June 15, 2015

Maria Ellis
Executive Secretary for MEDCAC
Centers for Medicare & Medicaid Services
Center for Clinical Standards and Quality
Coverage and Analysis Group
S3–02–01
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Program; Meeting of the Medicare Evidence Development and Coverage Advisory Committee—July 22, 2015; [CMS–3320–N]

Dear Ms. Ellis:

Lifeline Vascular Access appreciates the opportunity to present these comments related to Peripheral Artery Disease (PAD) and its treatment in more than 20 freestanding centers. The more than 50 credentialed physicians in our PAD centers are pleased to see this national forum for the discussion of PAD and its impact upon Medicare beneficiaries.

Specifically, the hearing asked for our comments related to the Clinical outcomes including reduction in pain; avoidance of amputation; improvement in quality of life and/or functional capacity including walking distance; wound healing; avoidance of cardiovascular events, including myocardial infarction, stroke, cardiovascular death, and all-cause mortality; and avoidance of harms from the interventions. The questions will further develop stratification related to asymptomatic PAD, intermittent claudication and Critical Limb Ischemia (CLI).

We would also like to highlight not only our center's outcomes (safety and efficacy) with patient satisfaction scores but also highlight the needs of the chronic kidney disease patient (CKD).

Introduction

Peripheral arterial disease (PAD) is highly prevalent in the United States [1-3]. Even though few deaths can be directly attributed to PAD, this disease has potent mortality implications. Asymptomatic PAD carries with it the risk of future compromised ambulation, lower extremity ulcers or the need for vascular surgery or amputation. Symptomatic disease directly affects functional capacity and quality of life by restricting ambulation. Both asymptomatic and symptomatic PAD are powerful independent predictors for cardiovascular events such as myocardial infarction, stroke, and cardiovascular death [4-6].

Chronic kidney disease (CKD) is also associated with an increased risk for cardiovascular events. It has been estimated that an individual with end stage renal disease (ESRD) has a cardiovascular mortality rate that is 15 times higher than that of the normal population. In fact a patient with CKD is 5 to 10 times more likely to die from a cardiovascular event then to progress to ESRD [7]. Available studies indicate that there is an increased incidence of PAD in hemodialysis patients. This gives affected patients to major risk factors for cardiovascular events. However, the evaluation of CKD patients for PAD has received very little attention. Therefore, they are less likely to receive appropriate treatment than are those, for example, with coronary artery disease.

Pathophysiology of PAD in CKD Patients

The pathophysiology of PAD in the CKD population differs from that observed in the absence of real disease. Traditional PAD is associated with intimal changes consisting of lipid-rich atheromatous plaques that can narrow the vessel and have the potential for rupture and subsequent thrombosis. In the CKD patient, in addition to these typical plaques, disease of the arterial medial layer in which increased collagen content, together with calcification, hyperplasia and hypertrophy of vascular smooth muscle cells, leads to arterial wall hypertrophy and increased arterial stiffness [8, 9]. It is thought that this medial calcification which characterizes the PAD seen in CKD patient is a result of the calcium and phosphate derangement is associated with renal disease.

Clinical Diagnosis of PAD

PAD is typically thought of as being associated with symptoms such as intermittent claudication, ulcers and rest pain. However, studies have shown that a minority of these patients actually present with these symptoms [1, 3, 10]. The ankle-brachial index (ABI) (Figure 1) has come to be regarded as the standard for making the clinical diagnosis of PAD. This noninvasive test is easily performed, reliable. Measurement of the ABI allows for the identification of both symptomatic and asymptomatic patients with PAD. It is common to be widely recommended as a screening test [6].

According to guidelines published by the American Heart Association and the Inter-Society Consensus for the Management of Peripheral Arterial Disease, the ABI is defined as the ratio between the higher of the systolic blood pressures of the 2 ankle arteries of the land in question (either the anterior or the tibial artery) and the higher of the 2 systolic blood pressures obtain in the upper extremities [6, 11, 12]. The significance of different ABI levels is shown in Table 1, an ABI between 0.9 and 0.4 is generally interpreted as mild to moderate PAD.

Table 1 – Significance of ABI Values

ABI	Significance
< 0.4	Severe PAD
0.9 – 0.4	Mild to moderate PAD
0.91 – 0.99	Borderline
1.0 – 1.29	Normal
>1.30	Abnormally high

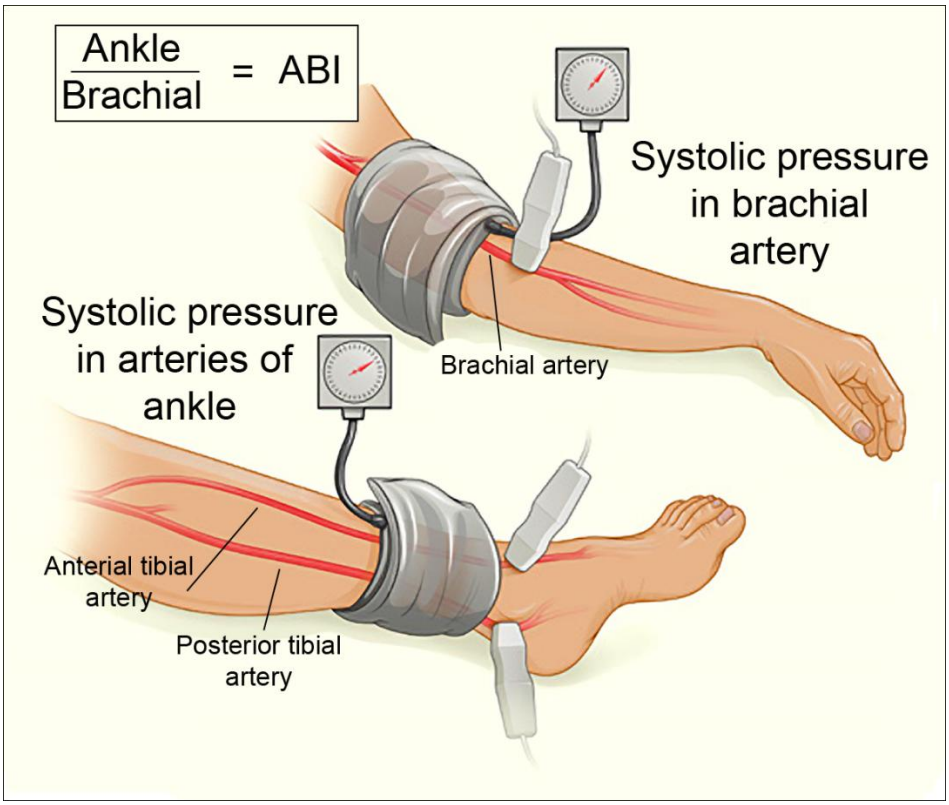

Figure 1 – Preforming the ankle-brachial index (ABI) test

Some investigators have questioned the use of the higher of the two ankle pressures for calculating the ABI, preferring to use the average [13] of both ankle artery pressures or to use the lower [14] of the 2 pressures for the calculation. A study was conducted based upon the hypothesis that the standard definition of ABI measurement based upon the higher of 2 ankle artery pressures under-estimated the true prevalence of PAD. In this investigation 831 patients admitted with chest pain for a diagnostic heart catheterization were evaluated [15]. Blood pressure in both the anterior and posterior tibial arteries was measured. The ABI was calculated in 2 ways - using the higher of the 2 ankle pressures (the standard definition) and using the lower of the 2 ankle pressures (modified definition). A total of 15 patients (1.8%) with an ABI > 1.5 were excluded from study. Three groups were defined and compared to determine differences in the incidence of cardiovascular events (cardiovascular death, myocardial infarction or stroke). These 3 groups were defined as *without PAD* (64.2%) having an ABI > 0.9, *with PAD* (25.0%) having an ABI < 0.9 according to the standard definition and *suspected PAD* (10.8%) having an ABI < 0.9 according to the modified definition (using the lowest pressure). The *without PAD* group had the lowest cardiovascular event rate whereas the event rates were comparable for the *with PAD* and *suspected PAD* groups (14.8%, 28.4% and 25.0% respectively). It was concluded from this study that the use of the standard definition for ABI overlooked a group of patients with an equally high risk for cardiovascular events.

It should be noted that some patients with CKD have a higher than normal ABI, > 1.30 [16]. In one study of 1,010 hemodialysis patients a high ABI was observed in 10.9% of the cases [17]. This is thought to represent a reflection of generalized stiffening of the lower limb arteries [18, 19] suggestive of a Mönckeberg-type atherosclerosis [20]. As will be discussed below, these cases have a poor prognosis.

Prevalence of Peripheral Arterial Disease (PAD)

Although CKD is a well-known fact that individuals with CKD are more likely to die of cardiovascular disease than to develop kidney failure. Additionally, the relationship between PAD and cardiovascular disease is well documented. However, the relationship between PAD and CKD has only been recognized in recent years.

In the general population

Peripheral arterial disease (PAD) is a common manifestation of the atherosclerotic disease process and its presence is associated with an increased risk of myocardial infarction and stroke [21-24]. The exact incidence of PAD depends somewhat on the method that is used to make the diagnosis. Intermittent claudication is often considered the cardinal symptom of PAD; however, epidemiologic studies have reported the prevalence of typical intermittent claudication in the adult population with PAD to be < 5% and in many cases < 2% [10, 25-27]. It has been shown that an ABI of < 0.90 correlates well with the presence of angiographic evidence of PAD [28]. Using this as the diagnostic criteria, PAD has been reported to affect from 12% to 14% of the general population and as many as 20% of individuals over the age of 75 [29]. This incidence of asymptomatic disease is important because epidemiological and clinical studies have demonstrated that the clinical impact of a low ABI on prognosis in subclinical PAD is similar to that in symptomatic PAD in the general population [1, 30]. Additionally, the extent of PAD severity as determined by measurement of ABI is positively associated with the occurrence of cardiovascular events [31].

In the CKD population

The incidence of PAD is higher in patients with chronic kidney disease (CKD) than in the general population [32]. Additionally, studies looking at the relationship between ABI measurements and renal function have shown a definite relationship with a higher incidence occurring with more advanced stages [33-37].

In the Cardiovascular Health Study (CHS), a cohort study of 5,888 adults aged 65 years or older, an inverse relationship between serum creatinine levels and ABI of < 0.90 was observed. Among the subset of CHS patients who underwent baseline serum creatinine measurement, 12% with renal insufficiency (defined as a serum creatinine level ≥ 1.3 mg/dL in women and ≥ 1.5 mg/dL in men) and 7% with normal renal function had an ABI of < 0.90 [35]. This association between renal insufficiency and a low ABI was found to be independent of patient age, diabetes, and other potential confounders [34].

The National Health and Nutrition Examination Survey reported that 24% of the population aged 40 years and older with an estimated creatinine clearance of < 60 mL/min/1,73 m2 or higher had an ABI < 0.90 compared with 3.7% of those with a clearance higher than this level [36].

In another study of 909 individuals with arterial hypertension [37], the prevalence of PAD was determined using ABI measurements. Patients were divided into 2 groups, those with a normal (ABI 0.9 - 1.4) and those with an abnormal ABI (ABI < 0.9). In this study, 8% of the subjects were found to have an abnormal value. In these cases the prevalence of CKD was 23.4% versus 11.2% in cases with a normal ABI. It was determined that the effect of eGFR on the likelihood of developing PAD was independent and statistically significant.

PAD in the CKD patient has been shown to correlate with an increased mortality rate. In a study of 1563 patients with CKD defined as an eGFR < 60 mL/min/1.73 m^2 [38], 573 subjects were diagnosed with PAD (ABI < 0.90). It was found that all-cause and cardiovascular mortality of CKD patients with PAD was increased 2.2 fold and 2.4 fold compared with CKD patients without PAD. Additionally, mortality of CKD patients significantly increased with decreasing ABI levels.

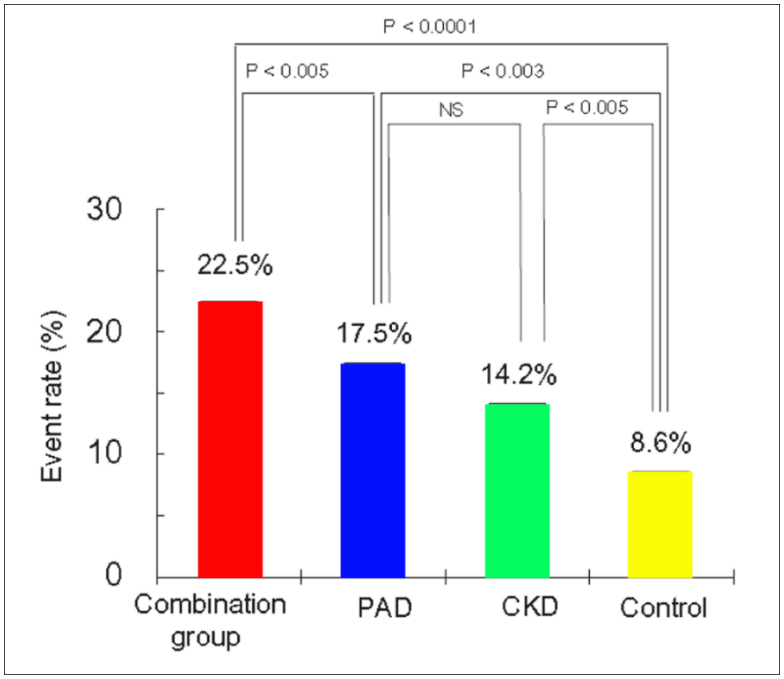

Figure 2 – Long-term event rate for PAD, CKD and combination of both compared to control group [29]

Another study was conducted to evaluate the impact of a combination of PAD and CKD in which a group of patients who had undergone coronary angiogram for the evaluation of chest pain was analyzed [29]. Patients on hemodialysis were excluded from this group. The cohort was divided into 4 groups according to presence of abnormal ABI (ABI < 0.9) and the presence of an abnormal eGFR (eGFR < 60 ml/min/1.73 m2). Using the combination of these 2 metrics, 4 groups were identified - Control group with an ABI >0.9 and an eGFR >60, PAD group with an ABI <0.9 and an eGFR >60, CKD group with an ABI >0.9 and an eGFR < 60 and Combination group with an ADI <0.9 and an eGFR <60. Long-term follow-up of 620 + 270 days was available and 89 patients (numbers in groups A-D were 94%, 18.5%, 15.2% and 28.3%, respectively). The long-term event rate is shown in Figure 2. The rate was 28.3% for patients with a combination of PAD and CKD compared to 9.4% for those without either condition. The adverse events used to define the long-term event rate were dead from any cause, stroke, and onset of acute coronary syndrome or heart failure.

In the dialysis population

Consistent with the inverse relationship between PAD and the severity of renal failure, the incidence of PAD appears to be even higher in the dialysis population that has been observed in either the general or the CKD populations. Several studies have reported the prevalence of an ABI < 0.90 among hemodialysis patients to be in the range of 30 to 38% [39-41].

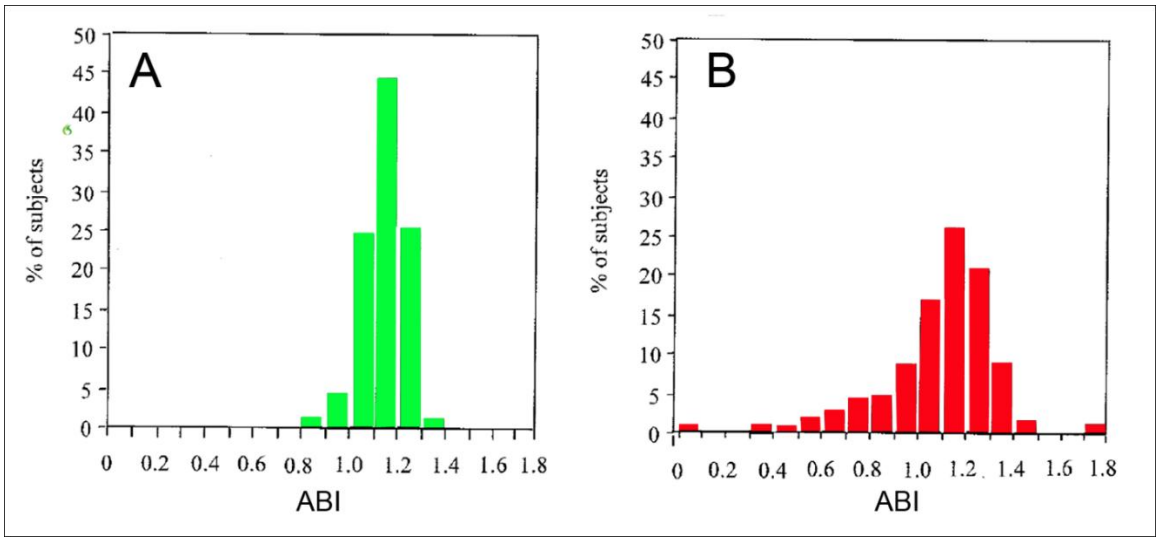

Figure 3 – Distribution of ABI measurements in healthy volunteers (A, n = 229) versus patients on hemodialysis (B, n = 1010) [17]

In order to evaluate the overall distribution of ABI in a population of hemodialysis patients, a cohort of 1010 patients was evaluated and compared with an age and gender matched control group of normal volunteers [17]. The results are shown in Figure 3 the mean value in the control group was 1.14 with males having a value that was significantly higher than females (1.15 versus 1.12). Only 0.67% of the subjects had an ABI < 0.9. In contrast, the ABI of hemodialysis patients was distributed broadly ranging from 0 to 1.75 a value < 0.9 was observed in 16.5% of the patient's and 10.9% of them had a value that was abnormally high, > 1.3.

The mean value for the hemodialysis patients was 1.07 which was significantly lower than that of the control group. Again, a significant difference was seen between male and female cases, 1.08 versus 1.05. During a two-year follow-up, 118 deaths were recorded in the hemodialysis group. Univariate regression analysis revealed a hazard ratio (HR) for an ABI < 0.9 versus 1.1 to 1.3 of 7.09. The HR was also significantly increased (4.83) for cases with even a mild reduction in ABI (0.9 to 1.0). Cases with an abnormally high ABI (> 1.3) were also associated with a significant increase in HR (2.20) indicating that this abnormality represents another risk factor for mortality in this group. Multivariate Cox analysis identified that ABI, age, cerebrovascular and coronary artery disease, and serum albumin level were variables that independently predicted all-cause mortality.

Management of PAD in the CKD Patient

The management of the CKD patient with PAD requires considerations into areas, systemic and local. Firstly, the presence of PAD is an indication of systemic disease (atherosclerosis) that is associated with an increased morbidity and mortality. Secondly, the presence of PAD places the patient at risk for compromised physical function, physical performance and the need for vascular surgery or amputation as a consequence of the leg ischemia that is present.

Medical therapy for PAD

Control of hypertension, the use of cholesterol-lowering agents, use of anti-platelet agents and changes in lifestyle such as exercise and smoking cessation are all important in the management of the systemic disease that is manifest as PAD. Specifics related to these areas of medical care are beyond the scope of this review; however, they are extremely important in the management of the CKD patient with PAD.

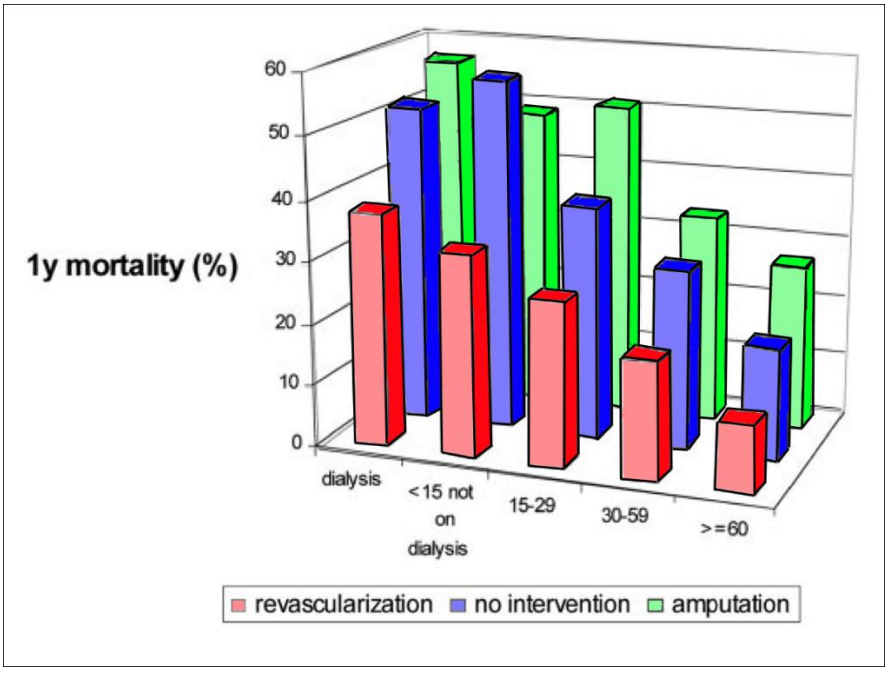

Figure 4 - 1 year mortality by management strategy and level of renal function [42]

Surgical therapy for PAD

Lower extremity surgical or percutaneous revascularization may be required for disabling claudication or for critical limb ischemia (rest pain, ischemic ulceration, or gangrene). Unfortunately, there are a number of studies which have shown a higher mortality rate and lower limb salvage rate for patients with advanced CKD who undergo these procedures [43-49]. Additionally, postoperative and 1 year mortality rates for patients undergoing lower extremity revascularization appeared to increase with declining renal function [50, 51]. This has caused concern as to defining the best approach to therapy in this group of patients.

In an attempt to evaluate the effects of different levels of renal function on the surgical management of PAD, a cohort of 6,227 male patients with limb ischemia was evaluated [42]. The patients were classified according to whether they underwent lower extremity revascularization, amputation or no procedure within the first 6 months following the diagnosis of critical limb ischemia, defined as ischemic rest pain, ulceration and/or gangrene. The association of renal insufficiency with revascularization and the association of management strategy with mortality within one year were measured. It was noted that at all levels of renal function, mortality risk was lowest for patients who underwent revascularization (Figure 4). Additionally, the one-year amputation rates among patients who underwent revascularization ranged from a low of 11% among those with an eGFR >60 to a high of 44% among those who were on dialysis (Figure 5). This this observation indicated a definite a definite advantage for treatment early in the progression of CKD.

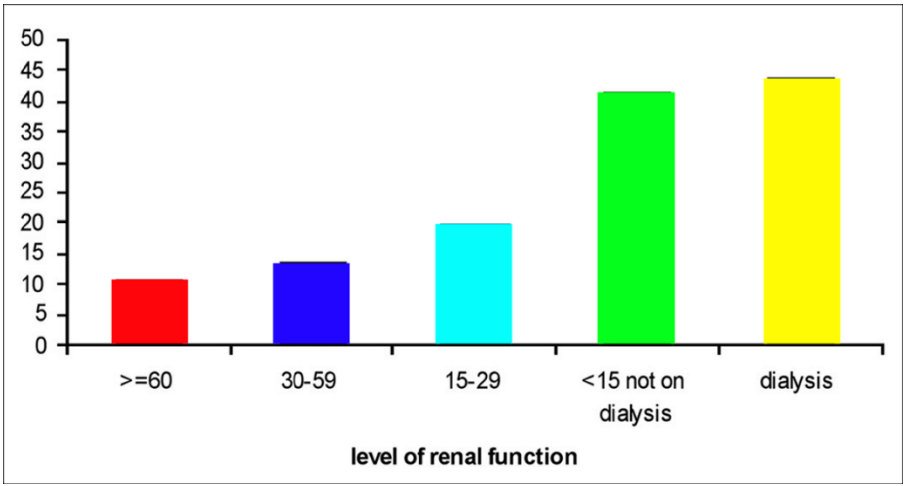

Figure 5 - Percentage of patients who underwent revascularization and underwent major amputation during the subsequent year [42]

In another study [52], data relating to postoperative morbidity and mortality of surgical revascularization or amputation for PAD from the United States Renal Data System was analyzed using propensity scores to account for confounding variables. Of the 317,533 patients initiated on dialysis during the one-year period of the study, 5,916 patients underwent amputation or revascularization within the first 6 months of initiating dialysis. In unadjusted logistic regression analysis, patients having amputations had a twofold higher odds of dying within 30 days of the procedure compared to the revascularization group. When adjusted for propensity scores and clinical variables, the amputated group still had 85% higher odds of dying within 30

days. There were 8.7% deaths within 30 days in the revascularization group compared to 16.0% deaths in the amputation group.

Outcomes from Lifeline Vascular Access Managed Centers

The Lifeline managed system for PAD care is delivered in state-of-the-art freestanding centers. They are all accredited under the Ambulatory classification of The Joint Commission. Data is available on 8,967 cases for the past 3 years.

The mean age of these 8,967 patients was 70.2 $\pm$ 0.12 years (95% CI – 70.0 – 71.0).

50.08% of the cases were in diabetics

Patient Demographics/Case Mix/Outcomes

12.1% of the patients had CLI

Procedures performed included Angioplasty, stent and atherectomy

Success Rate

Successful – 98.16% (4,898)
Unsuccessful – 1.48% (74)
Aborted – 0.36% (18)

Complications

None – 98.92% (4937)
Minor – 0.68% (34)
- Hematoma Grade I – 16
- Hematoma Grade II – 4
- Bleeding - 2
- Other – 12

Major – 0.40% (20)
- Hematoma Grade III – 4
- Arterial embolus – 6
- Bleeding - 4
- Other – 6

Procedure Time

Mean – 42.44 $\pm$ 0.45 minutes (95% CI – 33.0 – 35.0)

DAP

18.6750 $\pm$ 0.8309 mGy•m² (95% CI – 7.0460 – 20.3039)

Overall **Patient engagement scores** of 87.2% positive using a CAHPs type engagement survey instrument

The above data is consistent with previously reported data from the literature. Please note the above data is for previously diagnosed PAD requiring intervention consistent with the Consensus Guidelines on the

Treatment of Peripheral Artery Disease (2005). Patients were typically on medical management and/or had been prescribed exercise therapy.

Summary and Conclusions

There is a high prevalence of PAD in patients with CKD. Both asymptomatic and symptomatic PAD are powerful independent predictors for cardiovascular events such as myocardial infarction, stroke and cardiovascular death. There is also an increased incidence of these events in patients having only CKD. A combination of the two conditions magnifies the problem significantly. In spite of this association and increased risk, the evaluation of the CKD patient for PAD has received very little attention.

PAD is typically thought of as being associated with symptoms such as intermittent claudication; however, the majority of patients with this condition are asymptomatic. Unfortunately, asymptomatic PAD is also associated with serious adverse sequelae. The diagnosis of this condition has been standardized through the use of the ankle-brachial index (ABI) which is easily performed, reliable and noninvasive.

Management of the CKD patient with PAD should be directed at both the systemic disease and the ischemic extremity. Studies have shown that revascularization therapy is associated with a lower mortality rate than either no treatment or amputation even in cases with critical limb ischemia. Additionally, the requirement for subsequent amputation following revascularization is inversely related to the level of renal function present at the time of the primary procedure.

The current level of data presented in the medical literature clearly indicates that CKD patients would benefit significantly from an organized program of PAD screening and early institution of appropriate disease management principles.

As a member of the CardioVascular Coalition, we share their vision:

- Increased use of vascular care procedures can be associated with lower rates of amputations;
- Lowering the incidence of non-traumatic amputations through clinically appropriate intervention has the potential to reduce healthcare spending;
- Interventions that ultimately result in limb preservation offer the best possible clinical outcome;
- Vascular diagnostics are underutilized despite proven benefits of revascularization; and
- Patients with IC and CLI benefit from a comprehensive approach that can include risk factor modifications, exercise, and revascularization.

In addition to their comments, we wanted the opportunity to highlight the special needs of the renal patient in this compelling clinical scenario. Please contact me with any questions at (847) 388-2055.

Sincerely,

Richard Nee

General Manager, Lifeline Vascular Access

Lifeline Vascular Access Locations Providing Peripheral Arterial Disease Treatment

Vascular Health and Wellness, LLC	Albany	GA
Advanced Vascular Access Center	Bronx	NY
Dallas Vascular Center	Dallas	TX
Michigan Kidney Consultants	Southfield	MI
Michigan Kidney Consultants	Detroit	MI
East Side Vascular Access Center	Detroit	MI
Lifeline Dialysis Access Center	Allen Park	MI
Lifeline Vascular Center-Fort Lauderdale	Fort Lauderdale	FL
Fresno Nephrology Medical Group	Fresno	CA
Los Angeles Vascular Center	Inglewood	CA
West Tennessee Kidney Specialists	Jackson	TN
Vascular Access Centers	Las Vegas	NV
Greater Long Beach PAD	Long Beach	CA
Western Vascular	Mayaguez	PR
Lifeline Vascular and Interventional	Niceville	FL
Orange County Vascular AC	Orange County	CA
Desert Vascular Institute	Palm Desert	CA
Coastal Vascular and Interventional Ctr	Pensacola	FL
Quality Vascular Access Services	Elkins Park	PA
Metro Vascular Center	Philadelphia	PA
Virginia Surgical Vascular Center	Richmond	VA
Nephrology Associates Access Center	Riverside	CA
San Antonio Kidney Disease AC	San Antonio	TX
The Vascular Center at Westchester	Yonkers	NY

References

1. Selvin, E, Erlinger, TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. Circulation 2004; 110:738.
2. Diehm, C. [High morbidity rate, therefore: peripheral arterial disease screening from age 45 on! (interview by Dr. Ulrike Wepner)]. MMW Fortschr Med 2004; 146:10.
3. Meijer, WT, Hoes, AW, Rutgers, D, et al. Peripheral arterial disease in the elderly: The Rotterdam Study. Arterioscler Thromb Vasc Biol 1998; 18:185.
4. Golomb, BA, Dang, TT, Criqui, MH. Peripheral arterial disease: morbidity and mortality implications. Circulation 2006; 114:688.
5. Espinola-Klein, C, Rupprecht, HJ, Blankenberg, S, et al. Impact of infectious burden on extent and long-term prognosis of atherosclerosis. Circulation 2002; 105:15.
6. Hirsch, AT, Haskal, ZJ, Hertzer, NR, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 2006; 113:e463.
7. Foley, RN, Murray, AM, Li, S, et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. J Am Soc Nephrol 2005; 16:489.
8. Kanbay, M, Afsar, B, Gusbeth-Tatomir, P, Covic, A. Arterial stiffness in dialysis patients: where are we now? Int Urol Nephrol 2010; 42:741.
9. Chue, CD, Townend, JN, Steeds, RP, Ferro, CJ. Arterial stiffness in chronic kidney disease: causes and consequences. Heart 2010; 96:817.
10. Diehm, C, Schuster, A, Allenberg, JR, et al. High prevalence of peripheral arterial disease and co-morbidity in 6880 primary care patients: cross-sectional study. Atherosclerosis 2004; 172:95.
11. Greenland, P, Abrams, J, Aurigemma, GP, et al. Prevention Conference V: Beyond secondary prevention: identifying the high-risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing Group III. Circulation 2000; 101:E16.
12. Norgren, L, Hiatt, WR, Dormandy, JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg 2007; 45 Suppl S:S5.
13. McDermott, MM, Criqui, MH, Liu, K, et al. Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior tibial arterial pressures, and association with leg functioning in peripheral arterial disease. J Vasc Surg 2000; 32:1164.
14. Schroder, F, Diehm, N, Kareem, S, et al. A modified calculation of ankle-brachial pressure index is far more sensitive in the detection of peripheral arterial disease. J Vasc Surg 2006; 44:531.
15. Espinola-Klein, C, Rupprecht, HJ, Bickel, C, et al. Different calculations of ankle-brachial index and their impact on cardiovascular risk prediction. Circulation 2008; 118:961.
16. Liu, H, Shi, H, Yu, J, et al. Is chronic kidney disease associated with a high ankle brachial index in adults at high cardiovascular risk? J Atheroscler Thromb 2011; 18:224.

17. Ono, K, Tsuchida, A, Kawai, H, et al. Ankle-brachial blood pressure index predicts all-cause and cardiovascular mortality in hemodialysis patients. J Am Soc Nephrol 2003; 14:1591.
18. Hiatt, WR. Medical treatment of peripheral arterial disease and claudication. N Engl J Med 2001; 344:1608.
19. Orchard, TJ, Strandness, DE, Jr. Assessment of peripheral vascular disease in diabetes. Report and recommendations of an international workshop sponsored by the American Diabetes Association and the American Heart Association September 18-20, 1992 New Orleans, Louisiana. Circulation 1993; 88:819.
20. Young, MJ, Adams, JE, Anderson, GF, et al. Medial arterial calcification in the feet of diabetic patients and matched non-diabetic control subjects. Diabetologia 1993; 36:615.
21. Papamichael, CM, Lekakis, JP, Stamatelopoulos, KS, et al. Ankle-brachial index as a predictor of the extent of coronary atherosclerosis and cardiovascular events in patients with coronary artery disease. Am J Cardiol 2000; 86:615.
22. Tsai, AW, Folsom, AR, Rosamond, WD, Jones, DW. Ankle-brachial index and 7-year ischemic stroke incidence: the ARIC study. Stroke 2001; 32:1721.
23. Aronow, WS, Ahn, C. Prevalence of coexistence of coronary artery disease, peripheral arterial disease, and atherothrombotic brain infarction in men and women > or = 62 years of age. Am J Cardiol 1994; 74:64.
24. Murabito, JM, Evans, JC, Larson, MG, et al. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: the Framingham Study. Arch Intern Med 2003; 163:1939.
25. Belch, JJ, Topol, EJ, Agnelli, G, et al. Critical issues in peripheral arterial disease detection and management: a call to action. Arch Intern Med 2003; 163:884.
26. Newman, AB, Naydeck, BL, Sutton-Tyrrell, K, et al. The role of comorbidity in the assessment of intermittent claudication in older adults. J Clin Epidemiol 2001; 54:294.
27. Zheng, ZJ, Sharrett, AR, Chambless, LE, et al. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. Atherosclerosis 1997; 131:115.
28. Carter, SA. Indirect systolic pressures and pulse waves in arterial occlusive diseases of the lower extremities. Circulation 1968; 37:624.
29. Itaya, H, Shiba, M, Joki, N, Nakamura, M. Combined assessment of chronic kidney disease and subclinical peripheral artery disease used to predict future cardiac events. Nephrology (Carlton) 2010; 15:230.
30. Criqui, MH, Fronek, A, Barrett-Connor, E, et al. The prevalence of peripheral arterial disease in a defined population. Circulation 1985; 71:510.
31. Smith, FB, Lee, AJ, Price, JF, et al. Changes in ankle brachial index in symptomatic and asymptomatic subjects in the general population. J Vasc Surg 2003; 38:1323.
32. Ungprasert, P, Pornratanarangsi, S. Correlation between peripheral arterial disease and stage of chronic kidney disease. J Med Assoc Thai 2011; 94 Suppl 1:S46.
33. O'Hare, AM. Management of peripheral arterial disease in chronic kidney disease. Cardiol Clin 2005; 23:225.
34. Newman, AB, Shemanski, L, Manolio, TA, et al. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. The Cardiovascular Health Study Group. Arterioscler Thromb Vasc Biol 1999; 19:538.
35. Shlipak, MG, Fried, LF, Crump, C, et al. Cardiovascular disease risk status in elderly persons with renal insufficiency. Kidney Int 2002; 62:997.
36. O'Hare, AM, Glidden, DV, Fox, CS, Hsu, CY. High prevalence of peripheral arterial disease in persons with renal insufficiency: results from the National Health and Nutrition Examination Survey 1999-2000. Circulation 2004; 109:320.

37. Sarmento, C, Pereira, T, Maldonado, J, Conde, J. Peripheral artery disease and kidney function in hypertensive patients. Arq Bras Cardiol 2013; 100:362.
38. Wang, Y, Guo, X, Li, J, et al. Predictive value of ankle-brachial index to all-cause mortality and cardiovascular mortality in Chinese patients with chronic kidney disease. Vasa 2012; 41:205.
39. Al Zahrani, HA, Al Bar, HM, Bahnassi, A, Abdulaal, AA. The distribution of peripheral arterial disease in a defined population of elderly high-risk Saudi patients. Int Angiol 1997; 16:123.
40. Fishbane, S, Youn, S, Flaster, E, et al. Ankle-arm blood pressure index as a predictor of mortality in hemodialysis patients. Am J Kidney Dis 1996; 27:668.
41. Testa, A, Ottavioli, JN. [Ankle-arm blood pressure index (AABPI) in hemodialysis patients]. Arch Mal Coeur Vaiss 1998; 91:963.
42. O'Hare, AM, Bertenthal, D, Sidawy, AN, et al. Renal insufficiency and use of revascularization among a national cohort of men with advanced lower extremity peripheral arterial disease. Clin J Am Soc Nephrol 2006; 1:297.
43. Harrington, EB, Harrington, ME, Schanzer, H, Haimov, M. End-stage renal disease--is infrainguinal limb revascularization justified? J Vasc Surg 1990; 12:691.
44. Johnson, BL, Glickman, MH, Bandyk, DF, Esses, GE. Failure of foot salvage in patients with end-stage renal disease after surgical revascularization. J Vasc Surg 1995; 22:280.
45. Korn, P, Hoenig, SJ, Skillman, JJ, Kent, KC. Is lower extremity revascularization worthwhile in patients with end-stage renal disease? Surgery 2000; 128:472.
46. Lantis, JC, 2nd, Conte, MS, Belkin, M, et al. Infrainguinal bypass grafting in patients with end-stage renal disease: improving outcomes? J Vasc Surg 2001; 33:1171.
47. Lumsden, AB, Besman, A, Jaffe, M, et al. Infrainguinal revascularization in end-stage renal disease. Ann Vasc Surg 1994; 8:107.
48. Wassermann, RJ, Saroyan, RM, Rice, JC, Kerstein, MD. Infrainguinal revascularization for limb salvage in patients with end-stage renal disease. South Med J 1991; 84:190.
49. Whittemore, AD, Donaldson, MC, Mannick, JA. Infrainguinal reconstruction for patients with chronic renal insufficiency. J Vasc Surg 1993; 17:32.
50. O'Hare, AM, Feinglass, J, Sidawy, AN, et al. Impact of renal insufficiency on short-term morbidity and mortality after lower extremity revascularization: data from the Department of Veterans Affairs' National Surgical Quality Improvement Program. J Am Soc Nephrol 2003; 14:1287.
51. O'Hare, AM, Sidawy, AN, Feinglass, J, et al. Influence of renal insufficiency on limb loss and mortality after initial lower extremity surgical revascularization. J Vasc Surg 2004; 39:709.
52. Logar, CM, Pappas, LM, Ramkumar, N, Beddhu, S. Surgical revascularization versus amputation for peripheral vascular disease in dialysis patients: a cohort study. BMC Nephrol 2005; 6:3.