Exercise physiologists
Physical and occupational therapists
Nutritionists/dieticians

Patient Education resources

AHA Life's Simple 7

https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7

Preventative Cardiovascular Nursing Association

https://pcna.net/clinical-resources/patient-handouts/peripheral-artery-disease-tools-and-handouts/

American Heart Association

- https://www.heart.org/en/health-topics/peripheral-artery-disease/about-peripheral-artery-disease-pad
- https://www.heart.org/-/media/data-import/downloadables/8/e/8/pad-take-your-socks-off-downloadable-ucm-491938.pdf
- https://watchlearnlive.heart.org/index.php?moduleSelect=periad

American College of Sports Medicine

https://www.exerciseismedicine.org/assets/page_documents/EIM_Rx%20for%20Health_PAD.pdf

American College of Cardiology

- https://www.cardiosmart.org/~/media/Images/Infographics/2017/Peripheral-Artery-Disease.ashx
- https://www.cardiosmart.org/Heart-Conditions/Peripheral-Vascular-Disease
- https://www.cardiosmart.org/Original-Content/Walking-and-PAD
- https://www.youtube.com/watch?v=Nds4QN2C1bk#action=share

Henry Ford

https://www.youtube.com/watch?v=x8LmqxqoPb0&feature=youtu.be&list=PLeIzx72H9 229Z6W Cn- FA74SSDXDTxwrY

Circulation Foundation: Exercise for intermittent claudication

https://www.circulationfoundation.org.uk/news/new-infographic-intermittent-claudication

End of Life Resources

ECU Health Advanced Care planning https://www.vidanthealth.com/Manage-My-Health/Advance-care-planning

Conversation scripts for providers https://www.vidanthealth.com/Manage-My-Health/Advance-Care-Planning/Conversation-Scripts-for-Providers

Advanced Care Planning toolkit https://www.vidanthealth.com/getattachment/Manage-My-Health/Advance-Care-Planning-Steps/Advance-Care-Planning-Expanded-ToolKit.pdf?lang=en-US

Institute for Health "Conversation ready" http://www.ihi.org/engage/initiatives/ConversationProject/Pages/ConversationReady.aspx

National Institute on Aging https://www.nia.nih.gov/health/caregiving/advance-care-planning

Respecting Choices https://respectingchoices.org/

Resources for the Follow up Phase

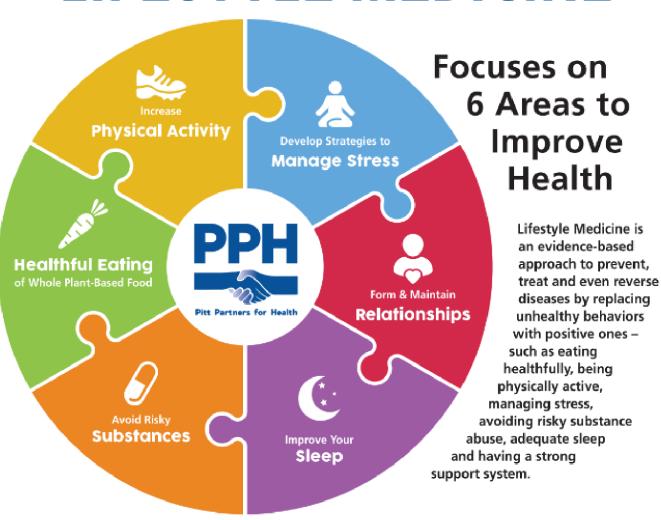
Amputee Coalition https://www.amputee-coalition.org/leg-amputation-guide/

US Department of Veterans Affairs website https://www.healthquality.va.gov/guidelines/Rehab/amp/



Working Together for a Healthier **Community**

LIFESTYLE MEDICINE



Graphic adapted from the American College of Lifestyle Medicine (ACLM)

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