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Protein-Energy Wasting, Risk Factors for Death and Composite Outcomes In CKD Patients Not Receiving Kidney Replacement Therapy

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Objectives : Protein–energy wasting (PEW) is a strong indicator of adverse outcomes such as all-cause mortality and cardiovascular events. Although this association has been reported primarily in patients with dialysis, it has not been clearly demonstrated in patients with non-dialysis–dependent chronic kidney disease (NDD-CKD). The current study aimed to evaluate the association of PEW with all-cause death or composite of any cardiovascular event and all-cause death in patients with NDD-CKD.

Methods : We evaluated the association of PEW with adverse outcomes in patients with NDD-CKD through a prospective cohort study. We analyzed clinical data from 1,847 patients with CKD (median follow-up duration was 6.94 years). The definition of PEW followed the International Society of Renal Nutrition and Metabolism criteria: serum albumin < 3.8 g/dL, body mass index < 23.0 kg/m², skeletal muscle mass < 19.7 kg in women, < 26.9 kg in men, and low dietary protein intake < 0.6 g/kg/day.

Results : During 6.94 years, 129 deaths and 264 composite outcomes (all cause death or cardiovascular events) occurred. In the Cox proportional hazards regression analysis, all-cause death and composite outcomes were significantly increased in the subgroups with two or more PEW parameters. All-cause death increased in patients with two PEW parameters (hazard ratio [HR], 2.777; 95% confidence interval [CI], 1.605–4.084; P < 0.001) and those with three or more PEW parameters (HR, 3.782; 95% CI, 1.814–7.888; P < 0.001). Composite outcomes also showed a significant increase in patients with two (HR, 2.164; 95% CI, 1.508–3.105; P < 0.001) and three or more PEW parameters (HR, 2.296; 95% CI, 1.296–4.068; P = 0.004). Significant increases of all cause death and composite outcomes were found among patients with two or more PEW parameters.

Conclusions : PEW was a strong indicator of all-cause death and composite outcomes among NDD-CKD patients.

Table 1.jpg



Table 1. Cox regression analysis of outcomes according to No. of PEW parameters after adjustment with confounding factors

No. of PEW parameters	Unadjusted		Model 1		Model 2		Model 3	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-Value	HR (95% CI)	P-value
All-cause death								
0	reference		reference		reference		reference	
1	1.486 (0.919-2.403)	0.106	1.567 (0.969-2.535)	0.067	1.345 (0.829-2.181)	0.23	1.669 (0.949-2.937)	0.076
2	3.360 (2.134-5.288)	<0.001	3.037 (1.926-4.789)	<0.001	2.511 (1.587-3.974)	<0.001	2.777 (1.605-4.084)	<0.001
≥3	5.723 (3.088-10.607)	<0.001	5.143 (2.772-9.544)	<0.001	3.011 (1.586-5.717)	<0.001	3.782 (1.814-7.888)	<0.001
Composite outcomes (cardiovascular event and all-cause death)								
0	reference		reference		reference		reference	
1	1.317 (0.968-1.793)	0.08	1.301 (0.956-1.770)	0.095	1.280 (0.941-1.742)	0.116	1.388 (0.967-1.990)	0.075
2	2.289 (1.682-3.115)	<0.001	2.225 (1.635-3.029)	<0.001	2.160 (1.213-3.270)	<0.001	2.164 (1.508-3.105)	<0.001
≥3	2.838 (1.738-4.633)	<0.001	2.278 (1.390-3.732)	0.001	1.992 (1.213-3.270)	0.006	2.296 (1.296-4.068)	0.004

Model 1 : adjusted for age and sex, Model 2 : adjusted for variables in model 1, in addition to underlying comorbidity (diabetes, hypertension, cardiovascular disease), Model 3 adjusted for variables in model 2, in addition to eGFR, Hemoglobin, cholesterol, HDL cholesterol, LDL cholesterol, high sensitivity C-reactive protein, total CO2. CI=confidential interval, HR=hazard ratio.