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ORIGINAL ARTICLE

Risk factors of accelerated progression of peripheral artery disease in hemodialysis

Shang-Reu Hsu [a], Ho-Ming Su [b,c], Ming-Chia Hsieh [a], Shin-Li Su [a], Szu-Chia Chen [d,*], Hung-Chun Chen [d,e]

[a] *Division of Endocrinology and Metabolism, Department of Medical, Changhua Christian Hospital, Changhua, Taiwan*
[b] *Division of Cardiology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*
[c] *Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[d] *Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*
[e] *Faculty of Renal Care, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*

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Abstract Ankle-brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) are markers for peripheral artery occlusive disease (PAOD) and arterial stiffness, respectively. The aims of this study were to assess whether PAOD and arterial stiffness progressed and to determine the risk factors for ABI and baPWV progression in patients on hemodialysis. This study enrolled 173 routine patients on hemodialysis. Both ABI and baPWV were measured by an ABI-form device at baseline and at 1 year of follow-up. Progression in ABI was defined as reduction in ABI exceeding 0.3, while baPWV measured at 1 year of follow-up exceeding that at baseline indicated baPWV progression. Comparison with baseline data showed increase in both prevalence of ABI < 0.9 ($p = 0.045$) and baPWV ($p = 0.028$) at 1 year of follow-up. Multiple linear regression analyses identified high fasting glucose and old age as independent factors of annual change in ABI and baPWV, respectively. Good control of blood sugar may contribute to delay the progression of peripheral artery disease in patients on hemodialysis.

* Corresponding author. Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, 100 Tzyou First Road, Kaohsiung 807, Taiwan.
E-mail address: scarchenone@yahoo.com.tw (S.-C. Chen).

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Introduction

A high prevalence of peripheral artery occlusive disease (PAOD) and increased artery stiffness have been reported in the end-stage renal disease (ESRD) population and are associated with increased morbidity and mortality [1—4]. There is growing evidence that uremia may predispose sufferers to PAOD progression and increased arterial stiffness with multiple pathogenic mechanisms involved, including deranged calcium/phosphate balance, secondary hyperparathyroidism, homocysteine, lipoprotein(a) metabolism, fluid overload, alterations in the angiotensin and endothelin systems, malnutrition, uremic toxins, oxidative stress, insulin resistance, and alterations in inflammatory and coagulation pathways [4,5].

A clinical device has been developed to automatically and simultaneously record the pulse waves of the brachial and posterior tibial arteries, using an automated oscillometric method. Using this device, we can easily and automatically calculate the ankle-brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) [6,7]. ABI has been reported to be a good marker for atherosclerosis and an ABI of <0.9 was useful in the diagnosis of PAOD [8—10], while baPWV has been taken as a good marker for arterial stiffness [11,12]. Previous cross-sectional studies have identified the risk factors of PAOD and increased artery stiffness in advanced chronic kidney disease and patients on hemodialysis, including old age, hypertension, diabetes mellitus (DM), previous coronary artery disease, previous cerebrovascular disease, wider pulse pressure, hyperlipidemia, malnutrition, and smoking [4,13,14]. However, there have been few studies evaluating the progression of PAOD and arterial stiffness longitudinally, or determining the risk factors of ABI and baPWV progression in patients on hemodialysis in Taiwan, an area with the highest prevalence of ESRD [15]. The aims of the present study were to assess the progression in PAOD and arterial stiffness and to determine the risk factors for ABI and baPWV progression in patients on hemodialysis.

Methods

Study design and participants

This is a prospective and observational study conducted at a single dialysis clinic in a regional hospital in Taiwan. All routine patients on hemodialysis in this hospital were included, except two patients who refused to be examined by an ABI-form device, four patients with atrial fibrillation, and six patients with both legs amputated due to complications of DM. Initially, 196 patients (91 men and 105 women) were included in this study. The ABI was measured twice within 1 year. During the follow-up period, 11 deaths were recorded in these 196 patients (5.6%), 10 patients were transferred to other hospitals, and two patients refused further examinations. Finally, 173 patients (80 men and 93 women) completed the study. The protocol was approved by our Institutional Review Board and all enrolled patients gave written, informed consent.

Hemodialysis

All patients underwent routine hemodialysis three times a week using a Toray 321 machine (Toray Medical Company, Tokyo, Japan). Each hemodialysis session lasting 3—4 hours was performed using a dialyzer with a blood flow rate of 250-300 mL/minute and a dialysate flow rate of 500 mL/minute.

Assessment of ABI and baPWV

Both ABI and baPWV might be influenced by hemodialysis [16]; hence, all measurements were made 10—30 minutes before hemodialysis. The measurements were taken using an ABI-form device (VP1000; Colin Co. Ltd., Komaki, Japan) [6,7,17] in a room with a temperature of around 25°C following a 5-minute rest upon arrival at the clinic. Occlusion and monitoring cuffs were placed tightly around the upper arms without blood access and with both sides of the lower extremities in the supine position. Dividing the ankle systolic blood pressure by the arm systolic blood pressure gave the ABI and the lower value of the ankle systolic blood pressure was used in the calculation. For measuring baPWV, pulse waves obtained from the brachial and tibial arteries were recorded simultaneously, and the transmission time, defined as the time interval between the initial increase in brachial and tibial waveforms, was determined. The transmission distance from the arm to each ankle was calculated according to body height. The baPWV value was automatically computed as the transmission distance divided by the transmission time. After obtaining bilateral baPWV values, the highest one was taken as the representative value for each participant. Both ABI and baPWV measurements were made at baseline and at the 1 year of follow-up. The automatic device and its reproducibility have been validated in previous research [17].

Collection of demographic, medical, and laboratory data

Demographic and medical data including age, sex, smoking history, and comorbidities were obtained from medical records and interviews with patients. Body mass index (BMI) was calculated as the ratio of weight in kilograms divided by the square of height in meters. Laboratory data were obtained from fasting blood samples using an autoanalyzer (Roche Diagnostics GmbH, D-68298 COBAS Integra 400, Mannheim, Germany). High-sensitivity C-reactive protein (Dade Behring Marburg GmbH, Germany) was measured using commercially available kits. Serum intact parathyroid hormone concentration was evaluated using a commercially available two-sided immunoradiometric assay (CIS Bio International, Gif Sur Yvette, France). Blood samples were centrifuged within 1 hour of collection and frozen at −20°C until analysis. Plasma homocysteine levels were determined by fluorescence polarization immunoassay using an IMx Homocysteine kit (Abbott Laboratories, Abbott Park, IL, USA). Blood samples were obtained within 1 month of enrollment. In addition, information regarding patient medications including aspirin, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, β-blocker, calcium channel blocker, and HMG-CoA reductase