Basic Diagnosis and Medical Treatment of Atherosclerotic Peripheral Arterial Disease (APAD)

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What is APAD? The terms PAD, vascular disease or peripheral vascular disease all connote different meanings to different people. Because of TV advertising PAD is often thought to be limited to the legs and none of these labels adequately reflects that atherosclerosis is the underlying cause of the disease. We have coined the term Atherosclerotic Peripheral Arterial Disease (APAD) to denote atherosclerosis as the underlying cause and to emphasize that it can occur in any peripheral artery.

What arteries are involved by APAD? The most common peripheral arteries involved are; atherosclerotic carotid artery stenosis; atherosclerotic subclavian or vertebral artery stenosis; atherosclerotic mesenteric arterial stenosis; atherosclerotic renal artery stenosis; atherosclerotic aorto, iliac, femoral, popliteal, and tibial stenosis. Just like Atherosclerotic Coronary Artery Disease (ACAD), patients with APAD require aggressive atherosclerosis risk factor management and lifestyle changes to effectively treat their APAD and avoid other atherosclerosis related morbid events.

Initial diagnosis and treatment for most all APAD lesions is based on history and physical exam and simple noninvasive diagnostic testing. There is usually no need for an invasive diagnostic or therapeutic procedure to be performed as first line diagnosis or therapy.

This article is a basic outline of the office approach to patients who may harbor APAD lesions. As noted, in most cases simple history and physical exam and noninvasive testing will allow accurate diagnosis of APAD and lead to secondary preventive measures outlined as “Life’s Simple 7” below. Also note that in this paper if you encounter the term “maximal risk factor reduction” it also includes instruction in lifestyle changes.

Identification of patients with Atherosclerotic Peripheral Arterial Disease (APAD).

Who are they? Medicare age and those over 50 who smoke, have diabetes and/or dyslipidemia. Finding an asymptomatic atherosclerotic lesion in a peripheral artery warrants maximal risk factor treatment and lifestyle changes for secondary prevention just as in patients with ACAD.

Atherosclerotic Coronary artery disease (ACAD)

The focus of this presentation is about identification of the patient who harbors Atherosclerotic Peripheral Arterial Disease (APAD). However in the APAD patient one must remember to ask about symptoms of Atherosclerotic Coronary Artery Disease (ACAD).

Conversely if a patient has ACAD and is on maximal atherosclerotic risk factor management and lifestyle modification, screening for asymptomatic APAD is not encouraged because the medical treatment of ACAD and APAD are the same. In the absence of specific symptoms of APAD (TIA, Claudication, mesenteric angina or renovascular HBP, etc.) there is no need to screen for APAD in the ACAD patient.
Outline of the general approach to evaluation of patients who may have APAD.

Start with the vital signs including BMI and waist circumference in order to identify patients who may have metabolic syndrome. One can also assess if the patient is hypertensive or prehypertensive. If you identify a patient with atherosclerosis in any peripheral artery as outlined below, the most important therapy that can be given is adequate treatment of their atherosclerotic risk factors and education about the needed lifestyle changes that the patient should make in order to decrease risk of suffering a morbid cardiovascular event.

The following are simple guidelines for patients you may see in your office who are suspected of harboring atherosclerotic disease in their peripheral arteries.

Atherosclerotic Subclavian artery stenosis.

Take BP in both arms routinely in all pts over the age of 50. If one arm is lower than the other by 20 torr systolic or more that may indicate the presence of a subclavian stenosis in the arm with the lower pressure. Most patients with subclavian artery stenosis are totally asymptomatic. The most common symptoms of subclavian stenosis are arm claudication and subclavian steal syndrome. Symptoms indicative of steal syndrome are dizziness, gait disturbance or imbalance/staggering, bilateral tunnel vision; presence of these symptoms could be a sign of true Vertebro-Basilar (VB) insufficiency and subclavian steal syndrome. On PE check for supraclavicular/infraclavicular bruits on the side with the lowest BP. The next step is a carotid duplex exam where one of the routine components is to look for retrograde flow in the vertebral artery on the side with lower BP. If reversal of vertebral flow is present and the patient has no symptoms it is called subclavian steal phenomenon. If the patient has VB insufficiency symptoms then it is called subclavian steal syndrome and may warrant correction of the subclavian lesion with angioplasty/stent or surgical reconstruction. The phenomenon is much more common than syndrome. Asymptomatic steal phenomenon does not warrant interventional correction of the subclavian lesion. However, since the subclavian lesion is almost always an atherosclerotic lesion, the patient requires maximal treatment of atherosclerotic risk factors and changes in lifestyle. Also
remember that the arm with the higher reading is the patient’s true BP and that arm only should be used for monitoring.

**When to refer?**

1. Significant arm claudication that interferes with daily activities.
2. Symptoms of true steal syndrome as outlined above.

**Atherosclerotic Carotid artery stenosis.**

**SYMPTOMATIC PATIENTS:** When patients present with an acute TIA or stroke and are within the six hour therapeutic window they should be sent immediately to the ED for “code stroke” evaluation. If the patient suffered a recent event and has fully recovered or has minor residual effects, and has evidence of carotid disease then same day referral to a vascular surgeon is needed.

**ASYMPTOMATIC PATIENTS:** In the asymptomatic patient there are no firm guidelines for screening for carotid stenosis with carotid duplex ultrasound and there are recommendations against routine screening for carotid stenosis like is practiced by groups such as “lifeline” screening. In the U.S. carotid stenosis causes 16% of strokes. In patients with known asymptomatic carotid disease the stroke risk is 2% per year or less. Intervention by endarterectomy or stenting carries a 2-4% risk which means there is a narrow therapeutic window in the asymptomatic patient. The number needed to treat (NNT) to prevent one neurologic event is prohibitive. Thus for fear of doing more harm than good the recommendation is not to screen the asymptomatic patient for carotid stenosis.

What about the asymptomatic patient with a carotid bruit? Not all bruits represent carotid stenosis. Transmitted murmurs, external carotid stenosis, venous hum, tortuous artery all can cause a bruit in the neck. When the patient is asymptomatic with a neck bruit, if they are already on maximal atherosclerotic risk factor reduction, then carotid duplex ultrasound is not necessary because even if a lesion is identified the treatment will be the same. If the patient is not on maximal risk factor management a carotid duplex ultrasound can be used to ascertain if there is carotid stenosis present. If atherosclerotic disease is identified, then maximal risk factor reduction is mandatory for secondary prevention.

**Who to refer for evaluation?**

1. All symptomatic patients go to ED for code stroke if within the six hour window for potential TPA or interventional capture.
2. Any symptomatic patient with evidence of carotid disease who is outside the six hour window. Here the choice is still immediate hospital admission or referral to a vascular surgeon.
3. Any ASYMPTOMATIC patient with a stenosis greater than 70%

**Atherosclerotic Renal artery stenosis and renovascular hypertension/ischemic nephropathy.**

Atherosclerotic renal artery stenosis is not a rare entity. The problem is that there are many patients who have unilateral or bilateral renal artery stenosis that does not cause the patient to have severe hypertension or renal insufficiency/failure. One frustration in evaluation of these patients is the kidney does not give up its secrets easily. After years of investigation using renal vein renins, split renal function studies, captopril renography and renal biopsy, all have failed to conclusively predict when correction of a renal artery stenosis will lead to improvement of BP control or renal function.
There are some clinical features that may help predict patients who might have unilateral or bilateral renal artery stenosis that is causing a problem that may be improved by a renal artery intervention. These are 1. Pediatric age pts with severe HBP or young to middle age females who may harbor fibromuscular dysplasia (FMD) 2. Older patients with abrupt onset of severe HBP, 3. Patients with well controlled HBP who suddenly go out of control requiring increased medication. 4. Any patient with flash pulmonary edema. 5. Patients with excessive (up to 20% increase may occur in NL patients especially those on diuretics) elevation of serum Cr with institution of ACE inhibitors or ARB’s. 6. Patients with severe HBP who rapidly lose renal function.

A renal artery duplex ultrasound with interrogation of the kidneys is a reasonable starting point in all of these scenarios. Interventional treatment with renal angioplasty/stent requires a lot of judgement and frank discussion with the patient about the likelihood of success. Current figures are that patients who undergo renal angioplasty or stent have a 30% chance of improvement, 30% chance of no change and a 30% chance of continued severe HBP or decline in renal function.

**Who to refer for evaluation?** Any patient with any of the clinical features 1-6 listed above.

**Atherosclerotic Mesenteric arterial stenosis; Chronic only**

In the elective setting chronic mesenteric ischemia is almost always manifested by the classic diagnostic triad; 1. Post prandial abdominal pain, 2. Food fear and 3. Weight loss, sometimes profound. Patients usually have a history of atherosclerosis in other peripheral arteries and on physical exam are found to have carotid or abdominal bruits along with pulse deficits in the lower extremities.

**Who to refer for evaluation?** As soon as chronic mesenteric ischemia is suspected, the patient should be referred to a vascular surgeon because left untreated this disease, over time, is uniformly lethal.

**Atherosclerotic Lower Extremity Arterial Occlusive Disease.**

**Limb threatening ischemia vs. Claudication.** The signs and symptoms of this disease fall into two categories. The first is limb threatening ischemia manifested by ischemic rest pain or ischemic tissue loss/gangrene. These patients all need referral to a vascular surgeon. Please note that ischemic rest pain is specific to location and method of relief of pain. This specificity is that the patient will go to bed at nite, fall asleep and shortly be awakened by burning pain or numbness in the forefoot. The patient will note that the symptoms are relieved by allowing the limb to hang over the side of the bed often with dependent rubor of the foot. Awakening increases cardiac output and placing the limb in a dependent position allows gravity to help increase distal perfusion to relieve the ischemic symptoms.

**The second category is patients who present with lower extremity claudication.** This is manifested by exertional lower extremity pain, weakness or tiredness in the large muscle groups such as the calf, thigh and buttock. The muscle level affected is related to the level of the atherosclerotic blockage. For aorto-iliac lesions there may be calf, thigh and buttock involvement. For superficial femoral and popliteal artery lesions the calf will be mainly involved. Occasionally the symptoms will involve the foot.

One hallmark is that the symptoms are extremely reproducible. The patient will relate that they can walk a set distance before the symptoms force them to rest and after a period of recovery the patient will be able to walk the same distance again and the symptoms will return. Walking distance will also vary when walking up a grade or carrying a heavy object. Both will decrease walking distance.
After obtaining this history the next step is the physical exam, specifically the aortic and lower extremity pulse exam. This begins with palpation of the abdominal aorta, both femoral, both popliteal and all four pedal pulses. Occasionally there will be an abdominal aneurysm palpable, but this is not the norm in patients with atherosclerosis. If one or both femoral pulses is diminished or absent, then the patient has atherosclerotic blockage in the aorta or iliac arteries. One should take the stethoscope and listen as there may be an audible bruit in the abdomen or groin. Likewise if the patient has a palpable femoral pulse and absent or reduced popliteal or pedal pulses, then the atherosclerotic occlusive disease is in the superficial femoral or popliteal arteries. Once again a stethoscope placed along the course of the superficial femoral artery may elicit finding a bruit.

One may also note hair loss, shiny skin and muscle atrophy in the lower extremities.

The next step is determining the Ankle Brachial Index or ABI. If the physical exam and ABI are not definitive in diagnosis of lower extremity APAD, then an exercise ABI is performed. This gives physiologic information about the status of the arterial circulation to the lower extremities with exercise and can effectively rule in or rule out claudication symptoms that are caused by lower extremity APAD.

As with all patients who have atherosclerosis maximal risk factor reduction and lifestyle modification is necessary. In addition, with claudicant patients, a supervised exercise walking program is first line therapy. Numerous studies show dramatic improvement in pain free walking distance and quality of life indicators with this therapy and it tends be more long lasting than catheter based or surgical interventions. In the long run these patients are best served with conservative measures reserving invasive interventions for those who are truly severely impaired by their claudication and who fail a walking program.

This is possible because claudication is a pure quality of life inhibitor. Revascularization does not save the patient’s life or preserve the limb. Risk of a claudicant patient losing a limb to amputation over 10 years is less than 5%. Maximal risk factor reduction and a supervised exercise walking program are therefore the mainstays of therapy.

Who to refer? 1. All patients with rest pain or tissue loss, institute maximal risk factor treatment first. 2. All patients with claudication who have failed maximal risk factor treatment and a walking program who are truly limited in their daily activities. Only then should discussion be held about invasive imaging and treatment of the arterial lesions. 3. All patients in whom the diagnosis of claudication is unclear from HPE and ABI.

Summary. APAD can be a systemic disease and may involve any of the major peripheral arteries. It can usually be diagnosed by history and physical exam and simple noninvasive tests. The mainstay of therapy is just like ACAD with maximal risk factor treatment and lifestyle changes. Invasive interventional imaging or treatment is not recommended or required in the vast majority of patients. Certainly not as first line therapy in patients who have not had their risk factors controlled.

RISK FACTOR REDUCTION FOR ALL PATIENTS WITH ATHEROSCLEROSIS

Treat dyslipidemia

Treat hypertension

Treat diabetes
Lifestyle changes

- Stop nicotine in all forms
- Follow a healthy diet.
  - One example is the American Heart Association diet which recommends limiting saturated fat (red meat, dairy products) to less than 7% of total intake and Trans fats to <1%, cholesterol <300mg/day and reducing sweets and sugar-sweetened beverages; eating at least two servings a week of fish and increasing your intake of vegetables, nuts, whole grains, and fruits. Other similar diets such as the Mediterranean diet is also recommended.
  - Restrict Sodium (salt) intake: < 2.5g/day for general population <1.5g/d for hypertensive patients.
- Exercise daily such as walking for thirty minutes
- Lose weight; target BMI 20-24

Recommendations for treatment of any patient with atherosclerosis. For all patients with peripheral atherosclerosis in any artery the current recommendation is for high intensity statin therapy regardless of lipid levels, control of DM (A1C<7) and blood pressure <140/90, smoking cessation therapy, regular daily exercise as simple as walking 30” per day and anti-platelet therapy such as 81mg daily ASA. In addition the recommendation is for a low carbohydrate, Mediterranean style diet which can be referenced on the internet. (Google “Mediterranean diet” and “Diabetic connect” for Mediterranean and low carb diet). The DASH diet is also used in patients who are hypertensive and is available on the internet. If the patient has lower extremity claudication a supervised exercise program is first line therapy prior to consideration of an interventional or surgical procedure.
Guideline-Recommended Prevention and Lifestyle Counseling Underused in PAD Patients

Fewer than half of patients with peripheral artery disease (PAD) in the United States (U.S.) receive guideline-recommended secondary prevention and lifestyle counseling to reduce the risk of cardiovascular events says new research published in the Journal of the American College of Cardiology. The study explores the trends in medical therapy and lifestyle counseling for U.S. patients with PAD between 2006 and 2013.

Using data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, Jeffrey S. Berger, MD, FACC, and Joseph A. Ladapo, MD, PhD, evaluated trends in the proportion of office visits with medication use and lifestyle counseling among patients with diagnosed PAD. Medication used was defined to include antplatelet therapy, statins, angiotensin-converting enzyme inhibitors (ACEI), angiotensin-receptor blockers (ARB), or cilostazol. Lifestyle counseling was defined as exercise or diet counseling and smoking cessation.

Overall results found that over the eight-year study period, the average number of ambulatory visits in the U.S. was 3,883,665; the mean age was 69.2 years. Comorbid coronary artery disease was present in 24.3 percent of visits. The authors note “the proportion of visits reporting use of medical therapy and lifestyle counseling was low and appears suboptimal in consideration of the substantial benefit of secondary cardiovascular prevention and lifestyle counseling.”

Any antiplatelet therapy was used in only 35.7 percent of visits, followed by statin use in 33.1 percent, ACEI or ARB in 28.4 percent and cilostazol in 4.7 percent. Exercise or diet counseling was used in only 22 percent of visits, while smoking cessation counseling or medication use occurred in 35.3 percent of visits for current smokers. Patients with comorbid coronary artery disease were more likely to be prescribed antiplatelet therapy odds ratio [OR], 2.6; 95 percent confidence interval [CI], 1.8-3.9), statins (OR, 2.6; 95 percent CI, 1.8-3.9), ACEI/ARB (OR, 2.6; 95 percent CI, 1.8-3.9) and smoking cessation counseling (OR, 4.4; 95 percent CI, 2.0-9.6).

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The results were much lower than expected, highlighting an opportunity to improve the quality of care in these high-risk patients, conclude Berger and Ladapo. They suggest that investments in new health care system strategies are required to ensure adequate resource use in PAD patients. “Although much attention is focused on novel therapies in PAD, a refocus on established therapies and healthy behaviors is clearly needed,” they write. “Attempts to increase patient and physician awareness of the benefits of lifestyle recommendations and secondary prevention may be necessary. In addition, systems of chronic disease management in which the use of nurses, other health care providers or information systems complements the role of physicians also may be helpful. Finally, efforts to monitor the prevention practices taking care of PAD patients may provide new incentives for quality care.”

In an ACC.org Journal Scan, Geoffrey D. Barnes, MD, MSc, FACC, writes the low rates of medication use and lifestyle modification recommendations found in the study are a call to action for all clinicians who care for patients with PAD. “We must do better to help prevent significant morbidity and mortality for the estimated 200 million patients with PAD globally,” he says.