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The ankle brachial index is associated with prognosis in patients with diabetic kidney disease

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ABSTRACT

Aims: Peripheral arterial disease (PAD) could be an additional risk factor for the clinical outcomes in different populations. The purpose of this study was to evaluate the influence of PAD on patients with diabetic kidney disease.

Methods: 362 persons with type 2 diabetes were followed-up for a mean 4.8 years grouped by ankle brachial index (ABI) (<0.9 vs. ≧0.9) and albuminuria (with or without). Primary and secondary outcomes were composite events (all-cause mortality, hospitalization for coronary artery disease, stroke, re-vascularization, amputation, and diabetic foot) and all-cause mortality.

Results: Inter-group differences in duration of diabetes, glycated hemoglobin, creatinine, and estimated glomerular filtration rate were significant. During the follow-up period, 53 composite events were recorded (14.7%) and 13 (3.5%) individuals died. Subjects with albuminuria plus ABI < 0.9 had higher risk of composite events than those with albuminuria but normal ABI ($p < 0.05$). The only trend difference between the two groups was in all-cause mortality. Albuminuria plus ABI <0.9 was associated with risk of composite events (hazard ratio [HR] 4.20, 95% confidence interval [CI] 1.77–9.92, $p = 0.001$) and all-cause mortality (HR 17.77, 95% CI 1.93–162.20, $p = 0.011$).

Conclusions: PAD might be an additional risk factor for adverse outcomes in patients with diabetic kidney disease. Further prospective data are required to validate this conclusion.

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1. Introduction

Globally, diabetes mellitus affected 371 million people in 2012 and this number is expected to increase to 552 million by 2030 [1,2]. Diabetic kidney disease, which is defined as albuminuria or decline of glomerular filtration rate, is a chronic microvascular complications of diabetes and the leading cause of hemodialysis in developed country [3]. Increasing urinary albumin excretion is also a strong risk factor for cardiovascular disease [4].

Type 2 diabetes mellitus is considered to be an independent risk factor for coronary artery disease (CAD) and peripheral arterial disease (PAD), whose risk is doubled [5–7]. Peripheral artery disease is clinically diagnosed by ABI, calculated as a ratio of ankle to arm systolic blood pressure, with a result of less than 0.9 being an independent predictor of cardiovascular and cerebrovascular events [8,9]. Furthermore, type 2 diabetes patients with PAD or peripheral arterial stiffness had 4.85 times more risk of major adverse cardiovascular events, defined as a composite of all-cause mortality, nonfatal myocardial infarction, repeated coronary revascularization, and ischemic stroke, compared to patients without diabetes and abnormality of ABI [10]. However, whether PAD could be a risk factor in addition to other complications is still controversial [11,12]. Accumulating evidence shows the association between PAD and prognosis is weaker in patients with type 2 diabetes compared to those without type 2 diabetes [13]. The aim of this study is to evaluate whether the co-morbidity of PAD influenced prognosis of a population with diabetic kidney disease.

2. Materials and methods

2.1. Patient population and clinical data

This was a retrospective chart review study and ethic approval is provided by the Taipei Veterans General Hospital, Taiwan (VGHIRB no.: 2012-07-029BC). Demographic and anthropometric characteristics, history of coronary artery disease or cerebrovascular disease, ABI of patients with type 2 diabetes, visiting the division of endocrinology and metabolism of Taipei Veterans General Hospital from July 1, 2005 to December 31, 2007, were reviewed. All ABI measurements were recorded using an Omron non-invasive vascular screening device (VP-1000, Omron Masusaka Company, Japan) for the purpose of screening for PAD. The pulse pressure was defined as the difference between systolic and diastolic blood pressure. Body mass index was calculated as the weight (kg) divided by the square of height (meters). The laboratory results within 3 months of ABI measurement, including HbA1C, serum creatinine, both baseline and updated results of estimation of glomerular filtration rate (eGFR) calculated by formula of the Modification of Diet in Renal Disease (MDRD) within months before the end of analysis, lipid profiles, and two consecutive daily urinary albumin excretion at the time of recruitment and within 6 months before the end of the outcome-analysis were recorded.

2.2. Groups and outcome definition

Enrolled patients were divided into 4 groups according to the combination of status of albuminuria (with or without albuminuria) and ABI (more or less than 0.9). To prevent interference from subjects with arterial stiffness as opposed to stenosis, subjects with ABI $>$ 1.3 were excluded in this study. Albuminuria was defined as daily urinary albumin excretion more than 30 mg. Outcomes up to August 31, 2011, were retrospectively reviewed. The primary outcomes were composite events which included all-cause mortality, hospitalization for CAD, stroke, carotid or peripheral revascularization, lower limb amputation, and hospitalization for diabetic foot, and the secondary outcome was all-cause mortality. The diabetic foot was defined as cellulitis or ulceration of lower extremities. For subjects with ABI $<$ 0.9, it was necessary to have concordance between the side with ABI $<$ 0.9 and diabetic foot.

2.3. Statistics

Continuous variables were expressed as mean $\pm$ standard deviation (SD) and were compared using an independent ANOVA test. The categorical variables were expressed as numbers and percentages and were compared using the Pearson chi-square test. The cumulative event free probabilities of primary and secondary outcomes were estimated using Kaplan–Meier analysis. The log-rank test was used to identify significant differences. All relevant variables were tested by univariate Cox proportional analysis and those with $p < 0.1$ were further subjected to multivariate Cox proportional analysis and HR with corresponding probability values were calculated. The SPSS software package (version 18, IBM Corporation, Armonk, N.Y., USA) was used for data analysis.

3. Results

3.1. Baseline characteristics

365 subjects were enrolled but 3 were excluded because ABI was more than 1.3. We analyzed the charts of 362 individuals with type 2 diabetes who were followed up for a mean duration of 4.8 years. Table 1 showed patients' baseline characteristics of the 4 groups. There were 191 patients in the group without albuminuria and ABI of $\geqq$0.9, 20 in the group without albuminuria but ABI of $<$0.9, 125 subjects with albuminuria and ABI $\geqq$ 0.9, and 26 individuals with albuminuria and ABI $<$ 0.9. There were significant differences among the 4 groups in duration of diabetes, HbA1C, creatinine, baseline and final eGFR, decline of GFR, and increment of daily urine albumin. Increment of daily urine albumin was found in 133 patients and decline of eGFR was observed in 267 subjects. The duration of diabetes, HbA1C, and daily urinary albumin excretion were significantly longer and higher in subjects with albuminuria and ABI $<$ 0.9. Furthermore, renal function, assessed according to serum creatinine and eGFR, was worse in subjects with albuminuria and ABI $<$ 0.9.

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