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CLINICAL RESEARCH

Associations of Dietary Protein and Energy Intakes With Protein-Energy Wasting Syndrome in Hemodialysis Patients

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Introduction: The associations of dietary protein and/or energy intakes with protein or energy wasting in patients on maintenance hemodialysis are controversial. We examined these in the Hemodialysis (HEMO) Study.

Methods: In 1487 participants in the HEMO Study, baseline dietary protein intake (grams per kilogram per day) and dietary energy intake (kilocalories per kilograms per day) were related to the presence of the protein-energy wasting (PEW) syndrome at month 12 (defined as the presence of at least 1 criteria in 2 of the 3 categories of low serum chemistry, low body mass, and low muscle mass) in logistic regression models. In additional separate models, protein intake estimated from equilibrated normalized protein catabolic rate (enPCR) was also related to the PEW syndrome.

Results: Compared with the lowest quartile, the highest quartile of baseline dietary protein intake was paradoxically associated with increased risk of the PEW syndrome at month 12 (odds ratio [OR]: 4.11; 95% confidence interval [CI]: 2.79–6.05). This relationship was completely attenuated (OR: 1.35; 95% CI: 0.88–2.06) with adjustment for baseline body weight, which suggested mathematical coupling. Results were similar for dietary energy intake. Compared with the lowest quartile of baseline enPCR, the highest quartile was not associated with the PEW syndrome at 12 months (OR: 0.78; 95% CI: 0.54–1.12).

Discussion: These data do not support the use of dietary protein intake or dietary energy intake criteria in the definition of the PEW syndrome in patients on maintenance hemodialysis.

Kidney Int Rep (2017) ■, ■–■; http://dx.doi.org/10.1016/j.ekir.2017.04.002
KEYWORDS: chronic kidney disease; hemodialysis; protein-energy wasting

The 1- and 3-year survival probabilities of patients on incident hemodialysis are dismal at 74% and 50%, respectively.[1] Low body mass index (BMI),[2–7] muscle mass,[4,8,9] percentage of body fat,[9,10] history of weight loss,[11,12] serum albumin,[13,14] and total cholesterol levels[15] are some of the strongest predictors of mortality in the population on maintenance hemodialysis (MHD). It is theorized that the previously described indicators of protein or energy depletion are the result of a wasting syndrome.[16–18]

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Received 7 November 2016; revised 6 April 2017; accepted 11 April 2017; published online 18 April 2017

An expert panel of the International Society of Renal Nutrition and Metabolism (ISRNM) defined the protein-energy wasting (PEW) syndrome as "the state of decreased body stores of protein and energy fuels (that is, body protein and fat masses)."[19] They also developed objective criteria for the clinical definition of the PEW syndrome in patients on dialysis and patients with chronic kidney disease (CKD) (Table 1).[20] Although it has been considered that kidney disease, protein, or energy depletion is due to wasting and not decreased nutrient intake,[17,21] the ISRNM panel included dietary protein (<0.8 g/kg per day) and energy intakes (<25 kcal/kg per day) as criteria for the PEW syndrome definition in patients on MHD. To our knowledge, the validity of these dietary definitions as indicators of the PEW syndrome

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Table 1. International Society of Renal Nutrition and Metabolism Panel protein-energy wasting syndrome criteria

Low serum chemistry	Serum albumin <3.5 g/dl[a]
	Serum cholesterol <100 mg/dl
Low body mass	BMI <23 kg/m^2
	Unintentional weight loss over time: 10% over 6 months
	Body fat percentage <10%
Low muscle mass	Reduced mid-arm muscle circumference area (reduction >10% in relation to 50th percentile of reference population)
Low dietary intake	DPI <0.60 g/kg/d in stage 2–5 CKD patients or
	DPI <0.80 g/kg/d in MHD patients
	DEI <25 kcal/kg/d

BMI, body mass index; CKD, chronic kidney disease; DEI, dietary energy intake; DPI, dietary protein intake; MHD, maintenance hemodialysis.
[a]The International Society of Renal Nutrition and Metabolism serum albumin criterion was based on Bromocresol green (BCG) method measurement. In the HEMO study, serum albumin was measured by the nephelometry method, which is approximately 0.3 g/dl lower than that obtained with BCG method.[20]

has not been examined; therefore, we analyzed these in a retrospective analysis of the Hemodialysis (HEMO) study.[22,23]

MATERIALS AND METHODS

The details of the HEMO Study design were described elsewhere.[22,23] In brief, the HEMO study was a 2-by-2 factorial design randomized control trial of standard- or high-dose hemodialysis and high- or low-flux dialyzers. Eligibility criteria were patients aged 18 to 80 years old who underwent in-center hemodialysis 3 times per week for ≥3 months. A total of 1846 participants were randomized in 15 clinical centers from March 1995 to October 2000, and followed until December 2001.

Trained study coordinators following standardized protocols conducted study visits. Demographics and comorbidity data were obtained with standardized questionnaires. The heights of the patients, obtained at study entry, and postdialysis weight measurements, obtained monthly, were used to calculate BMI. mid-arm muscle circumference was calculated from mid-arm circumference, and triceps skinfold thicknesses were measured with previously published protocols.[24] Body fat percentage was calculated as: body fat percentage $= (1.20 \times \text{BMI}) + (0.23 \times \text{age}) - (10.8 \times \text{sex}) - 5.4$, (sex: females $= 0$, males $= 1$). Details of dietary assessment in the HEMO study were published elsewhere.[25] Serum albumin was measured at a central laboratory by nephelometry. Equilibrated normalized protein catabolic rate (enPCR) were calculated from formal urea kinetic models using both single and double pool Kt/V urea. Total serum cholesterol was assessed locally at each clinical center laboratory.

Definitions of PEW syndrome individual criteria and categories are summarized in Table 1. Because the goal of the present analyses was to examine the relationships of baseline dietary protein intake (DPI) and dietary energy intake (DEI) with the rest of the PEW

Table 2. Baseline characteristics by dietary protein intake and dietary energy intake groups (N = 1487)

	Low DPI <0.8 g/kg/d (*n* = 608)	High DPI ≥0.8 g/kg/d (*n* = 879)	*P* value	Low DEI <25 kcal/kg/d (*n* = 957)	High DEI ≥25 kcal/kg/d (*n* = 530)	*P* value
Age (yr)	59.1 ± 12.7	56.0 ± 14.8	<0.001	59.4 ± 12.6	53.4 ± 15.7	<0.001
Black (%)	66.4%	63.0%	0.18	67.2%	59.4%	0.003
Male (%)	35.4%	49.5%	<0.001	38.0%	54.0%	<0.001
ESRD duration (yr)	2.0 (1.0, 4.1)	2.3 (0.9, 5.2)	0.10	2.0 (0.9, 3.9)	2.7 (1.0, 6.5)	0.001
Fistula (%)	28.5%	38.7%	<0.001	28.4%	45.5%	<0.001
Kt/V group (%)	50.2%	50.2%	1.00	49.8%	50.8%	0.74
Flux group (%)	51.5%	49.9%	0.56	50.4%	50.9%	0.83
Smoking (%)	46.1%	51.1%	0.06	47.2%	52.3%	0.06
Alcohol use (%)	14.5%	16.8%	0.22	13.9%	19.4%	0.005
Diabetes (%)	51.5%	37.4%	<0.001	51.5%	28.1%	<0.001
Atherosclerotic conditions (%)	45.7%	39.1%	0.01	44.7%	36.6%	0.002
Cancer (%)	9.0%	7.8%	0.41	8.6%	7.9%	0.67
Congestive heart failure (%)	9.5%	11.5%	0.23	10.9%	10.4%	0.77
DPI (g/kg/d)	0.62 (0.51, 0.71)	1.10 (0.93, 1.36)	<0.001	0.74 (0.58, 0.92)	1.22 (1.02, 1.48)	<0.001
DEI (kcal/kg/d)	15.6 (12.4, 18.9)	26.4 (21.4, 32.7)	<0.001	17.6 (13.7, 21.2)	31.3 (27.5, 37.1)	<0.001
TPI (g/d)	44.7 (37.2, 52.7)	72.0 (62.2, 85.8)	<0.001	52.1 (41.6, 66.2)	74.4 (63.3, 89.6)	<0.001
TEI (kcal/d)	1162 (936, 1433)	1692 (1401, 2048)	<0.001	1225 (1012, 1497)	1962 (1697, 2308)	<0.001
enPCR (g/kg/d)	0.98 (0.83, 1.14)	1.04 (0.90, 1.22)	<0.001	1.01 (0.86, 1.17)	1.02 (0.88, 1.21)	0.38
Body weight (kg)	75.1 (65.8, 85.1)	63.8 (56.0, 72.3)	<0.001	72.0 (63.0, 83.1)	61.3 (54.0, 68.8)	<0.001

DEI, dietary energy intake; DPI, dietary protein intake; enPCR, equilibrated normalized protein catabolic rate; ESRD, end-stage renal disease; TEI, total energy intake; TPI, total protein intake.