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Lower Extremity Amputation Risk Factors Associated With Elevated Ankle Brachial Indices and Radiographic Arterial Calcification

Eric Lew, DPM, AACFAS [1], Nicole Nicolosi, DPM [1], Georgeanne Botek, DPM, FACFAS [2]

[1] *Resident, Department of Podiatric Medicine and Surgery, Kaiser Permanente Medical Center–Cleveland Clinic, Cleveland, OH*
[2] *Staff, Orthopaedic and Rheumatologic Institute, Cleveland Clinic, Cleveland, OH*

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ABSTRACT

An elevated ankle brachial index (ABI) resulting from medial artery calcification, or Mönckeberg's arteriosclerosis, is commonly seen in patients with diabetes mellitus or end-stage renal disease. Recent data have found an association between elevated ABIs and cardiovascular morbidity and mortality. The purpose of the present study was to evaluate the prognostic significance of high ABIs, poorly compressible arteries, and radiographic artery calcification compared with low ABIs in predicting lower extremity amputation and morbidity. A retrospective review was conducted of patients who had undergone a lower extremity amputation from July 1, 2011 to August 31, 2012. A total of 129 patients (140 lower extremity amputations) were categorized into 3 groups: a low ABI (<0.9), a normal ABI (0.9 to 1.3), and a high ABI (>1.3) or poorly compressible arteries. Of the 129 patients, 31 (22.14%), 36 (25.71%), and 73 (52.14%) were in group 1, 2, and 3, respectively. The prevalence of diabetes was greatest in group 2 ($p = .016$). A high percentage of radiographic arterial calcification was found in all 3 groups ($p = .003$). Statistically significant differences were also found in groups 1 and 3 for peripheral arterial disease ($p < .001$), chronic kidney disease ($p < .001$), coronary artery disease ($p = .021$), revascularization history ($p < .001$), and tobacco use ($p = .012$). A U-shaped relationship between the ABI and comorbidity was found, suggesting an elevated ABI is as equally prognostic as a low index in predicting the need for amputation.

Medial artery calcification (MAC), or Mönckeberg's arteriosclerosis, is calcification of the tunica media of medium-size vessels and affects patients with diabetes mellitus (DM) or end-stage renal disease. The pathogenesis of MAC is believed to stem from multifactorial etiologies promoting the osteogenic process involved in calcinosis formation in vascular smooth muscle cells (1,2). MAC is not associated with luminal obstruction; however, a decrease occurs in arterial vessel wall elasticity and compliance, which can lead to a reduction in perfusion and formation of atherosclerosis. Patients with MAC and concomitant intimal calcinosis or peripheral arterial disease (PAD) might have even greater malperfusion in the lower extremity (LE) and an associated poorer prognosis. PAD in these patients is difficult to diagnosis using the noninvasive ankle brachial index (ABI) secondary to the noncompressible nature of the increased arterial wall stiffness (3–5). An ABI is elevated in the presence of MAC and incompressible vessels (3,4).

The clinical significance of an elevated ABI is not as well understood as that of a low ABI and its association with PAD (5). Recent studies have suggested that patients with an elevated ABI have a greater risk of cardiovascular morbidity and mortality and that it should be considered a PAD equivalent (3,5–8). Other studies have indicated that an elevated ABI and the radiographic presence of MAC are significant risk factors for LE complications (7–12). The purpose of the present retrospective cohort study was to evaluate the prognostic significance of high ABIs, poorly compressible arteries (PCAs), and radiographic artery calcification (RAC) compared with a low ABI for LE amputation and morbidity in these patient populations. We hypothesized that a high ABI, PCA, and RAC would be significant clinical findings associated with high rates of LE amputation and poor healing.

Patients and Methods

The present study was a 13-month retrospective review of adult LE amputations distal to the knee performed within the Foot and Ankle section of the Orthopedics and Vascular Surgery departments from July 1, 2011 to August 31, 2012 at the Cleveland Clinic (Cleveland, OH). This investigation was conducted with institutional review board approval. LE amputation surgical cases were identified from an electronic medical record database. We explored the distribution of ABIs and evaluated the variables for an association with the ABI. The patients who had been diagnosed with PAD, DM, or chronic kidney disease (CKD) according to their electronic medical record were

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Address correspondence to: Eric Lew, DPM, AACFAS, Department of Podiatric Medicine and Surgery, Kaiser Permanente Medical Center–Cleveland Clinic, 9500 Euclid Avenue, NA-40, Cleveland, OH 44195.
E-mail address: eric.j.lew@dmu.edu (E. Lew).

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Fig. 1. An anteroposterior radiograph demonstrating medial artery calcification involving multiple pedal arteries in a patient with diabetes mellitus and chronic kidney disease.

Fig. 2. A lateral radiograph demonstrating intimal and medial artery calcification in the tibial arteries of a patient with end-stage renal disease.

included for review. The diagnosis of PAD was determined from the patient's clinical history, physical examination findings, and the results of noninvasive vascular studies, including an ABI of <0.9. When the ABI was considered unreliable, other noninvasive vascular studies, such as the arterial duplex, pulse volume recordings, toe perfusion pressure, or transcutaneous oximetry, were used. We excluded amputations resulting from trauma, digital deformity, vasculitic or rheumatologic conditions, cancer, clotting disorders, or pulmonary transplantation. Additionally, we excluded those without a complete noninvasive arterial evaluation.

The patient age and sex were recorded. The preoperative ABIs were categorized into 1 of 3 groups: a low ABI (<0.9); a normal ABI (0.9 to 1.3); and a high ABI (>1.3) or PCA. The presence of RAC as demonstrated using plain radiography or computed tomography angiography. Also, whether perioperative revascularization procedures had been conducted was also recorded. The other comorbidities reviewed included coronary artery disease (CAD), myocardial infarction (MI), hypertension, dyslipidemia (HLD), polyneuropathy, and tobacco use. The recorded complications included additional proximal amputation or a nonhealing amputation site, defined as a healing time >30 days. Ischemia and infection were closely evaluated as a primary cause of complications. The outcomes of the present study were determined from a review of the medical records. Each case was reviewed by 2 of us (E.L., N.N.).

Statistical Analysis

Descriptive statistics were computed comparing the 3 ABI groups. The continuous variables are presented using the mean ± standard deviation and the categorical variables as counts and percentages. The associations between the categorical variables and ABI ranges were tested using either Pearson's chi-square test or Fisher's exact test. The latter test was used for situations in which small cell counts made the assumptions of the chi-square test questionable.

Significant associations were explored using multiple comparisons between the ABI ranges to identify exactly which ranges differed. Pairwise comparisons of the average age among the ABI ranges were performed using linear model estimates of the differences for each of the 3 pairs of ranges (normal versus low, high versus low, and high versus normal). Pairwise comparisons of the odds of each feature among the ABI ranges were performed using either the chi-square or Fisher exact test with 2-by-2 subtables, as appropriate. The p values for each family of tests were adjusted using Holm's step-down procedure to obtain the desired family-wise error rate. All analyses were performed using R software, version 2.15.4 (R Project for Statistical Computing, Vienna, Austria). A significance level of .05 was used for all testing.

Results

A total of 155 patients had undergone ≥1 LE amputations at or below the knee from July 1, 2011 to August 31, 2012 within the Foot and Ankle and Vascular Centers at the Cleveland Clinic. The total number of cases was 168. After applying the exclusion criteria, we arrived at a final study sample of 129 patients and 140 LE amputations. The average patient age was 67 years, and 76% of the patients were male. The average follow-up length was 14.08 weeks. Of these LE amputation cases, 31 (22.14%) had a low ABI (<0.9; group 1), 36 (25.71%) had a normal ABI (0.9 to 1.30; group 2), and 73 (52.14%) had a high ABI (>1.3) or PCA (group 3).

DM was present in 101 cases (72.1%), PAD in 106 (75.7%), and CKD in 75 (52.1%). RAC (Figs. 1 and 2) was present in 129 cases (92.1%; $p < .003$). The incidence of DM was most prevalent in group 2 (88.89%; $p = .016$; Table 1). However, the incidence of DM was also high in groups 1 and 3 (58.06% and 69.86%, respectively). From the pairwise comparisons of the average age among the ABI ranges, the patients with a low ABI were significantly older than were the patients with a normal or high ABI ($p < .004$). However, no significant differences were found in the average age of those in the normal and high ABI groups. Estimates for the differences in the average age were also computed. From these, we estimated that patients with a low ABI were on average 9.3 years older than were patients with a normal ABI and 6.7 years older than were patients with a high ABI.

PAD was most prevalent in groups 1 (96.77%) and 3 (84.93%; $p < .001$). The incidence of CKD was significantly greater in groups 1 (54.84%) and 3 (65.75%; $p < .001$). The incidence of perioperative revascularization ($p < .001$), CAD ($p = .021$), and tobacco usage