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The value of Doppler waveform analysis in predicting major lower extremity amputation among dialysis patients treated for diabetic foot ulcers☆

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ABSTRACT

Aims: This study examined the predictors for lower extremity amputation (LEA) in patients with diabetic foot ulcers according to kidney function and, in the case of dialysis patients, specifically evaluated the vasculature with the ankle–brachial index (ABI) and Doppler waveforms.

Methods: Among 658 diabetic patients admitted to the Diabetic Foot Care Center, 286 had an estimated glomerular filtration rate (eGFR) $\geq$ 60 ml/min per 1.73 m^2, 275 had an eGFR $<$ 60, and 97 patients were under maintenance dialysis. All clinical variables were analyzed. A specialist retrospectively reviewed Doppler images of 78 of the patients in dialysis to evaluate peripheral arterial disease.

Results: Forty-two percent of patients with eGFR $<$ 60 presented with ABI $\leq$ 0.90. For ABI values $>$ 1.40, the proportion of dialysis patients (31.3%) was greater than the proportion of patients with eGFR $<$ 60 (5.3%). Wagner wound classifications, reduced serum albumin levels, and low ABI values were the predictors for major LEA among patients in the non-dialysis groups. Nevertheless, these indicators were not predictive of the risk of amputation in diabetic patients on dialysis. The presence of poor monophasic waveforms in the dorsalis pedis artery or posterior tibial artery served as an independent predictor (odds ratio: 7.61; $P = 0.008$) for major LEA among dialysis patients. The sensitivity and specificity were 88.0% and 59.6%, respectively.

Conclusions: Poor monophasic Doppler waveforms of below-the-knee arteries, commonly found among dialysis patients in treatment for diabetic foot ulcers, can serve as an independent predictor for major LEA.

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Abbreviations: CFA, common femoral artery; SFA, superficial femoral artery (proximal segment); PA, popliteal artery; PTA, posterior tibial artery (distal segment); DPA, dorsalis pedis artery.
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1. Introduction

Diabetic patients with chronic kidney disease (CKD) tend to suffer foot ulceration that subsequently requires lower extremity amputation (LEA) [1–3], which is mainly associated with peripheral arterial disease (PAD) [2,3]. The convenience and effectiveness of the ankle–brachial index (ABI) measurements has led to its frequent use for PAD evaluation [4,5]. An ABI equal to 0.90 or less has been considered indicative of atherosclerosis in peripheral arteries, and a value greater than 1.40 is considered indicative of incompressible stiffness or medial calcification in the lower limb arteries [4,5]. However, when the arteries exhibit both stiffness and stenosis, the ABI values are confounded and their diagnostic sensitivity reduced [6,7]. Noncompressible ABI values are commonly observed in diabetic patients, especially those with advanced CKD [8–10]. Although a lower ABI has been proven to predict amputation outcome in patients with diabetic foot ulcers (DFU) [11], its applicability has never been proven among diabetic patients with advanced CKD.

Several non-invasive measurements such as the toe-brachial index, transcutaneous oxygen pressure, segmental pressures, pulse volume recordings, and Doppler waveform analysis were recommended for evaluating PAD in patients with noncompressible ABI values according to Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II) [5] and the guideline from the American Heart Association [4]. Doppler waveform analysis during duplex ultrasonography has the merit of quantitatively localizing stenosis by measuring the blood flow of lower extremity arteries [12].

In this study, we stratified patients with DFU in different stages of CKD and retrospectively reviewed the color Doppler images of the patients group with high prevalence of arterial stiffness. In addition to elucidate the characteristics of PAD in each group, we also identify the predictors for amputation.

2. Materials and methods

2.1. Study subjects, clinical information, and management of foot ulcers

From January 2009 to December 2010, 658 patients hospitalized consecutively for limb-threatening foot ulcers [13] in the Diabetic Foot Care Center at Chang Gung Memorial Hospital were enrolled. The Institutional Review Board of Chang Gung Memorial Hospital approved the study protocol (No. 101-0826B). The medical history included information on the patient's age, sex, body mass index, duration of diabetes, concurrent cardiovascular disease, cigarette smoking, initial Wagner grading of the foot lesion, and initial laboratory data (hemoglobin, leukocytes, C-reactive protein, serum albumin, serum creatinine, glycated hemoglobin [HbA1c], low-density lipoprotein cholesterol [LDL cholesterol], high-density lipoprotein cholesterol [HDL cholesterol], total cholesterol, and triglycerides). Foot lesions were graded according to the Wagner classification: grade 0 (absence of skin lesions and hyper-keratosis below or above bony prominences); grade 1 (skin and immediate subcutaneous tissue ulceration); grade 2 (deeper lesions that may penetrate to the tendon, bone, or joint capsule); grade 3 (deep tissue involvement, with the possibility of osteomyelitis); grade 4 (gangrene of some portion of the toes or forefoot); and grade 5 (the entire foot is gangrenous) [14].

All patients were under the care of a multidisciplinary team of diabetologists; cardiologists; vascular, plastic, and orthopedic surgeons; nutritionists; and nursing personnel [11,15]. Major decisions, including those related to revascularization and amputation, were made according to current guidelines [4,5,16] and team consensus for individualized treatment [11,15]. A minor LEA was defined as any amputation distal to the ankle joint, while a major LEA was defined as any amputation through or proximal to the ankle joint.

All diabetic patients were divided into 3 groups: 286 subjects had an estimated glomerular filtration rate (eGFR) of $\geq$60 ml/min per 1.73 m^2 (eGFR $\geq$ 60 group), 275 subjects had eGFR of $<$60 ml/min per 1.73 m^2 but were not on dialysis (eGFR $<$ 60 group), and 97 subjects had end-stage renal disease and were on maintenance dialysis therapy (dialysis group: 91 on hemodialysis and 6 on peritoneal dialysis). The eGFR was calculated using the Modification of Diet in Renal Disease Study equation: 175 $\times$ serum creatinine (exp[$-$1.154]) $\times$ age (exp[$-$0.203]) $\times$ (0.742 if female) [17].

2.2. Color duplex ultrasound scan and ABI measurements

Measurements for the duplex ultrasound scan and ABI were simultaneously obtained as part of the standardized assessment in all our patients. These examinations were performed by cardiologists within 7 days of admission [15]. Patients rested in a supine position until a stable blood pressure was obtained for at least 5 min. ABI values obtained from the side with the lesion were categorized into 3 groups according to the latest guidelines from American Heart Association [4]. ABI values from 0.91 to 1.40 were considered normal, ABI values $\leq$ 0.90 were considered indicative of occlusive PAD, and ABI values $>$ 1.40 suggested noncompressible arteries or arterial stiffness.

Duplex ultrasound scans were performed using a Hitachi Aloka ProSound ALPHA 7 Premier machine (Aloka, Tokyo, Japan). A linear array transducer (UST-5412; frequency range, 5–13 MHz, Aloka, Tokyo, Japan) was used to survey 5 arterial segments, including the common femoral artery (CFA), the proximal segment of the superficial femoral artery (SFA), the popliteal artery (PA), the distal segment of the posterior tibial artery (PTA), and the dorsalis pedis artery (DPA). The detection points for these arteries were 10–20 mm proximal and distal to the femoral bifurcation, over the popliteal fossa, behind the medial malleolus, and at the dorsum of the foot, respectively. Arteries below-the-knee (BTK) were defined as either PTA or DPA. Images of Doppler waveforms were obtained at midstream of the vessel at an angle of $<60^\circ$ [18].

2.3. Color images of Doppler waveform analysis for dialysis patients

In the more than 31% of the individuals in the dialysis group with an ABI $>$ 1.40, the arterial stiffness significantly decreased