Peripheral arterial disease: causes, symptoms and treatments

Peripheral artery disease is an under-diagnosed, chronic and progressive disease caused by narrowing of the arteries outside of the heart and brain. Previously called peripheral vascular disease (PVD), PAD is now recommended to describe atherosclerotic disease affecting the lower or upper extremity arteries (Creager, et al., 2008). Symptoms of PAD are often variable or not present; therefore, diagnosis is often missed. Risk factors are the same as coronary artery disease (CAD), with tobacco use and diabetes mellitus (DM) having the most significant impact. Primarily the result of atherosclerosis, PAD manifests with chronic, insufficient tissue perfusion and ischemia, potentially complicated by a thrombotic or embolic event. The ACC/AHA classifies the disease in 4 categories: asymptomatic, claudication, critical limb ischemia (CLI), and acute limb ischemia (ALI) (Hirsch, 2006). Current guidelines suggest the use of resting ankle-brachial index (ABI) for diagnostic confirmation of patients with suspected or known lower extremity PAD, defined by an ABI < 0. 90 (Center for Disease Control: Peripheral Arterial Disease Fact Sheet, 2010). Screening patients for PAD is reserved for those with exertional leg symptoms, a non-healing leg ulcer, patients greater than age 65, greater than age 50 with a history of smoking or DM, or less than 50 with DM and another risk factor (Hirsch, 2006). Routine screening for asymptomatic PAD, however is not recommended. Early diagnosis of PAD can help prevent progression and complications both peripherally and systemically. Without general population screening, the early diagnosis of asymptomatic PAD depends on the ability of the health care provider to evaluate risk, take a detailed history, and pick up on subtle physical exam findings. If diagnosed in early stages, lifestyle and risk factor modification,

medications, and vascular procedures can be utilized to decrease morbidity and mortality.

2. Epidemiology

PAD currently affects nearly 12% (8 million) of Americans, beginning at the age of 40. The prevalence increases with age: 1-2% in 40-49 year olds, 3-5% in 50-59 year olds, 5-6% in 60-69 year olds, 9-11% in 70-79 year olds, and 21-26% in > 80 year olds (CDC, 2010). As people with chronic illness are living longer, the prevalence of PAD will likely increase in the future. Men are affected more than women in the younger population, but the incidence is nearly equal in the older population. There is also a 2. 4-fold prevalence increase in African Americans compared to the non-Hispanic white population (Criqui et al., 2005). The prevalence for PAD in the US is similar to that of other developed countries (Paraskevas, 2011). In the presence of CAD or cerebrovascular disease (CVD), there is a 50 to 75% chance that PAD is also present, as atherosclerosis is a systemic disorder. Oftentimes, in the presence of both PAD and CVD, one disease might remain silent because the other limits exercise by claudication or angina.

3. Pathogenesis

The most common cause of PAD is atherosclerosis. Atherosclerosis is an inflammatory disease that is a result of a chain of step-like insults to the arteries. The disease process is initiated by endothelial injury and dysfunction, leading to a fatty streak, causing a fibrotic plaque, and potentially ending with a complicated lesion.

The initial injury to the endothelial cells, the inner lining of the artery wall, can be caused by many of the risk factors seen in PAD: smoking, hypertension, diabetes, hyperhomocystinemia, dyslipidemia, and increased C-reactive protein levels. Additionally, autoimmune phenomena, vessel shear, and increases in fibrinogen levels can cause endothelial damage. An inflammatory mediated cascade is initiated at the site of injury, resulting in an accumulation of macrophages. After adherence to the vessel wall, the macrophages release free radicals and then begin to migrate through the endothelial surface into media of the vessel. Lipid localization and accumulation also occurs at the site of endothelial injury, leading to free radical oxidation of low-density lipoproteins (LDL). Hypertension, smoking and diabetes also increase oxidation of LDL. Oxidized LDL initiates smooth muscle proliferation as well as abnormal vasoconstriction. Macrophages then engulf the oxidized LDL and penetrate the intima of the vessel, creating what is known as a foam cell. The accumulation of many foam cells in the intimal layer of the artery creates a fatty streak, the earliest visible lesion of atherosclerosis. Over time, smooth muscle cells proliferate, produce collagen, migrate over the fatty streak, and evolve into a fibrous plaque, the hallmark of established atherosclerosis. Ultimately the lesion may evolve to contain large amounts of lipid; if it becomes unstable, denudation of overlying endothelium or plaque rupture then initiates the coagulation cascade and can result in thrombotic occlusion of platelets and fibrin in the overlying artery.

The lesions of atherosclerosis are often segmental and localized to large and medium-sized vessels. They are typically seen at arterial branch points,

which are sites of increased turbulence, altered shear stress, and intimal injury. Typically located in multiple sites, stenosis and occlusion are most often seen in the abdominal aorta and iliac arteries (30% of symptomatic patients), the femoral and popliteal arteries (80-90% of patients), and the tibial and peroneal arteries (40-50% of patients) (Bartholomew & Olin, 2006).

4. Classification

PAD has three primary systems of classification. The Fontaine Classification and the Rutherford Classification are used to grade the severity of clinical symptoms in patients (see table 1). Even with a similar extent and level of disease progression, presence of and severity of symptoms may vary from one person to another. Both the Rutherford and the Fontaine Classifications are used more routinely in research settings and are utilized less in clinical practice. However, as the'2005 ACC/AHA guidelines point out, a way of standardized communication between clinicians is important, and it is suggested to describe a patient's status as 1) Asymptomatic, 2) Claudication, 3) Critical Limb Ischemia, or 4) Acute Limb Ischemia.

Asymptomatic

Asymptomatic PAD is simply described by the absence of claudication symptoms of the legs.

Claudication

The term claudication is derived from the Latin verb 'claudicare', meaning to limp (Norgren et al., 2007). Claudication is one of the most common

manifestations of PAD and is defined by reproducible, ischemic muscle pain. Claudication occurs during physical activity secondary to inadequate blood flow and is relieved after a short rest. In order to be classified as claudication, the pain must be exertional, reproducible, and relieved within 10 minutes of rest (Creager et al., 2012). Atypical leg pain also falls amongst this class in the absence of symptoms of CLI.

Critical limb ischemia

CLI describes patients with chronic, ischemic rest pain, ulcers or gangrene, which can be attributed to arterial occlusive disease (Norgren et al., 2007). CLI implies chronicity, distinguishing it from acute limb ischemia.

Acute limb ischemia

ALI is defined by a sudden decrease in limb perfusion, which poses a potential threat to limb viability. Presentation is typically up to 2 weeks following the acute event. (Norgren et al., 2007).

5. Risk factors

Most risk factors for PAD are the same as those of CVD: older age, hypertension, diabetes, dyslipidemia, tobacco use, a family history of atherosclerosis, obesity, sedentary lifestyle, and high homocysteine or C-reactive protein levels. Of the risk factors, diabetes and smoking should be of high focus to the clinician, as they are the strongest modifiable risk factors.

Smoking

Smoking has been shown to enhance endothelial dysfunction and alter both lipid metabolism and anticoagulation (Lu & Creager, 2004). An interesting case-control study (Cole et al., 1993) estimated that 76% of PAD is attributable to smoking, with a 7-fold increase in previous smokers and 16-fold increase in current smokers. Smoking cessation is associated with a rapid decline in the incidence of claudication, which equates to that in non-smokers after 1 year of stopping (Tendera, 2011).

Diabetes mellitus

The other strongest risk factor for PAD is diabetes, with a proportionate correlation of incidence and prevalence with the duration the patient has been diabetic. There is a 2-4 fold increased risk for PAD with diabetes and approximately 30% of PAD patients in primary care suffer from diabetes. A 1% increase in HgA1C Is associated with 28% increase in the risk of PA (Paraskevas, 2011). Because of the decreased sensation associated with poor circulation around the feet in diabetes, claudication might be a lacking symptom and initial presentation of PAD might be with ulceration, infection, or gangrene.

Hypertension

Hypertension is a risk factor for PAD, although, to a weaker extent than diabetes and smoking. The Framingham Heart Study showed an increased risk of IC by 2. 5 fold for men and fourfold for women with hypertension, with a proportional risk with the severity of hypertension (Murabito et al., 1997).

Dyslipidemia

Dyslipidemia is a risk factor for PAD, highly related to its contribution to atherosclerosis. The ratio of total cholesterol to HDL was found to be the best predictor of PAD in the Framingham study. The Study also found that cholesterol levels over 270 had a twofold increase of frequency of IC (Murabito et al., 1997). Additionally, focus should be of total cholesterol, LDL, triglycerides, and lipoprotein (a) in PAD patients.

Inflammatory risk markers

Elevated levels of C-reactive protein (CRP), were found to have a 2. 5 fold increase in PAD development in the Physicians Health Study (Hirsch et al., 2006). CRP, an inflammation risk marker, has become a valuable measurement of risk in healthy individuals (Suominen, 2008). Currently, other inflammatory 'biomarkers' are being studied for their ability to increase recognition for disease and thereby improve care (Cooke & Wilson, 2010). A recent prospective cohort study of 1, 000 ambulatory elderly Japanese subjects for 8 years revealed that B2M, cystatin-C, and CRP were all independent mortality predictors, the most informative being B2M (ShinkaI, 2008).

Hyperviscosity and hypercoagulable states

Elevated fibrinogen levels, a known risk factor for thrombosis, can cause an alteration in microcirculation, and in turn, worsen claudication symptoms of PAD. Hyperviscosity and hypercoagulability are considered to be risk factors for and indicate poor prognosis of PAD (Norgren, 2007).

Hyperhomocysteinemia

Evidence shows a direct correlation of high homocysteine levels and atherosclerosis, leading many to believe that elevated levels directly increase the risk for developing PAD. Approximately 30 to 40% of patients with PAD have high levels of homocysteine (Hirsch et al., 2006). There has been recent speculation, however, on whether elevated homocysteine levels actually relate to primary cause or possibly are just a major mediator of PAD, as a marker of endothelial or systemic oxidative stress (Hoffman, 2011).

6. Clinical Manifestations

A complete cardiovascular and peripheral vascular history is indicated if any risk factors or potential symptoms of PAD are present, including atypical symptoms that may limit walking ability. Family history of PAD, CVD, CAD, CKD and aneurisms should be included. Clinical manifestations differ in relation to their classification.

Asymptomatic

PAD can be very difficult to diagnose clinically since approximately half of all patients are asymptomatic (Hirsch, 2006). If asymptomatic, the patient will have no symptoms of claudication, no symptoms of ischemic pain, and no limitation in walking distance. Past medical history, tobacco use, family history, and physical exam findings are key for further workup and diagnosis in these patients. Other vascular symptoms that, if positive, could indicate the need for further PAD workup are: erectile dysfunction, post-prandial abdominal pain with associated anorexia or weight loss, upper extremity exertional pain, symptoms suggestive of angina, or transient or permanent neurological symptoms.

Intermittent claudication

Intermittent claudication is considered the hallmark symptom of PAD. Patients may describe leg pain that is aching, numbing, heavy in nature, fatiguing or cramping. It typically affects the muscles of the calves and feet, below the origin of arterial compromise. It can also occur in the buttock or thigh, indicating arterial compromise in the femoral artery. Although intermittent claudication is the classic symptom of PAD, it is actually only present in 10% of patients with the disease (Domino, 2012). Patients with co-morbidities that prevent sufficient activity to produce limb symptoms (i. e. congestive heart failure, severe pulmonary disease, musculoskeletal disease, deconditioned) make it difficult to assess for claudication.

Atypical leg pain is a much more common manifestation of PAD, affecting 40-50% of patients (Domino, 2012). Often, atypical pain is a result of comorbidities, physical inactivity, or alterations in pain perception. It might present similarly to IC, but not be severe enough to stop walking and rest. Alternatively, it might not resolve after 10 minutes of rest or might be present both with exertion and rest (Mohler, 2010). Hirsch explained atypical leg pain as any discomfort in the legs or heels that is present at rest or during exercise and may not be confined to the muscle. He also notes the higher prevalence, like in CVD, of atypical PAD symptoms in women (2012). '

The Edinburgh Claudication Questionnaire (see table 2) is an additional tool that has been shown to be 91% specific and 99% sensitive for diagnosing intermittent claudication in symptomatic patients. It is composed of a series

of six questions and a pain diagram that can be self-administered by the patient (Sontheimer, 2006).

Critical limb ischemia

CLI, characterized by persistent rest-pain and tissue loss, affects 1-2% of patients with PAD (Hirsch et al., 2005). Rest pain related to critical limb ischemia is typically severe in nature and might only be relieved by opiates. It often is worse when the leg is supine and might improve by having the leg dependent. It often manifests as nocturnal burning pain, located on the arch of the foot. Inquiry of sleeping position might aid in diagnosis, as many patients will sleep in a chair or with their leg hanging over the bed to prevent, lessen or alleviate pain.

Non-healing or slowly healing wounds below the level of the knee are also associated with critical limb ischemia. The patient might report a purple or black color change in the toes or foot, which can be a sign of gangrene or necrosis. Oftentimes, this will be seen on the digits or the heel, especially if the patient is bedridden. Local trauma, poor fitting shoes, or local heat can also cause ulceration (Norgren et al., 2007).

Acute limb ischemia

Acute limb ischemia is a medical emergency. The patient will likely present with sudden onset of severe leg pain, possibly accompanied by extremity weakness, numbness, coolness, and pallor. Severe cases may cause loss of motor function (Hallett, 2008). History taking should include the symptoms and severity of the current presentation (present illness) as well as

background information pertaining to etiology, differential diagnosis and concurrent disease (Norgren et al., 2007).

7. Physical Exam

The physical exam for suspected or known PAD includes a focused cardiovascular and complete peripheral vascular system exam. The ACC/AHA guidelines suggest the following physical exam elements be completed in all patients with suspected or known PAD:

Palpate the carotid pulses and note carotid upstroke and amplitude. Auscultate the carotids, abdomen and flank for bruits. Palpate the abdomen and note the presence of the aortic pulsation and its maximal diameter. Palpate the pulses at the brachial, radial, ulnar, femoral, popliteal, dorsalis pedis, and posterior tibial sites. Perform Allen's test when knowledge of hand perfusion is needed. Auscultate both femoral arteries for the presence of bruits. Pulse intensity should be assessed and should be recorded numerically as follows: 0, absent; 1, diminished; 2, normal; and 3, bounding. The shoes and socks should always be removed and the feet inspected for color, temperature, and integrity of the skin and intertriginous areas' (2006).

It is also important to measure the blood pressure in both arms because upper extremity PAD, specifically subclavian steal, can present with differences of 15 mm Hg or more systolically between arms (Mohler, 2007). There is a 96% specificity of PAD and 93% for CVD when seen (Clark et al., 2012).

Some findings suggestive of severe PAD, including distal hair loss, trophic skin changes, and hypertrophic nails, should be sought and recorded. The

most reliable physical findings for PAD include absent or diminished pedal pulses, the presence of a femoral artery bruit, skin color abnormalities, and coolness of the skin (Hirsch, et al., 2006).

ALI

Patients with ALI may initially present with a combination of five symptoms, known as the ''5 Ps'': pain, pulselessness, pallor, paresthesia, or paralysis. Additional findings indicating advanced ALI are muscle rigor, tenderness, or findings of pain with passive movement (Norgren, 2007).

Laboratory evaluation

The aim of the laboratory assessment in patients with asymptomatic or symptomatic disease is to detect major risk factors of CVD. There are no current guidelines for routine or diagnostic lab work in these patients. CBC with platelet count, Hg A1C, CRP, fibrinogen, fasting lipid profile, serum creatinine, and urinalysis for glucosuria and proteinuria might all be helpful when considering risk factors or coexisting diagnosis (Sontheimer, 2006).

In patients with ALI, electrocardiogram, standard chemistry, CBC, prothrombin time, partial thromboplastin time and creatinine phosphokinase level should be obtained. If hypercoagulable state is suspected, additional studies seeking anticardiolipin antibodies, elevated homocysteine concentration and antibody to platelet factor IV should be ordered (Norgren, 2007).

8. Differential diagnosis

PAD has a diversity of causes beyond atherosclerosis, including thromboembolic, infiammatory, or aneurysmal disease; by trauma, adventitial cysts, or entrapment syndromes; or by congenital abnormalities. Establishment of an accurate diagnosis is necessary if individual patients are to receive ideal pharmacological, endovascular, surgical, or rehabilitative interventions (Hersch, 2006). See Table 3 for common differential diagnoses for IC.

Differential diagnosis for ALI has three primary entities. The first, CHF, in the presence PAD, can present similarly when severe low output states lead to lack of pulse and to classic findings of pain, pallor, paresthesia, and paralysis. Although a similar presentation to ALI, angiography will not show an occlusion. Second, deep vein thrombosis can present as a large, swollen, and painful leg. The leg might appear blue due to venous infarction, but without paleness. Pulses may be absent secondary to thrombotic occlusion. Lastly, acute spinal cord compression can imitate CLI, with pain, paresthesia, and paralysis; however, normal skin color and pulses will be present (Sontheimer, 2006).

9. Diagnostic evaluations

Noninvasive Testing

Noninvasive testing can help detect early PAD and, with appropriate intervention, help prevent progression to critical leg ischemia and amputation. In addition, it predicts future ischemic cardiac and cerebral

events and thus can be used to detect persons who would benefit from medical therapy.

Ultrasound

Ankle brachial-index

A standard part of the initial PAD evaluation is the measurement of arterial pressures, by means of the ABI. Patients who have a pertinent history or physical examination suggestive of PAD should proceed to objective testing including an ABI. The test is done with the use of a sphygmomanometer cuff placed just above the ankle and a doppler to measure the systolic pressure of the posterior tibial or dorsalis pedis arteries. The systolic blood pressure is then placed in a ratio equation comparing the systolic pressure of the arm on the same side. Current guidelines recommend using the ABI to establish the diagnosis of PAD in patients with suspected disease, defined as individuals with one or more of the following: exertional leg symptoms, nonhealing wounds, age 65 years and older, or 50 years and older with a history of diabetes or smoking, or less than 50 with DM and another risk factor (Rooke, et al., 2011). The normal range of ABI is 1. 00 to 1. 40 and ABI values of 0. 91 to 0. 99 are considered borderline. ABI from 0. 71 to 0. 9 indicates mild PAD and 0. 41 to 0. 7 indicates moderate disease. An ABI of less than 0. 4 is indicative of severe ischemia. If ABI is found greater than 1. 4, calcified vessels should be suspected and additional diagnostic studies are warranted (Domino, 2012). ABIs with readings this high are commonly seen in patients with diabetes, renal insufficiency, or other diseases causing vascular calcification.

In patients with pertinent claudication but normal ABI results, additional exercise testing with ABI measurements can be ordered. The procedure requires an initial measurement of the ABI at rest. The patient might be asked to walk (typically on a treadmill at 3. 2 km/h (2 mph, 10%'12% grade) until their claudication pain is reproduced (a maximum of 5 minutes), after which the ABI is again measured. A decrease in ABI of 15%'20% would be diagnostic of PAD. Walking exercises in the hallway or in a stairwell can be used as an alternative to a treadmill if unavailable (Norgren, 2007).

The ABI is a noninvasive, inexpensive, office-based test that can reliably be performed by most trained healthcare personnel. The ABI is an accurate and diagnostic measure for PAD, with a sensitivity of 95% and specificity of 100% in detecting PAD with an ABI less than 0. 9. This ABI risk prediction for PAD has recently been demonstrated to be independently valuable and its use would add incrementally to the Framingham risk score .(Fowkes,'2008). The test can confirm the diagnosis of PAD, even in patients who are asymptomatic, and is useful in the differential diagnoses of leg symptoms to identify vascular etiology (Hirsch et al., 2006). However, ABI is intended for office-based and vascular laboratory diagnostic use and is not intended to serve as a population screening tool. The use of ABI measurement should be used as diagnostic workup of suspected disease or in the presence of known risk factors, not for general screening of asymptomatic patients. This recommendation was based on the fact that the treatment of asymptomatic PAD, beyond standard cardiovascular assessment and treatment, does not improve major health outcomes (Screening for Vascular Disease, 2009).

Toe Brachial Index (TBI)

Similar to the ABI, the TBI is a quick and cost effective way to establish the diagnosis of PAD. With the use of smaller cuffs and careful technique to preserve accuracy, measurement of digital perfusion can be established when small-vessel arterial occlusive disease is present. For patients with non-compressible posterior tibial or dorsalis pedis arteries, the TBI is a useful alternative to the ABI (Norgren, 2007).

Segmental leg pressures

The extent and location of PAD can be further defined with the measurement of segmental leg pressures (SLP). Obtained the same way as the ABI, segmental leg pressures differ in that they are done at the level of the thigh and calf. Similar limitations with non-compressible pedal arteries can potentially altar accuracy and alternative testing should be done.

Pulse volume recordings

Also useful for establishing PAD diagnosis, pulse-volume recordings (PVR) measure arterial perfusion, even in patients with non-compressible vessels. PVR is also useful to monitor limb perfusion after revascularization procedures. Limitations include a decrease in accuracy in more distal segments, abnormal readings in patients with low cardiac stroke volume, and providing only qualitative, not quantitative, measurement of perfusion. Both SLP and PVR provide more of an objective assessment of the location and presence of PAD'both alone are 85% accurate in detecting significant stenosis compared to angiography, but when used together, a 97% diagnostic accuracy has been reported (Norgren et al., 2007).

Doppler velocity waveform analysis

Arterial velocity waveform analysis is a useful study that uses a continuous-wave doppler at multiple sites in the peripheral circulation. This test visualizes the arteries with sound waves and measures the blood flow in an artery to indicate the presence of a blockage.' Healthy peripheral vessels will have a triphasic pattern and progress to a biphasic and, ultimately, monophasic appearance in patients with significant PAD. When assessed over the posterior tibial artery, a reduced or absent forward flow velocity was highly accurate for detecting PAD. Measurements are useful to provide an accurate assessment of lower extremity PAD location and severity, to follow lower extremity PAD progression, and to provide quantitative follow-up after revascularization procedures. While the test is operator-dependent, it provides another diagnostic method in patients with noncompressible tibial arteries (Norgren et al., 2007).

Duplex ultrasound (DUS)

Arterial duplex ultrasonographic examination is also used to diagnose PAD, but is primarily used to investigate anatomic location and degree of stenosis in pre-diagnosed PAD. It can delineate between stenotic and occlusive lesions above the level of the knee, which makes it useful in assessing the need of endovascular or surgical intervention as well as selecting potential sites of anastomosis. Current guidelines recommend its use for routine surveillance after femoral-popliteal or femoral-tibial bypass (Rooke et al., 2011). Duplex ultrasonography combines the waveform analysis and velocities of doppler imaging. The sensitivity and specificity of the diagnosis

of stenosis greater than 50% of the vessel diameter from the iliac to the popliteal arteries are each approximately 90-95% (Rybicki, 2009).

Imaging

Imaging is indicated for patients in whom the decision has been made to proceed with revascularization when a suitable lesion is demonstrated.

Magnetic resonance angiography (MRA)

Although not the gold standard for PAD imaging, MRA has become the first line of pre-surgical imaging in many centers across the country. The sensitivity and specificity for detection of stenosis when greater than 50% in diameter is 90% to 100%. It is more accurate in detecting significant stenosis for pre-operative planning than DUS. The major limitation of using MRA is the risk of nephrogenic systemic fibrosis (NSF), related to its use of gadolinium, and alternative study is indicated in patients with abnormal renal function (Rybicki, 2009). MRAs are contraindicated in patients that have any form of metal inside their body: pacemakers, defibrillators, intracranial metallic stents, clips, coils, or other devices.

Computed tomographic angiography (CTA)

CTA of the extremities may be considered to diagnose the presence of and anatomical location ofsignificant stenosis in patients with PAD and is used primarily as a substitute for MRA in the presence of contraindications. Although the risk is less than of gadolinium, contrast materials must be used, and precautions should still be considered in patients with abnormal kidney function. Like MRA, sensitivity and specificity for detection of stenosis

greater than 50% in diameter is 90% to 100%. Its major limitation is visualization in the presence of significant calcified atheromatous disease, and testing should be avoided in these patients (Rybicki, 2009).

Invasive diagnostic testing

Contrast angiography

Contrast angiography is the gold standard and definitive method of anatomical evaluation under some circumstances (i. e. acute limb ischemia), because it offers the benefit simultaneous intervention, if needed. This test is invasive and it carries risk of bleeding, infection, embolism, contrast allergy, and contrast nephropathy. This method provides the most detailed information about the arterial anatomy and is recommended for evaluation of patients when revascularization is contemplated, to help develop an individualized diagnostic plan, select access sites, identify significant lesions, and to ensure the need for invasive evaluation. Noninvasive imaging modalities, such as MRA, CTA, and color flow duplex imaging, may be used in advance of invasive therapy. Follow-up evaluation is necessary 2 weeks after contrast angiography to evaluate renal function, presence of insertion site injury, and to detect any possible delayed adverse effects, such as atheroembolism. (Rybicki, 2009).

10. Medical management

The medical management goals of claudication are: risk factor modification, a supervised exercise program, the use of antiplatelet drugs, and possibly, medication for symptom improvement.

Risk factor modification

Smoking cessation

Since smoking is one of the two most jeopardizing, modifiable risk factors of PAD, it is imperative to address this issue with patients. In 2011, the ACC/AHA updated the guideline, advising practitioners to ask patients who are current or former smokers about the current status of their tobacco use at every visit. Patients with current use should be assisted with counseling and developing a quit plan that may include pharmacotherapy and/or referral to a smoking cessation program. Individuals with preexisting PAD who use tobacco should be advised by each of their clinicians to stop as well as being offered behavioral and pharmacological treatment. In the absence of contraindication or other compelling clinical indication, one or more of the following pharmacological therapies should be offered: varenicline, bupropion, and nicotine replacement therapy (Rooke et al., 2011).

Glycemic control

It is well known that better glycemic control can help prevent microvascular complications such as retinopathy and neuropathy. Unfortunately, no studies have correlated the effects of glycemic control in patients with PAD. Current PAD guidelines coincide with that of the current American Diabetes Association guidelines, which recommend a HbA1c <7. 0%. Metformin is an effective first-line pharmacotherapy and can be useful if not contraindicated (Rooke, et al., 2011).

Dyslipidemia control

Current cholesterol goals for PAD are based on the ATP III guidelines: 1) LDL-C goal of <100 mg/dL, 2) LDL-C goal of <70 mg/dL is reasonable for very high risk patients, and 3) if triglycerides are fi200 mg/dL, non'HDL-C''should be <130 mg/dL, whereas non'HDL-C <100 mg/dL for very high risk patients is reasonable (Smith, et al., 2011). In the presence of PAD, the first line of therapy for reducing a patient's cholesterol is not only therapeutic lifestyle changes (dietary modification and incre