INTRODUCTION

Peripheral arterial disease (PAD) affects approximately 20% of adults older than 55-years of age and is a powerful predictor of myocardial infarction, stroke, and death due to systemic vascular disease.\(^1\) PAD is a manifestation of atherosclerotic disease, with recent attention focused on its presence in the lower extremity. PAD is grossly underestimated in the population, and its prevalence is increasing as life expectancy increases.\(^5\) With the increased prevalence, it is imperative that the podiatric physician be able to identify patients with early signs of PAD. The aim of this paper is to identify the prevalence, clinical impact, associated symptoms, effects on the quality of life, and emerging therapeutic modalities for the effective identification and treatment of peripheral arterial disease.

PAD is an abnormal condition that leads to the progressive stenosis, occlusion, or aneurysmal dilation of the aorta and non-coronary branches.\(^1\) Peripheral arterial occlusive disease is analogous to PAD, but excludes vasoreactive or aneurysmal disorders. The end stage of PAD is known as critical limb ischemia (CLI). CLI is sustained, severe decrease of leg blood flow, which if untreated, would lead to rest pain, ulceration and eventual limb loss.\(^1\) A term typically misused to describe PAD is peripheral vascular disease (PVD). This historic term includes noncardiac disease that affects the circulatory system and encompasses pathology of arterial, venous, and lymphatic circulation.

RISK FACTORS

The risk factors implicated in PAD are preventable with the exception of age and genetics. Preventable factors associated with atherosclerosis are smoking, diabetes, obesity, dyslipidemia, hyperhomocysteinemia, hypertension, and hypercoagulability.\(^2\)\(^4\) Smoking is the number one preventable factor that leads to atherosclerosis, and is directly correlated with intermittent claudication and the amount of cigarettes smoked.\(^7\) There is a 40-50% five-year mortality rate in patients that smoke and have intermittent claudication.\(^2\)\(^4\) Diabetics have a 200-400% increased chance of developing atherosclerosis and tend to develop PAD a decade earlier than nondiabetics. Twenty-five percent of all leg revascularizations are in diabetic patients, and lower extremity amputation is seven-fold higher in diabetics with PAD than in nondiabetics with PAD.\(^5\)\(^4\) Perhaps the deadliest combination of all risk factors is the diabetic patient who smokes.

PATHOGENESIS

Initially, the disease is characterized by fatty deposits within the tunica intima of medium and large arteries. Stenosis of the arterial wall occurs secondary to stable or unstable plaque accumulation. Stable plaque accumulation, as the name implies, is likely to remain in the area of origin, fixed to the respective tunica. The plaque may then calcify, leading to stenosis of the iliac, femoral, and/or popliteal arteries. This is the pathogenesis of intermittent claudication. The stenosed artery prevents adequate perfusion to sustain the demand of the active muscle, thus leading to clinical symptoms. These symptoms generally take place one level below the stenosed artery. Gluteal pain, hip pain, thigh pain, and impotence are secondary to stenosis of the abdominal aorta or iliac arteries. Thigh and calf symptoms indicate stenosis at the femoral artery or its branches. A stenosed popliteal artery leads to pain in the calf, ankle, or the foot.\(^3\) The occlusion that occurs is broken down into stages according to Fontaine. Stage I is no
symptoms, Stage II is intermittent claudication, Stage III is rest pain, and Stage IV is gangrene. Table 1 shows each stage with recommended treatment options.

Unstable plaque, though, has the potential to embolize and may cause acute ischemic events. Acute lower limb ischemia following aortic surgery is commonly termed trash foot (Figures 1, 2). The triad of thigh and foot pain, livedo reticularis, and intact peripheral pulses is considered to be pathognomonic for cholesterol embolization. This condition predominantly affects the elderly (mean 66 years). It may also affect patients with a history of hypertension (61%), atherosclerotic cardiovascular disease (44%), renal failure (34%), and aortic aneurysm (25%). Unstable plaques may embolize spontaneously from prosthetic grafts, after manipulation of the aorta by cardiac catheterization, or by simply dislodging of atherosclerotic debris from proximal arteries. The most common area of embolus to the lower extremities is from the infrarenal arteries. Sharma performed a retrospective study of 1,011 patients undergoing infrarenal aortic and infrainguinal vascular surgery from 1986-1993. They identified 29 patients (2.9%) with evidence of atheroembolism with one-third (44.8%) of the emboli caused by iatrogenic manipulation of the vascular tree and the remaining patients with spontaneous emboli. The sources of emboli were in the abdominal aorta, iliac and femoropopliteal arteries. Trash foot occurred in 19 patients (7 bilateral) and occlusions of tibioperoneal/digital arteries were seen in 7. Multiple treatment regimens have been generally unsuccessful in altering the course of the disease process.

Table 1

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Evidence of PAD</td>
<td>Intermittent Claudication</td>
<td>Rest Pain</td>
<td>Gangrene</td>
</tr>
<tr>
<td>- No further treatment required</td>
<td>- Order NIVS,</td>
<td>- Order NIVS,</td>
<td>- Consult Vascular</td>
</tr>
<tr>
<td></td>
<td>- Consult Vascular team</td>
<td>- Consult Vascular team</td>
<td>- Surgical</td>
</tr>
<tr>
<td></td>
<td>- Start- Pharmacotherapy</td>
<td>- Surgical Intervention</td>
<td>- Revascularization</td>
</tr>
<tr>
<td></td>
<td>pharmacotherapy intervention</td>
<td></td>
<td>- Amputation</td>
</tr>
</tbody>
</table>

Figure 1. Typical trash foot appearance.

Figure 2. Trash foot appearance.
The most significant impact on the disease can be made by its prevention. Prevention and treatment includes heparin, embolectomy, lumbar sympathectomy, aspirin, and prostaglandins. The high morbidity and mortality of atheroemboli demand prompt recognition and treatment, as well as attempts at prevention to achieve good results.

**PATIENT EVALUATION**

Evaluation must begin with a detailed history touching on all aforementioned risk factors. A comprehensive vascular review of systems is necessary if patients are at risk for PAD. Table 2 provides the physician with a framework of pertinent questions to help assess the level of suspected PAD. Documentation of the onset of symptoms, correlation with distance walked before pain, and the rest time required for the resolution of symptoms should be recorded at each visit to evaluate the progression or regression of the disease.

Physical examination for suspected PAD starts with dermatologic exam. The color, temperature, turgor, and texture of the skin are evaluated for atrophic changes. Dependency rubor test is performed when evaluating an atrophic foot with erythema. The limb is elevated above the level of the heart and the erythema is monitored. If the foot becomes pale, this is a positive test indicating severe ischemia. From a vascular standpoint, dorsalis pedis, posterior tibial, popliteal and femoral pulses must always be assessed and can be graded as nonpalpable, weakly palpable, palpable, and bounding. When pulses are nonpalpable, utilization of a 5-7 megahertz hand held Doppler to determine signal intensity and quality is important. The signal intensity and quality are described as monophasic, biphasic, or triphasic. Pedal deformities must also be assessed especially in areas with bony prominences, which may lead to ulceration. When PAD is suspected, the next step is to obtain non-invasive vascular studies (Table 3).

**Non-Invasive Vascular Studies**

Non-invasive vascular studies (NIVS) are excellent diagnostic tools to evaluate PAD. NIVS will give insight into areas of occlusion and type of treatments that are needed. Table 4 provides a list of normal and abnormal values of different NIVS.

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**Table 2**

**QUESTIONS TO ASK IF PAD IS SUSPECTED**

- What kind of leg discomfort do you experience? Fatigue, aching, numbness, or pain?
- Does this discomfort occur in one or both legs?
- Where is the primary site(s) of discomfort (gluteal, thigh, calf, or foot)?
- When you walk, is the discomfort in the muscles or joints? Which discomfort limits your walking?
- How long have you had this discomfort?
- How long does it take for the discomfort to resolve once you stop walking?
- Do you have to sit, stand, or bend over, to get relief from symptoms?
- Can the symptoms be reproduced reliably by walking for the same amount of time or distance?
- Do you develop pain in the foot when you lay down flat? Are these symptoms relieved if you place your leg below your heart?

**Table 3**

**PHYSICAL FINDINGS THAT WARRANT NIVS**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Abnormal Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin quality</td>
<td>Warm to Cool</td>
</tr>
<tr>
<td>Pulse</td>
<td>Weakly or Non-Palpable</td>
</tr>
<tr>
<td>Toenails</td>
<td>Dystrophic</td>
</tr>
<tr>
<td>Intrinsic Muscle</td>
<td>Atrophy</td>
</tr>
<tr>
<td>Hair Growth</td>
<td>Absent</td>
</tr>
<tr>
<td>Doppler</td>
<td>Mono- or Biphasic</td>
</tr>
<tr>
<td>Leg Dependency</td>
<td>Rubor to Palor</td>
</tr>
</tbody>
</table>
Table 4

**TYPICAL NIVS - NORMAL AND ABNORMAL VALUES**

<table>
<thead>
<tr>
<th>NIVS</th>
<th>Normal</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABI&lt;sup&gt;18&lt;/sup&gt;</td>
<td>1.0-1.10</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>PVR&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Steep Upstroke, Sharp Peak Dicrotic Notch</td>
<td>Extended Upstroke, Loss of Dicrotic Notch, Extended Downstroke</td>
</tr>
<tr>
<td>Segmental Pressures&lt;sup&gt;20&lt;/sup&gt;</td>
<td>20-30mmHg Drop</td>
<td>&gt;30mmHg Drop</td>
</tr>
<tr>
<td>TCpO2&lt;sup&gt;23&lt;/sup&gt;</td>
<td>&gt;60mmHg</td>
<td>&lt;60mmHg</td>
</tr>
<tr>
<td>Pulse Oximetry&lt;sup&gt;22&lt;/sup&gt;</td>
<td>&gt;2% Difference Between Finger and Toe Saturation</td>
<td>&lt;2% Difference Between Finger and Toe Saturation</td>
</tr>
<tr>
<td>SPP&lt;sup&gt;20&lt;/sup&gt;</td>
<td>&gt;50mmHg</td>
<td>&lt;50mmHg</td>
</tr>
</tbody>
</table>

Ankle brachial index (ABI) is a test comparing the brachial artery systolic pressure to the ankle systolic pressure. Some recommend that the ankle pressure be taken as an average of the dorsalis pedis and posterior tibial systolic pressures,<sup>23</sup> while others recommend the highest of the ankle pressures be used. The ABI value is calculated by dividing the ankle systolic pressure by the brachial systolic pressure. The normal ABI is 1.0-1.1.<sup>23,25</sup> A patient with an ABI of <0.9 is considered to have early PAD.<sup>22,23</sup> ABI values of 0.5-0.8 correlate to 1 occlusion and values <0.5 indicate multilevel occlusion. One must be aware that non-compressible vessels, secondary to calcification, will give falsely raised values (>1.1).<sup>24,25</sup>

Pulse volume recordings are performed by applying blood pressure cuffs to the thigh, upper calf, lower calf, midfoot, and digits (Figure 3). The cuffs are inflated to 65mm Hg so that the recordings taken reflect arterial pulse. The systolic waveform is then recorded. The normal waveform is seen as a steeply sloped upstroke, a sharp peak (systolic), and a dicrotic notch in the down stroke (Figure 4A). Typically in PAD patients, there is a loss of dicrotic notch, decreasing the slope of the down stroke and also an extended upstroke. (Figure 4B) In severe cases, one may note a flat-lined waveform.

Photoplethysmography (PPG) may be used to assess the cutaneous microcirculation in digits (Figure 5). Infrared light is transmitted through the skin and is reflected back from the blood of the microcirculation. The amount of reflected light correlates with the volume of blood, and there is no quantitative value. PPG only records changes in blood volume. The results of PPG will be in waveforms, as in PVRs.
Segmental pressures are used to evaluate the area of occlusive disease. Again, as in PVRs, blood pressure cuffs are applied to the thigh, upper calf, lower calf, midfoot, and digits. The cuffs are inflated and then systolic pressures are measured at each cuff site (Figure 6). The systolic pressures are compared from proximal to distal (Figure 7). A difference greater than 20-30 mm Hg per segment is indicative of peripheral arterial occlusive disease. The occlusion is between the 2 areas (i.e., thigh to high calf) where the pressure drop is found. When comparing with the contralateral limb, a difference of >40 mm Hg is also suggestive of an occlusion.

Another modality utilized at our institution is transcutaneous oxygen pressure monitoring (TcOM) (Figure 8). TcOMs reveal the oxygen pressure at different sites, and are another test of microcirculation. This study is usually performed by a well-trained respiratory therapist. The patient is placed on 100% oxygen via nasal cannulae. The sensors used warm the skin to greater than or equal to 43 degrees C to increase blood flow and skin permeability. A normal oxygen pressure is >60 mm Hg in the lower extremity. An oxygen pressure of <60 mm Hg is strongly indicative of PAD. Keep in mind that obesity, edema, cellulitis, bony prominences, thickened skin, and decreased temperature may falsely decrease the value.

Digital pulse oximetry is also used at our institution. This tests oxygen saturation at the level of the pedal digits compared with the fingers. Both normal values should be 98-100%. The technique for this study is performed first by thoroughly cleaning the digits with alcohol. Next, the leg is elevated above heart level for 5 minutes and the oximeter is placed directly on the digit to be tested. The saturation level is allowed to normalize and is then recorded. This value is then compared with that of the index finger. A value of less than 2% difference compared with the finger value is deemed abnormal and indicative of PAD. A study
by Parameswaran showed this test shown to be as accurate as ABL.  

A new machine, Sensilase (Vasamed, Eden Prairie, MN), has been introduced that allows for skin perfusion pressure (SPP) testing (Figure 9). This device uses a laser sensor that is placed at the site to be measured and a cuff is then placed over the sensor and inflated past systolic pressure. As the cuff deflates, the pressure at which capillary flow returns is measured. This measurement is the skin perfusion pressure. Normal SPP is >50 mm Hg, but values less than 30 mm Hg are consistent with CLI and also correlate with decreased healing potential.  

Imaging modalities such as conventional angiography (CA), magnetic resonance angiography (MRA), digital subtraction angiography (DSA), and computed tomographic angiography (CTA) provide direct images of the vascular tree and reveal specific areas of stenosis. MRA is a completely non-invasive modality, whereas, CA, DSA, and CTA require peripheral intraenous access to administer contrast. CA is the gold standard in assessing peripheral occlusions. X-ray beams are shot through the area to be assessed and contrast dye is then injected into the vessel. An occlusion is noted when the contrast flow is impeded or restricted. Intervention, which will be described later, may then be instituted.

MRA is a means to obtain projection and cross-section images of arteries. MRA does not evaluate the flow through these vessels, but it does identify occlusions. In DSA, 2 images are recorded. The first is precontrast (mask image) and the second is after administration of the contrast (opacification image). The images are processed and the tissues that are not affected by the contrast are digitally subtracted. CTA uses rotating device that emits x-ray beams through the area of interest. The x-ray beams are computer analyzed and a three-dimensional picture of the arteries in question are obtained. CTA does give a representation of blood through the arteries and veins. A major drawback of using DSA and CTA is that they require a high amount of dye. This means they are contraindicated in patients with dye allergies and they may also cause nephropathy, especially in patients with renal impairment. An MRA would be of great value in one of these situations. MRA, DSA, and CTA have been proven useful in determining the location and extent of stenosis and may help in deciding whether endovascular versus surgical intervention is needed.  

**CONSERVATIVE TREATMENT**

The goals of conservative treatment for patients with peripheral arterial disease are the preservation of the affected limb, decreasing the need for revascularization, and improving function. Treatment starts with prevention by education. The clinician must educate the patient about modifying their individual risk factors. Strict glycemic control, diet, ideal body weight, exercise, smoking cessation, cholesterol and hypertension control are important points to emphasize with all patients. Patients should be encouraged to start a routine exercise program consisting of a 35-50 minute walking program 3 to 5 times per week. The patient will walk until the initiation of symptoms, rest until resolution of the symptoms, and then continue to walk for the remaining allotted time. It is well-documented that patients are more likely to continue with an exercise program if it is performed under a supervised setting. Referral to a dietitian for education and management of caloric intake to obtain ideal body weight is recommended to improve outcome. If the patient continues to have symptoms after implementing the conservative therapy, pharmacological agents should be employed (Table 5).
Table 5

PAD MEDICATIONS AND INFORMATION

<table>
<thead>
<tr>
<th>Medication</th>
<th>Method of Action</th>
<th>Half Life</th>
<th>Indications</th>
<th>Dosing/Scheduling</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentoxifylline</td>
<td>xanthine derivative</td>
<td>0.4 - 0.8 hrs</td>
<td>Indication: Intermittent claudication</td>
<td>400 mg TID</td>
<td>Do not use in recent cerebral or retinal hemorrhage. Monitor prothrombin with patients on Warfarin. Monitor renal function with renal impairment. Contraindicated in CHF. Monitor for thrombocytopenia and leukopenia. Smoking decreases cilostazol exposure by 20%.</td>
</tr>
<tr>
<td>(Trental®)</td>
<td>Hemorrheologic agent</td>
<td>Metabolites are renally excreted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cilostazol</td>
<td>Quinolinone derivative</td>
<td>11-13 hrs</td>
<td>Indication: Intermittent claudication</td>
<td>100 mg BID</td>
<td>GI bleeding 2%</td>
</tr>
<tr>
<td>(Pletal®)</td>
<td>Phosphodiesterase III inhibitor</td>
<td>Cytochrome P-450</td>
<td></td>
<td>50 mg BID</td>
<td>Incidence increases with concomitant aspirin and NSAIDs use.</td>
</tr>
<tr>
<td></td>
<td>Vasodilator</td>
<td></td>
<td></td>
<td>with co-administration of CYP450 drugs</td>
<td>TTP 4 per million</td>
</tr>
<tr>
<td></td>
<td>and platelet inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>ADP inhibitor</td>
<td>11 days</td>
<td>Reduction of Atherothrombotic events Recent MI, Recent Stroke or Established Peripheral Arterial Disease</td>
<td>75 mg daily patients.</td>
<td></td>
</tr>
<tr>
<td>(Plavix®)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SURGICAL TREATMENT

Historically, the gold standard for revascularization of critically ischemic limbs has been vascular bypass. A number of newer procedures have been discovered and noted to be as efficacious as bypass. Advanced techniques such as percutaneous endovascular procedures have gained popularity with distinct advantages over bypass surgery. Bypass surgery is associated with high morbidity and mortality, graft failure, and the use of the great saphenous vein. Interventional therapy offers a reasonable alternative to complicated attempts at surgical bypass in high-risk patients. These techniques include percutaneous transluminal angioplasty (PTA), stenting, mechanical, and rotational debulking techniques (arthrectomy). Interventional techniques have been proven to restore blood flow to the ischemic limb; however, debate centers around the long-term patency of the procedure. Two randomized controlled studies suggest that the patency rate is equal for surgical and percutaneous transluminal techniques when comparing ABI index at a period of less than 3 years. It should be noted that with CLI patients, patency is less important than the restoration of blood flow. The tissue in patients with nonhealing ulcers or gangrene requires high levels of oxygen and nutrition for tissue repair. This means that any of the procedures may be successful for treatment of CLI wounds. Once wound healing has occurred, less oxygen is required to keep the limb asymptomatic.

One of the interventional techniques is subintimal angioplasty. A guide wire is inserted into the subintimal track at the occlusion’s origin. This guide wire is pushed forward past the lesion and allowed to re-enter at the end of the obstruction, restoring blood flow. Utilization of a stent with this procedure has been described with slight improvement of inflow to the lower extremity, but long-term studies remain pending.
Due to the diffuse, multi-level disease associated with CLI, a debulking strategy prior to balloon angioplasty is warranted in many cases. Debunking is important to facilitate the crossing of total occlusions and will transform a diffuse, polymorphic lesion into a more easily balloon stenosis thus reducing the risk of distal embolization. There are multiple plaque excision systems marketed today. SilverHawk Plaque Excision System (Fox Hollow Technologies, Redwood City, CA) is a catheter-based plaque excision device allowing percutaneous removal of atheromatous material. The excimer laser assisted angioplasty device utilizes a flexible optic catheter to deliver UV energy in short pulse duration. This ablates tissue on contact and with short pulse duration, prevents increase in temperature of nearby tissues.

Other mechanical thrombectomy devices include AngioJet (Possis Medical) and the new Trellis thrombectomy device (Bacchus Vascular). The AngioJet shoots jets of high-speed saline solution through a catheter tip. The plaque then dissolves into small pieces that are vacuumed back through the catheter. Unlike earlier technology, the AngioJet removes the clot entirely, eliminating the possibility of shower emboli. The Trellis Thrombectomy System contains a drug dispersion catheter with proximal and distal occlusion balloons, which help prevent distal embolization and systemic release of the infused thrombolytic agent. After inflating the distal balloon, the thrombolytic agent is infused and held at the target site by inflation of the proximal balloon. An oscillating dispersion wire optimizes dispersal of the thrombolytic agent as the thrombus is mechanically fragmented. The liquefied thrombus is then aspirated.

CASE PRESENTATIONS

Case 1: The Good
A 55-year-old male with past medical history of non-insulin diabetes mellitus for 5 years and 30 pack-year smoking history presented for complaint of leg cramping. On further questioning, the patient related a history of cramping of the bilateral lower extremities when ambulating a distance of 2 blocks, requiring him to sit for relief of pain. On physical examination, the patient had weakly palpable dorsalis pedis, posterior tibial, and popliteal pulses. His capillary fill time was less than 5 seconds and his skin temperature was warm to warm from proximal to distal with absence of pedal hair growth. Also noted were onychodystrophy, xerosis, and intrinsic muscle atrophy (Figures 10, 11).

The patient was diagnosed with intermittent claudication and NIVS were ordered. The NIVS revealed an ABI of 0.8 with blunting of PVR waveforms and evidence of trifurcation disease. The patient was placed on Plavix and enrolled at our Joslin’s institute for diabetes. At Joslin’s, he received extensive education on glycemic control, enrolled in a smoking cessation program, and was placed on statin therapy. He was also referred to a podiastist for diabetic shoes. On subsequent follow-up, the patient had adequate glycemic control, had stopped smoking, and his symptoms of intermittent claudication had resolved.

Case 2: The Bad
A 70-year-old female with past medical history of diet-controlled diabetes mellitus for 10 years, and 40 pack-year smoking history presented to the emergency room with a supination external rotation stage IV ankle fracture. The patient was taken to the operating room and underwent open reduction and internal fixation then was placed in a cast. On routine follow-up the patient presented to clinic where the cast was removed and gangrenous changes were observed (Figures 12, 13). The patient was referred to a vascular specialist where an angiogram was performed. There were multi-segmental occlusions and the patient subsequently underwent endovascular intervention with restoration of blood flow. The patient was able to heal uneventfully and has had no further problems (Figure 14).

Case 3: The Ugly
A 65-year-old male with past medical history of insulin-dependent diabetes mellitus for 25 years presented to the emergency room secondary to deep space infection of the foot. The patient underwent an incision and drainage of the deep space abscess (Figure 15). However, non-invasive and angiographic studies revealed severe ischemia with multi-segmental disease. The patient had prior open bypass to the extremity and despite extensive efforts to save the limb the patient underwent a
below-knee amputation. The patient eventually went on to an AKA due to a non-healing BKA stump (Figure 16).

**CONCLUSION**

Peripheral arterial disease is a manifestation of atherosclerosis, a systemic vascular process. The staggering statistics presented in this paper should prompt the podiatrist to initiate a systemic evaluation for the patients suspected of having PAD. In the face of suspected PAD, we must take the right steps in preventing further progression of the disease, whether it means sending the patient for NIVS or consulting the proper specialist. The
early identification of PAD has been shown to decrease the morbidity and mortality of patients affected by this disease. The necessary steps in evaluating and aiding the patient with PAD are; taking a good history, identifying risk factors, performing a complete exam, ordering relevant NIVS, obtaining necessary consults, and initiating proper therapy.

**REFERENCES**


