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Predicting clinical outcomes using phase angle as assessed by bioelectrical impedance analysis in maintenance hemodialysis patients

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ABSTRACT

Objective: Protein–energy wasting is common in patients on hemodialysis and is an independent risk factor for adverse events. The aim of this study was to retrospectively investigate whether phase angle (PA), known as a nutritional marker, can predict various clinical outcomes in patients with end-stage renal disease (ESRD) who are receiving hemodialysis.

Methods: Using bioelectrical impedance analysis (BIA), PA was obtained every 6 mo, and patients were divided into two groups according to baseline PA: group A included patients with PA $\geq$4.5°, and group B included patients with PA <4.5°.

Results: We followed 142 patients for a median of 29 mo (12–42 mo). We found that a decrease in PA was associated with an increased risk for death that persisted after adjusting for age, sex, and comorbidities (hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.33–0.97). Cardiovascular events were not associated with PA ($P = 0.685$). We found that PA predicted the occurrence of infection, independent of age, sex, and comorbidities (HR, 0.65; 95% CI, 0.45–0.94). Although levels of hemoglobin did not differ between groups during the study period, patients in group B received higher doses of erythropoiesis-stimulating agents and intravenous iron than those in group A ($P = 0.004$ and 0.044, respectively). In longitudinal analyses, we did not find increases in PA over time in patients who had a mean dialysis adequacy $\geq$1.4, daily protein catabolic rate $\geq$1.2 g/kg, or total carbon dioxide level $\geq$22 mmol/L.

Conclusions: PA assessed in a simple manner using BIA provides practical information to predict clinical outcomes in ESRD patients on maintenance hemodialysis.

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Introduction

Protein–energy wasting (PEW) is a syndrome characterized by decreased body stores of protein and energy sources [1]. This condition is prevalent in patients with chronic kidney disease (CKD), especially those with end-stage renal disease (ESRD) requiring maintenance dialysis. Although the prevalence of this condition varies depending on the assessment method, previous surveys have reported that 18 to 75% of dialysis patients are malnourished [2,3]. PEW is an important determinant of mortality and morbidity in patients on dialysis. Several studies have demonstrated that it is closely associated with increased rates of hospitalization and death [4,5]. Furthermore, studies have shown that it may be a contributing factor in the development of cardiovascular disease (CVD) and infection [6,7], which are major concerns in patients with CKD. However, improving nutritional status is challenging in patients with ESRD who are undergoing maintenance dialysis because PEW can be induced by several factors including not only inadequate diet, but also uremia-induced alterations such as increased energy expenditure,

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chronic inflammation, metabolic acidosis, endocrine disorders, comorbid conditions, and dialysis per se [7]. Accordingly, an integrated approach ranging from identification of malnourished patients to treatment of wasting is required.

Although several clinical, nutritional, and biochemical parameters have been used, no single parameter has been established to provide reliable information on the overall nutritional status patients on maintenance dialysis [1,8]. Bioelectrical impedance analysis (BIA), which is a fast, noninvasive, and reproducible technique, appears to be a promising tool for monitoring the nutritional status of these patients [9]. Among various parameters obtained from BIA, phase angle (PA) is assumed to indicate cell integrity and shows a good correlation with other nutritional parameters [10,11]. Moreover, previous studies have confirmed that PA can be used as a nutritional indicator to predict mortality in ESRD patients on maintenance dialysis [11–13]. Nevertheless, although studies have shown an association between PA and mortality, the correlations between PA and other important clinical outcomes such as CVD, infection, or anemia are unclear.

In this study, we retrospectively evaluated whether low PA was associated with the occurrence of CVD, infection, and mortality among ESRD patients receiving maintenance hemodialysis. Differences in anemia management according to PA also were explored. Furthermore, we assessed longitudinal changes in PA over time with a specific focus on whether optimizing CKD management can improve PA in patients on hemodialysis.

Materials and methods

Patients

Patients with ESRD who are receiving outpatient maintenance hemodialysis at Chung-Ang University Hospital in Seoul, Korea, were recruited between October 2011 and October 2015. The study included adult patients who had been on hemodialysis for ≥3 mo. Among 147 patients on maintenance hemodialysis, body composition was evaluated in 145 patients. We excluded three patients for the following reasons: One did not have baseline laboratory data and two were followed up for <1 mo after body composition analysis. Thus, the study included 142 ESRD patients on maintenance hemodialysis.

After examination of body composition, patients were followed up until death, hospitalization due to cardiovascular events or infection, or loss to follow-up. This study was approved by the Institutional Review Board of Chung-Ang University Hospital.

Data collection

All demographic and clinical data were collected from electronic medical records. Age, sex, height, body weight, causes of ESRD, duration of renal replacement therapy, types of dialysis access, and intradialytic weight gain in kilograms were collected. Comorbidity burden was assessed using the modified Charlson comorbidity index (CCI) [14]. Age was excluded to calculate the modified CCI, but was used for adjustment in multivariate analyses. Additionally, information regarding the use of erythropoiesis-stimulating agents (ESAs) and intravenous (IV) iron was reviewed.

All blood samples were drawn under fasting conditions before the first-in-week dialysis sessions, except postdialysis blood urea nitrogen (BUN). Dialysis adequacy (Kt/V_{urea}) and protein catabolic rate (PCR) also were estimated using a single pool urea kinetic model [15]. Laboratory results were measured every 6 mo during the study period.

Body composition analysis

Body composition was assessed every 6 mo using a multifrequency BIA device (InBody S10, Biospace, Seoul, South Korea), with the measurement performed within 30 min after the start of dialysis on the day of the first dialysis session after the weekend [16]. Eight electrodes were placed on the surface of the thumb, fingers of the hand, and ball of the foot and heel with the patient in the supine position. Using reactance (Xc) and resistance (R) obtained from BIA at 50 kHz, PA was estimated by the follow formula: PA (°) = arctangent (Xc/R) × (180°/π). Patients were divided into two groups based on the initial PA value: group A included patients who had a PA ≥4.5° and group B included patients with a PA <4.5° [17,18].

Outcome measurements

The correlation of PA with several variables known to be associated with nutritional conditions was evaluated. We then explored whether PA could

Table 1
Baseline characteristics of ESRD patients receiving maintenance hemodialysis

Variables	Total (N = 142)	Group A* (n = 77)	Group B* (n = 65)	*P* Value
Age, y	64 ± 13	61 ± 12	67 ± 13	0.007
Male, n (%)	75 (52.8)	51 (66.2)	24 (36.9)	<0.001
Dialysis duration, mo	22 (5–57)	19 (7–46)	25 (3–64)	0.954
Diabetes, n (%)	81 (55.9)	36 (46.8)	45 (69.2)	0.007
Charlson comorbidity index	7 ± 2	6 ± 2	7 ± 2	0.006
Central venous access, n (%)	5 (3.5)	0 (0.0)	5 (7.7)	0.018
BMI, kg/m^2	22.5 (20.4–24.9)	23.4 (21.5–25.8)	21.1 (19.4–23.4)	0.018
Interdialytic weight gain, kg	1.8 ± 0.7	1.9 ± 0.7	1.6 ± 0.7	0.011
Hemoglobin, g/dL	10.6 ± 1	10.8 ± 0.9	10.5 ± 1.1	0.071
Albumin, g/dL	3.8 ± 0.3	3.9 ± 0.3	3.7 ± 0.4	<0.001
Glucose, mg/dL	153.0 (124–242.3)	140.0 (118.5–195.5)	180.0 (134–274)	0.002
BUN, mg/dL	68.6 ± 18.9	73.3 ± 18.6	63 ± 18	0.001
Creatinine, mg/dL	9.0 ± 2.6	10.1 ± 2.6	7.6 ± 2.1	<0.001
Total cholesterol, mg/dL	139.5 (121.5–163.3)	143.0 (123–168)	135.0 (118.5–161)	0.347
Triacylglycerol, mg/dL	108.5 (81.8–149.3)	114.0 (85.5–150.5)	105.0 (76–143)	0.759
LDL cholesterol, mg/dL	72.5 (61.8–95)	75.0 (61.5–96.5)	72.0 (62–93)	0.314
Uric acid, mg/dL	7.9 ± 1.6	8.4 ± 1.5	7.2 ± 1.5	<0.001
CRP, mg/L	1.9 (0.8–4.5)	1.8 (0.8–3.9)	2.0 (0.8–4.8)	0.200
TCO_2, mEq/L	23.1 ± 3.1	22.6 ± 2.9	23.6 ± 3.2	0.063
Intact PTH, pg/mL	214.3 (132.2–351.6)	240.3 (151.4–378.4)	201.5 (115.1–304.2)	0.690
Calcium, mg/dL	8.6 ± 0.7	8.7 ± 0.7	8.5 ± 0.7	0.277
Phosphorus, mg/dL	5.0 ± 1.5	5.4 ± 1.5	4.6 ± 1.4	0.001
Kt/V_{urea}	1.6 ± 0.3	1.6 ± 0.3	1.7 ± 0.2	0.076
PCR, g/kg daily	1.0 ± 0.2	1.0 ± 0.2	0.9 ± 0.2	0.072
PA, °	4.6 ± 1.0	5.3 ± 0.7	3.7 ± 0.6	<0.001

BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; LDL, low-density lipoprotein; PA, phase angle; PCR, protein catabolic rate; PTH, parathyroid hormone; TCO_2, total carbon dioxide

Continuous variables are expressed as mean value ± standard deviation or median (interquartile range), and categorical variables are expressed as number (percentage)

* Group A included patients who had a PA ≥4.5° and group B included patients with a PA <4.5°.

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