PREVALENCE AND CORRELATION FACTORS OF PERIPHERAL ARTERIAL DISEASE IN HEMODIALYSIS PATIENTS DEFINED BY ANKLE-BRACHIAL INDEX (ABI)

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Background: Cardiovascular diseases including peripheral arterial disease (PAD) are highly prevalent among hemodialysis patients. PAD is one of the important manifestations of systemic atherosclerosis and is related to poorer quality of life among patients with end-stage renal disease (ESRD). In this study, we evaluated the prevalence and correlation factors of PAD in hemodialysis patients using the ankle-brachial index (ABI).

Method: We enrolled 68 patients including 21 DM patients with ESRD undergoing hemodialysis. PAD was defined by an ABI of ≤ 0.9. Correlation factors including DM, age, hemodialysis duration (vintage), albumin level, Kt/V, Ca × P production, and iPTH were analyzed.

Results: We found that the DM group has higher rate of PAD than the all-patients group (non-DM + DM) (PAD/total: 32% vs. DM with PAD/DM, 55%, p < 0.05). There was no significant difference in ABI value for the all-patients group with different dialysis durations. However, the difference in ABI value between non-DM patients on dialysis for less than 1 year and those on dialysis for more 10 years was significant (p < 0.05). There was no significant difference in ABI value between patients of different ages for both all-patients and non-DM patients groups. The PAD group had significantly lower albumin level than the non-PAD group (p < 0.05). There were no significant differences in Kt/V, Ca × P production and iPTH values between the PAD and non-PAD groups.

Conclusion: In this study, PAD was more prevalent among DM patients on hemodialysis. The albumin level was significantly lower in the PAD group. The ABI value was significantly lower in non-DM patients on dialysis for more than 10 years than in those on dialysis for less than 1 year. (Acta Nephrologica 2010; 24: 42-46)

Key words: Peripheral arterial disease, ankle-brachial index, hemodialysis.

INTRODUCTION

Uremic patients on hemodialysis are associated with higher incidence of cardiovascular morbidity and mortality.\textsuperscript{1,2} Cardiovascular diseases include coronary artery disease, congestive heart failure, and peripheral arterial disease (PAD). PAD refers to obstructive atherosclerosis of lower extremities and is traditionally defined by an ankle-brachial index (ABI) of ≤ 0.9.\textsuperscript{3} It is an important manifestation of systemic atherosclerosis and results in poorer quality of life among patients with end-stage renal disease (ESRD).\textsuperscript{4,5}

Diabetes mellitus (DM), aging, cigarette smoking, hypertension, and hyperlipidemia are risk factors for PAD in non-ESRD patients.\textsuperscript{6,7} Cheung et al. and O’Hare et al. observed that smoking, DM, aging, duration of dialysis, serum albumin level, parathyroid hormone (PTH), Kt/V may be associated with PAD in ESRD patients on hemodialysis.\textsuperscript{7,8} ABI is a non-invasive and reliable diagnostic test for PAD. ABI of 0.9 or less is about 95% sensitive and 100% specific values for PAD detection.\textsuperscript{9,10} In this study, we used ABI to evaluate prevalence and correlation factors of PAD in hemodialysis patients.

MATERIALS AND METHODS

Patients and Independent Variables

We included a systemic sample of patients who were on hemodialysis at Sinlau Hospital, Tainan, Taiwan in October 2007. The study population consisted of 68
patients. The inclusion criteria were as follows: written informed consent, ABI measurement made, and availability for periodical follow-up visits for one year. The mean age of subjects was 64 ± 11 years. There were 26 male and 42 female, among which 21 had DM. The exclusion criterion was liver cirrhosis.

The variables studied included age, calcium × phosphorus product values (mg²/dl²), iPTH (pg/ml) levels, albumin (g/ml) levels, dialysis duration, and Kt/V. Kt/V was determined according to the procedure proposed by Daugirdas JT.\textsuperscript{11}

**ABI Measurement**

The ABI measurement was performed as described by Ono et al.\textsuperscript{12} In brief, ABI was determined in all participants using the ABI-form (VS-1000, Colin, Japan), which measures BP from bilateral arm and ankle (brachial and posterior tibial arteries, respectively) simultaneously by an oscillometric method. The BP was measured before performing hemodialysis. The patients were at rest in supine position for at least 15 min for the BP to stabilize. The systolic pressure of the arm without dialysis access and the lower value of the ankle systolic pressure were used for the calculation. ABI was calculated by the ratio of the ankle systolic pressure divided by the arm systolic pressure. The ABI was assessed once in each patient. Patients having ABI of 0.9 or less were defined as having PAD.

**Statistical Analyses**

Data were expressed as mean ± SD. The one-way analysis of variance (one-way ANOVA) was performed for ABI associated with dialysis duration and age. If the difference in ANOVA results was significant, the unpaired t-test was performed between groups. Other group comparisons were performed by unpaired t-test. P < 0.05 was considered significant.

**RESULTS**

**Prevalence of PAD**

Among all patients, 22 were found to have PAD according to ABI measurement. There were 12 patients with DM in these 22 PAD patients. The PAD percentage in the all-patients group (non-DM + DM) was 32%, while that among DM patients was 55%. There was significant difference in PAD prevalence between the all-patients and DM groups (p < 0.05) (Fig. 1).

**Correlation between ABI values and dialysis duration**

Fig. 2 shows the relationship between ABI value and dialysis duration in both groups. As shown in Panel A (p > 0.05), the mean ± SD of ABI in the all-patients (non-DM + DM) group was as follows: duration < 1 year, 1.04 ± 0.13; duration 1-5 years, 0.90 ± 0.27; duration 6-10 years, 1.02 ± 0.20; and duration > 10 years, 0.94 ± 0.13. As shown in Panel B (p < 0.05), the mean ± SD of ABI in the non-DM group was as follows: duration < 1 year,
1.10 ± 0.13; duration 1-5 years, 0.96 ± 0.23; duration 6-10 years, 1.04 ± 0.21; and duration > 10 years, 0.93 ± 0.12. There was no significant difference in ABI value among all patients with different dialysis durations, but the difference in ABI value between non-DM patients on dialysis for less than 1 year and those on dialysis for more than 10 years was significant (p < 0.05).

**Correlation between ABI values and age**

The mean ± SD of ABI for all patients (non-DM + DM) of different age groups was as follows: 40-50 y/o, 1.04 ± 0.09; 51-60 y/o, 1.10 ± 0.21; 61-70 y/o, 0.96 ± 0.20; and > 70 y/o, 0.83 ± 0.30 (p > 0.05). The mean ± SD of ABI for non-DM patients of different age groups was as follows: 40-50 y/o, 1.04 ± 0.09; 51-60 y/o, 1.00 ± 0.24; 61-70 y/o, 1.03 ± 0.13; and > 70 y/o/0.90 ± 0.26 (p > 0.05). As can be seen, the difference in ABI value for all patients and non-DM patients of different age groups was not significant.

**Albumin level in PAD and non-PAD**

Albumin level was found to be lower in the PAD group than in the non-PAD group (PAD: 3.47 ± 0.31 vs. non-PAD: 3.61 ± 0.35; p < 0.05). The difference was statistically significant (Fig 3).

**Kt/V, Ca × P, and iPTH values in PAD and non-PAD**

Kt/V value was found to be higher in the PAD group than in the non-PAD group (PAD: 1.88 ± 0.10 vs. non-PAD: 1.78 ± 0.09; p > 0.05). Ca × P value was lower in the PAD group than in the non-PAD group (PAD: 43.61 ± 14.65 vs. non-PAD: 45.73 ± 12.14; p > 0.05). Similarly, iPTH value was lower in the PAD group than in the non-PAD group (PAD: 214.83 ± 249.68 vs. non-PAD: 260.64 ± 293.11; p > 0.05). However, there were no statistically significant differences in Kt/V, Ca × P, and iPTH values between the PAD and non-PAD groups.

**DISCUSSION**

PAD is a marker for general cardiovascular diseases and also a prognostic factor for a higher mortality rate. The ABI, which has high sensitivity and specificity, has become an easy and reliable technique for PAD diagnosis. The present study revealed the high prevalence (32%) of PAD in the lower limbs of our patients on hemodialysis. The prevalence of PAD among DM patients on hemodialysis was even higher (55%). The prevalence of PAD among individuals aged ≥ 40 years was 4.3% in the United States. Among CKD patients, the prevalence of PAD is about 24%. In this study, DM patients on hemodialysis are more likely to develop PAD than the all-patients group (non-DM + DM) on hemodialysis.

Patients who are on dialysis may have unique factors associated either with the dialysis process or with ESRD itself for PAD formation. Such processes may include oxidative stress, chronic inflammation, vascular calcification, or exposure to atherogenic factors associated with dialysis or uremia. Therefore, the dialysis duration may effect formation and progression of atherosclerosis. We found no significant difference in ABI value in the all-patients (non-DM + DM) group with different dialysis durations. However, for the non-DM patients, the ABI value showed significant difference among patients with different dialysis durations. Non-DM patients on dialysis for more than 10 years had statistically significant lower ABI value than those on dialysis for less than 1 year. O’Hare et al. reported a statistically significant,
positive, independent association of peripheral vascular disease with vintage (hemodialysis duration). The dialysis duration that is more than 10 years may effect formation and progression of PAD, especially in non-DM hemodialysis patients.

Data from the National Health and Nutrition Examination Survey revealed that the prevalence of PAD in the age group of 50-59 yr is 2.5% and increases to 14.5% in the age group of > 70 yr. In our hemodialysis group, the mean ABI value was lower in the age group of > 70 yr than in the age group of 40-50 yr. Nevertheless, the difference in ABI value among the different age groups was not statistically significant.

In this study, the serum albumin level was found to be statistically lower in the PAD group than in the non-PAD group. PAD is an atherosclerotic process that is associated with chronic inflammation. Chronic inflammatory states are often associated with impaired nutrition and hypoalbuminemia. Hypoalbuminemia in ESRD has been found to be a risk factor for PAD and general vascular morbidity. There was no statistical difference in Kt/V value between the PAD and non-PAD groups. O’Hare et al. reported that Kt/V was negatively associated with PAD. Data from Dialysis Outcomes and Practice Patterns Study (DOPPS) revealed no significant correlation between Kt/V and PAD. The correlation between Kt/V and PAD should be studied further with other data sets.

The higher prevalence of cardiovascular disease in ESRD has been attributed to arterial calcification. Secondary hyperparathyroidism and the effect of Ca × P may be involved in the mechanisms responsible for cardiovascular diseases. We did not find significant difference in levels of Ca × P and iPTH between the PAD and non-PAD groups in this study. O’Hare et al. reported that peripheral vascular disease is negatively associated with parathyroid hormone. Data from DOPPS revealed that PAD was not associated with calcium, phosphate, calcium-phosphate product and parathyroid hormone. Guerrero et al. reported that there is no significant difference in levels of iPTH in PAD patients. London et al. found significantly lower iPTH and adynamic bone in ESRD patients with aortic calcification and stiffness.

In view of these findings, the relationship between PAD and Ca × P and parathyroid hormone must be further studied.

This study had several limitations. First, the number of patients in this study was small. Second, this was a cross-sectional study, not longitudinal study. Third, there is no defined upper limit for ABI, but most studies use 1.3 as the cutoff point. ABI values can be elevated among patients with extensive medial artery calcification of the lower extremities, which prevents occlusion of blood flow by the blood pressure cuff. This may result in an unusually high ABI reading. The present analysis may underestimate the prevalence of PAD in patients on hemodialysis because of the high prevalence of vascular calcification in this group. It should also be stressed that ABI ≥ 1.3 is more prevalent in hemodialysis patients than in control subjects. Initially, it was believed that these supernormal ABI measurements were inconclusive. However, it was reported that high ABI (≥ 1.3) also had poor prognosis for all-cause and cardiovascular mortality as ABI < 0.9 in hemodialysis patients. Therefore, evaluating the toe brachial BP index (TBBP) is an alternative for overcoming the false elevation of ABI due to calcification.

In conclusion, we found a higher prevalence of PAD among patients on hemodialysis. The serum albumin
level was significantly lower in the PAD group. ABI was statistically lower in non-DM patients on dialysis for more than 10 years than in those on dialysis for less than 1 year.

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REFERENCE