

# Peripheral Arterial Disease and the CKD Patient: The Case for Early Screening, Diagnosis, and Minimally Invasive Revascularization

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Peripheral arterial disease (PAD) is a general term used to describe obstructive atherosclerosis of the lower extremities. PAD occurs when cholesterol or plaque builds up in the arteries outside the heart—typically in the legs or pelvis—limiting normal blood flow and increasing the risk of heart attack or stroke. PAD is more common in patients with chronic kidney disease than in the general population. Patients with impaired renal function have a greater than twofold risk of developing PAD, and in the dialysis population, the incidence of clinical PAD is 15%. We discuss the importance of early screening and diagnosis of this serious circulatory problem, and include a checklist that any member of the renal team can use to discuss symptoms with patients.

**P**eripheral arterial disease (PAD) accounts for significant morbidity and mortality among end-stage renal disease (ESRD) patients.<sup>1</sup> Due to a lack of consensus regarding treatment options and the poor outcomes associated with traditional surgical revascularization and amputation for the ESRD population, screening for PAD remains a controversial topic.<sup>2</sup> However, there is evidence that supports aggressive screening, diagnosis, medical treatment, and revascularization prior to amputation to reduce mortality. Non-surgical interventions are available to re-establish circulation to the lower extremities, thereby decreasing or resolving symptoms associated with PAD such as claudication and skin ulceration.<sup>3</sup> PAD is common in ESRD patients, and nephrology professionals understand how an amputation can impact the prognosis for effective dialysis. At Vascular Access Centers, we have developed and implemented a protocol for patient education, screening, diagnosis, and minimally invasive treatment of PAD.<sup>4</sup> Furthermore, we are successfully treating patients with minimally invasive procedures in the outpatient setting.

## PAD in the General Population

In the United States, PAD affects approximately 8 million adults over the age of 40. Intermittent claudication, exertional leg-muscle discomfort that is relieved with rest, is the classic presenting symptom that may lead to a diagnosis of PAD. However, fewer than 20% of patients will experience claudication.<sup>5</sup> Asymptomatic PAD is important because there is evidence to suggest that the progressive nature of the underlying PAD is identical, whether the patient experiences symptoms or not.<sup>5</sup>

With the progression of the disease, patients are at even greater risk of developing critical limb ischemia (CLI). CLI is defined as extremity pain at rest or as impending limb loss with the presence of non-healing ulcers or gangrene. If left untreated, it usually leads to major limb amputation within 6 months.<sup>5</sup>

The ankle-brachial blood pressure index (ABI) is an easy test to diagnose a patient with PAD.<sup>6</sup> In fact, clinicians who rely on claudication alone are likely to miss 85-90% of cases of PAD.<sup>5</sup> The ABI, while effective in diagnosing PAD in general, is not reliable in all patients.

Patients with arterial calcification, such as chronic kidney disease patients, will present with falsely elevated ABI. The use of pulse volume recording (PVR) waveform testing will identify a greater number of patients with PAD earlier.

## Limb Amputations

According to a report published in 2004 by the Sage Group out of Atlanta, approximately 160,000 amputations are performed annually in the United States because of PAD.<sup>2</sup> Depending on the patient population, procedural mortality rates range from 4% to 30% and morbidity from 20% to 37%.<sup>1</sup>

There are significant costs to amputations, both economic and social. It is estimated that of the patients who have undergone a below the knee amputation, less than half (40%) will achieve full mobility. Similarly, of those patients with an above the knee amputation, only an estimated 20% will achieve full mobility. Additionally, the report goes on to say that the amputation costs are estimated at \$10 billion annually.<sup>2</sup>

In the later stages of PAD, when CLI develops, the blood flow to the extremities

is so limited that ulcers and gangrene can develop. According to the Sage Group report, 6 months after CLI develops, 20% of those patients will die and another 35% will need an amputation.<sup>1</sup>

## Advances in Minimally Invasive Procedure Technology

For some patients with PAD, despite changes they make in their physical activity, diet, smoking cessation, and medication use, minimally invasive or surgical procedures are required to restore adequate blood flow to the extremity.<sup>3</sup>

In the 1990s, the myth that balloon and stent technology was not effective in the lower extremities may have been somewhat appropriate because this technology was new. However, between 2000 and 2005, data began to emerge that reflected improved technologies.

Adjunctive technologies, including pharmacological support and novel wire and crossing technologies, now make it possible to achieve a CLI procedural success rate of 96-97% with contemporary balloon and stent technology.<sup>7</sup>

Early stent design technology suffered from significant fracture rates. However, recent results from the RESILIENT trial demonstrated a less than 5% fracture rate at 12 months versus angioplasty. The newer stents on the market boast a less than 1% fracture rate and are highly kink resistant.<sup>8</sup>

Balloon technology has also advanced to include specialized cutting surfaces and drug coatings, and the clinical trials on this technology demonstrate very high patency rates (85%) at 12 months (THUNDER Trial).<sup>9,10</sup> The question of whether balloon angioplasty and stent technology work in the lower extremities was investigated in the BASIL trial, and the results showed that endovascular therapy was equivalent to fem-pop bypass at 3 years.<sup>11</sup>

Minimally invasive procedures are done under local anesthesia and conscious sedation. This combination suits these procedures perfectly in the outpatient clinic setting because of the low risk to patients. Therefore, it makes sense that, given the advances in technology, the growing body of evidence demonstrating improvement in patency rates, and the low risk of procedural complications, that minimally invasive pro-

cedures using balloon and stent technology continue to be positioned as clear alternatives to more invasive surgical procedures. In the ESRD population, with demonstrated poor wound healing, the use of minimally invasive procedures provide a clear advantage.

## Current PAD Diagnosis Guidelines for ESRD

The incidence of clinical PAD in the CKD Stage 5 population, according to data from the U.S. Renal Data System, is 15%.<sup>12</sup> Subclinical PAD prevalence is presumed to be much higher. A guideline for assessing the presence of PAD is in place for patients initiating dialysis (Kidney Disease Outcomes Quality Initiative [KDOQI] Guideline 10; *Table 1*).<sup>13</sup>

## Evidence for Stronger Screening Guidelines and Use of Minimally Invasive Revascularization Prior to Surgical Measures and Major Amputation

At the time the KDOQI guidelines for cardiovascular disease were written, the authors noted that more randomized, controlled clinical trials were needed for

a more robust guideline. However, several compelling editorials and studies suggest that screening for PAD and treating with revascularization may be indicated in the ESRD and CKD population in general. These articles are summarized below.

### Renal Insufficiency and Use of Revascularization Among a National Cohort of Men With Advanced Lower Extremity Peripheral Arterial Disease<sup>14</sup>

Although PAD is prevalent in patients with CKD, little is known about the disease management in this group. "The percentage of patients who underwent revascularization within 6 months of initial diagnosis of critical limb ischemia decreased in patients with CKD."<sup>14</sup> A larger percentage underwent either major amputation or neither major amputation or revascularization. Therefore, patients with CKD are less likely to have revascularization procedures. Despite recommendations by some authors for aggressive primary amputation in CKD patients, this did not result in favorable outcomes. In fact, even among patients with CKD, "mortality is lowest among patients who have critical limb ischemia and receive a revascularization procedure either with or independent of amputation."<sup>14</sup>

**TABLE 1. Current Kidney Disease Outcomes Quality Initiative (KDOQI) cardiovascular guideline 10: peripheral vascular disease (PVD).\***

10.1. Diagnosis of peripheral arterial disease (PAD)
10.1a. At the time of dialysis initiation, all patients should be evaluated for the presence of PVD.
10.1b. Evaluation should include physical examination including assessment of arterial pulses and skin integrity.
10.1c. Further specialized studies, such as duplex ultrasound or invasive testing, should be undertaken if abnormalities are detected upon physical examination and interventions are considered.
10.2. Approach to therapy of PVD
10.2a. Patients with PVD should be treated in the same manner as the general population in regard to smoking cessation, lipid-lowering therapy, glycemic control, blood pressure control, and the use of ACE inhibitors and antiplatelet agents. In addition, supervised exercise regimens and medications to increase vasodilation should be considered in patients with claudication and without critical limb ischemia. Established national guidelines, similar to those for stroke, are not available for PVD in the general population.

Adapted from KDOQI Cardiovascular Guidelines: Guideline 10: Peripheral Vascular Disease.<sup>13</sup>  
 \*KDOQI recognizes that screening using ankle-brachial blood pressure index (ABI) in dialysis patients is weak; ABI may be falsely elevated in patients on dialysis because of vascular calcification.

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**TABLE II. Symptom checklist for peripheral arterial disease.**

Do you hear patients complain about the following issues? Your patients could be at risk for leg amputation due to peripheral arterial disease (PAD). Use the checklist below to talk with your patients about this serious circulatory problem that can affect people with chronic kidney disease.

## Are You at Risk for PAD?

PAD is a serious circulatory problem in which the blood vessels that carry blood to your arms, legs, brain, or kidney become narrow or clogged. It affects more than 8 million Americans, most over the age of 50. People with PAD are at a significantly increased risk for stroke and heart attack.

### Answer these questions to determine if YOU are at risk for PAD.

1. Do you have chronic kidney disease (CKD), high blood pressure, or diabetes?
2. Do you experience discomfort when walking?
3. Are you able to walk five blocks without stopping?
4. Do you dangle your feet off a couch or bed to relieve discomfort?
5. Do you experience foot or toe pain that disturbs your sleep?
6. Are your toes pale, discolored, or bluish?
7. Do you have skin wounds or ulcers on your feet or toes?
8. Have you ever been told you have diminished or weak pulses in your feet (pedal pulses)?
9. Have you had vascular surgery on your legs?
10. Do you have an infection of the leg(s) or feet that may be gangrenous (blackened skin tissue)?
11. Have you experienced hair loss below the knee over time?
12. Do you have thin, shiny skin below the knee?
13. Have you experienced hair loss below the knee over time?
14. Are your feet always cold? Or is one foot always colder than the other?

**If you answered YES to any of these questions, alert your doctor that you may be at risk for PAD. It could save your life.**

Source: Vascular Access Centers. Used with permission.

### Lower Extremity Peripheral Arterial Disease Among Patients with End-Stage Renal Disease<sup>15</sup>

PAD accounts for significant morbidity and mortality among CKD patients. PAD is accepted to be more prevalent in the ESRD population and is responsible for significant morbidity and death in this population. "Future research efforts should focus on the development of an optimal screening strategy for patients with ESRD."<sup>15</sup> Effective screening would allow us to identify patients who are likely to benefit from preventive measures such as smoking cessation and exercise programs, which have been proved to prevent critical limb ischemia. When indicated, revascularization results in a lower morbidity and mortality than amputation alone.<sup>15</sup>

### PAD: A Guide for Nephrologists<sup>16</sup>

"PAD is an often overlooked and under-diagnosed condition in patients with CKD."<sup>16</sup> Individuals with CKD are at an increased

risk for developing Cardio-Vascular Disease (CVD), which includes Coronary Artery Disease (CAD) and PAD. Nephrologists are the primary physician for many patients with CKD, particularly those on dialysis. The patient population on dialysis is particularly at risk for PAD. Therefore, Nephrologists and Nephrology professionals should be knowledgeable about the disease process and treatments for PAD.<sup>16</sup>

### Combined Effect of Chronic Kidney Disease and Peripheral Arterial Disease on All-Cause Mortality in a High-Risk Population<sup>17</sup>

CKD (glomerular filtration rate [GFR] > 60) and PAD are independent predictors of mortality. The overall 6-year mortality rate in this study was 28% (n = 284). Patients with PAD and CKD had the highest 6-year mortality rate at 45%. Patients with CKD alone had a 28% mortality rate. Patients with PAD alone had a 26% rate. Patients with neither condition had an 18% mortality rate.<sup>17</sup>

### Surgical Revascularization Versus Amputation for Peripheral Vascular Disease in Dialysis Patients: A Cohort Study<sup>18</sup>

Surgical treatment of PAD in dialysis patients is controversial. Amputation might be associated with a higher mortality in this population. Where feasible, revascularization might be preferable over amputation in dialysis patients. Symptomatic peripheral vascular disease in dialysis patients should not automatically result in amputation.<sup>18</sup>

### Predicting 6-Month Mortality for Patients Who Are on Maintenance Hemodialysis<sup>19</sup>

Cohen and colleagues developed a prognostic tool for predicting mortality among hemodialysis patients with certain co-morbid conditions. Patients with PAD had a relatively high hazard ratio, which is an indicator of poor 6-month survival and high mortality.<sup>19</sup>

### Percutaneous Transluminal Angioplasty Is Feasible and Effective in Patients on Chronic Dialysis With Severe Peripheral Arterial Disease<sup>20</sup>

Surgical revascularization in ESRD patients can be difficult due to calcified distal vessels, resulting in poor limb salvage outcomes and high rates of perioperative mortality. Therefore, a less invasive approach, such as percutaneous transluminal angioplasty (PTA), represents a safe and effective option in most patients with PAD.<sup>20</sup> While prospective data supporting PTA in ESRD patients have been scarce, a retrospective review was conducted on 107 patients followed between 2000 and 2004. These were ESRD patients on chronic dialysis with symptomatic PAD, consecutively treated by PTA. The results indicated that PTA is safe and effective in this highly complex patient population, with a technical success rate of 97%, and a 73% limb salvage rate at the 1-year follow-up. With limb salvage rates similar to the highest reported for surgical alternatives, the data suggest that PTA should be a first-line treatment option for symptomatic PAD instead of more costly invasive surgical options.<sup>20</sup>

### Case Study

#### ESRD Patient With Positive Screening, Diagnosis, and Treatment for PAD

Patient B, a 78-year-old African-American male, presented to Vascular Access Center of Washington DC on 6/14/2010 with a thrombosed upper right thigh AV graft. Patient B has a history of hypertension, type 2 diabetes, and smoking 1 pack a day for 20 years, but quit 10-15 years ago (Figures 1 and 2). Upon arrival at the Center, patient B was given a PAD Screening Questionnaire. He answered "yes" to questions that indicated bilateral claudication and reported that he experienced a decreased quality of life related to decreased mobility. It was noted that bilateral pedal pulses were non-palpable. Because patient B is an ESRD patient, he was referred for PVR waveform testing. The test results indicated severe, bilateral PAD. Patient B was then recommended for angiogram (Figure 3). Dr. James F.



**FIGURE 1.** Patient B's legs, with no obvious signs of PAD. Often severe PAD will not present visible symptoms, so screening is imperative.

McGuckin performed bilateral aortic run-off and confirmed bilateral disease distal to and in the tibio-peroneal trunk. On 7/29/2010, Dr. McGuckin performed angioplasty of the anterior tibial, posterior tibial, and peroneal arteries. Patient B reported that pain decreased immediately following the procedure. Pulses were palpable to the pedal level in the left leg following the procedure. Because of the successful outcome, patient B was scheduled to return and received similar treatment to his right leg on 8/29/2010.

Without proper screening, patient B would have continued to have decreased mobility and an increased risk of develop-



**FIGURE 2.** Patient B's feet. With minimally invasive measures, limbs can be saved from amputation.



**FIGURE 3.** Angiogram shows severe below the knee arterial disease. Patient B has only a very small supply of blood and vital oxygen to his lower extremity.

ing CLI. With CLI, patient B might end up with a major amputation, decreasing his overall quality of life and survival.

With screening, patient B now has clear bilateral arterial run-off. He can return to a more active lifestyle with a decreased risk for CLI and amputation (Figure 4).



**FIGURE 4.** Patient B's diseased posterior tibial artery after treatment. Prior to angioplasty, there was no visible blood flow to the patient's foot. Without screening, this patient's limb would have been at risk for amputation.


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## Conclusions

In conclusion, PAD affects over 8 million individuals in the United States and is understood to be a grossly underdiagnosed disease. The incidence of PAD is higher in patients with CKD and especially those on dialysis. According to USRDS data, 15% of all patients on dialysis have clinical PAD. It is assumed that many more have subclinical PAD. PAD coupled with CKD Stage 5 indicates higher mortality than in patients with CKD Stage 5 alone. There is evidence that patients who are treated with revascularization rather than aggressive amputation have a higher survival rate. Minimally invasive procedures are available for treatment without wound healing complications.

Therefore, future research efforts and guidelines should be focused on screening, early diagnosis, and treatment of PAD and CLI with minimally invasive endovascular revascularization rather than major amputation alone.

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