The Prognostic Importance of Protein Energy Wasting in Chronic Kidney Disease: A Sectional Monocentric Study

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Abstract

Aim: The purpose of this study is to determine the frequency of Protein Energy Wasting (PEW) in individuals with chronic kidney disease (CKD) and evaluate the relationship between PEW and anthropometric measurements, biochemical parameters, and nutritional status of individuals.

Method: The study was conducted with 119 predialysis individuals aged 19 and over with CKD. The biochemical parameters and anthropometric measurements of the participants were evaluated, and their nutritional status was determined by Subjective Global Assessment (SGA) and PEW criteria. Nutritional status was classified as good, moderate nutritional deficiency, and severe malnutrition according to SGA. The presence of PEW was accepted if ≥3 categories for PEW were met.

Results: According to SGA, 20.2% of the individuals had moderate/severe malnutrition and 8.4% PEW. It was determined that with the increase in the number of PEW criteria in individuals, the body weight, body mass index (BMI), upper middle arm circumference, triceps skin fold thickness and body fat percentage; serum total protein, albumin, calcium and magnesium levels; intake amounts of many macro and micro nutrients have decreased significantly. It was detected that BMI (26.8%), albumin (18.6%), fiber (14.1%) and magnesium (15.7%) were the parameters most explaining the number of PEW criteria met by individuals.

Conclusion: PEW was related to anthropometric measurements, biochemical parameters and nutrient intakes. So, using the PEW tool at certain intervals from the moment of diagnosis will be a practical and effective intervention in reducing the prevalence of malnutrition.

Keywords: Anthropometric measurements, nutrition, chronic kidney disease, malnutrition, protein energy wasting.

Kronik Böbrek Hastalıklarında Protein Enerjisi İsrafının Prognostik Önemi: Kesitsel Tek Merkezli Bir Çalışma

Öz

Amaç: Bu çalışmanın amacı kronik böbrek hastalığı (KBH) olan bireylerde Protein Enerji Kaybı (PEK) sıklığını belirlemek ve PEK ile bireylerin antropometrik ölçümleri, biyokimyasal parametreleri ve beslenme durumları arasındaki ilişkiyi değerlendirmektir.

Yöntem: Çalışma 19 yaş ve üzeri KBH'li 119 diyaliz öncesi birey ile gerçekleştirildi. Katılımcıların biyokimyasal parametreleri ve antropometrik ölçümleri değerlendirilerek beslenme durumları Subjektif Global Değerlendirme (SGD) ve PEK kriteri ile belirlendi. Beslenme durumu SGA'ya göre iyi, orta derecede beslenme yetersizliği ve ciddi beslenme yetersizliği olarak sınıflandırıldı. PEK için ≥3 kategorinin karşılanması durumunda PEK'in varlığı kabul edildi.

Bulgular: SGD'ye göre bireylerin %20,2'sinde orta/ciddi malnütrisyon, %8,4'ünde PEK vardı. Bireylerde PEK kriterlerinin sayısının artmasıyla birlikte vücut ağırlığı, beden kütle indeksi (BKİ), üst orta kol çevresi,

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ETHICAL STATEMENT: The study was approved by the Ankara University Ethics Committee (Date: 18.06.2019, Decision No: 231) and the study was conducted in accordance with the principles of the Declaration of Helsinki.

triseps deri kıvrım kalınlığı ve vücut yağ yüzdesinin; serum toplam protein, albümin, kalsiyum ve magnezyum düzeyleri; birçok makro ve mikro besinin alım miktarları önemli ölçüde azalmıştır. Bireylerin karşıladığı PEK kriteri sayısını en çok açıklayan parametrelerin BKİ (%26,8), albümin (%18,6), posa (%14,1) ve magnezyum (%15,7) olduğu belirlendi.

Sonuç: PEK antropometrik ölçümler, biyokimyasal parametreler ve besin alımıyla ilişkiliydi. Dolayısıyla tanı anından itibaren PEK aracının belirli aralıklarla kullanılması malnütrisyon prevalansının azaltılmasında pratik ve etkili bir müdahale olacaktır.

Anahtar Sözcükler: Antropometrik ölçümler, beslenme, kronik böbrek hastalığı, malnütrisyon, protein enerji kaybı.

Introduction

Chronic kidney disease (CKD) is a costly worldwide health problem and its prevalence is increasing rapidly[1]. Malnutrition, which is seen at a high rate in individuals with CKD[2-4], is one of the important complications of CKD and causes negative results in terms of quality of life, morbidity and mortality[5]. Malnutrition has various causes such as decreased energy and protein intake, increased energy expenditure, anorexia, hormonal and metabolic changes[6].

Different definitions and diagnostic methods are used for malnutrition seen in individuals with CKD. In order to eliminate this confusion and to evaluate all aspects of nutritional and metabolic disorders such as cachexia, malnutrition and inflammation seen in CKD, the use of the concept of "Protein Energy Wasting (PEW)", which is associated with increased mortality in CKD population, has been recommended by the International Society of Renal Nutrition and Metabolism (ISRNM)[7]. PEW has been defined as the decrease in body protein stores and energy sources[8]. The existence of at least three of the parameters of biochemical markers, decreased body weight (BW), decreased muscle mass, decreased daily protein or energy intake in a patient is considered as presence of PEW, by ISRNM[9]. In various studies, PEW was evaluated in individuals with CKD and a relationship was found between the course of the disease and the presence of PEW[10-12]. However, studies with PEW evaluation in individuals with CKD who do not receive dialysis treatment are limited. Therefore, in this study, it was aimed to evaluate the relationship between the number of PEW criteria met by adult CKD patients not receiving dialysis treatment, and anthropometric measurements, biochemical parameters and nutritional status.

Material and Methods

General Plan of the Study

The sample size of the study was calculated using the G-Power program (version 3.0) using the values (2.2±0.8, 2.8±1.4, 3.5±1.8 and 3.3±1.4) in a similar study (Jagadeswaran et al., 2019) with a significance level of 0.05 and a power of 0.95. Accordingly, it was determined that a sample of at least 84 people would be sufficient for this study. This study was conducted in accordance with the principles of the Declaration of Helsinki on a total of 119 individuals, 72 men and 47 women, with CKD over the age of 19, who came to Ankara Bilkent City Hospital. The research comprised individuals who did not have a cardiac pacemaker, did not have an intellectual handicap, and hadn't undergone a surgical operation within the previous 30 days. Research data were

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collected using a survey form and face-to-face interview technique and by obtaining informed consent from individuals. The research data started to be collected after obtaining the ethics committee approval, which numbered 231-14 and date 18/06/2019 from the Ankara University Ethics Committee and the institutional permission.

Anthropometric Measurements and Evaluation of Blood Pressure

BW (kg), body fat percentage (BFP,%) and lean body mass (LBM, kg) measurements of individuals made with Tanita BC 545 N brand analyzer. The BW (kg)/height (m^2) formula was used to calculate the Body Mass Index (BMI). A BMI below 23 kg/m^2 is considered an indicator for PEW by ISRNM[9]. Upper middle arm circumference (UMAC) and triceps skinfold thickness (TSFT) measurements of the patients were made in accordance with the technique[13]. The middle arm muscle circumference area (MAMCA), which was used to evaluate the status of having PEW, was calculated according to the [UMAC (cm)-(π×TSFT (cm)]²/4π-10 formula for men and [UMAC (cm)-(π×TSFT (cm)]²/4π-6,5 for women and was evaluated according to percentile values[14]. It was accepted that one of the PEW criteria was met if the MAMCA was more than 10% lower than the 50th percentile.

The blood pressure measurements of the participants were made three times after 20 minutes of rest with a digital sphygmomanometer, and the systolic and diastolic blood pressure values were recorded by taking the average of the last two to determine the result.

Evaluation of Protein Energy Wasting

For the diagnosis of PEW, the criteria suggested by the ISRNM under four different categories were used. These categories were serum biochemistry (serum albumin <3.8 g/dL, serum prealbumin <30 mg/dL, serum cholesterol <100 mg/dL), body mass (BMI <23 kg/m^2, unintentional weight loss: >5% in 3 months or >10% in 6 months, total body fat percentage <10%), muscle mass [muscle wasting: >5% in 3 months or >10% in 6 months, decrease in the mid-arm muscle circumference area (reduction >10% in relation to 50th percentile of reference population), appearance of creatinine] and daily nutrient intake (Protein intake <0.8 g/kg/day for the dialysis patient, <0.6 g/kg/day for the predialysis patient, daily energy intake <25 kcal/kg/day). For this study, serum albumin <3.8 g/dL criterion from category 1, BMI <23 kg/m^2 criterion from category 2, decrease in middle arm muscle circumference area (reduction >10% in relation to 50th percentile of reference population) criterion from category 3, protein intake below 0.6 g/kg/day criterion from category 4 have been evaluated. PEW was accepted if at least three of these four categories were present in a patient (provided that at least one criterion in each category was met)[9].

Determination and Evaluation of Food Consumption Status

Three-day food consumption records were taken from the patients to determine the food consumption status. All the foods consumed by the patients in the last 72 hours were questioned with the Food and Food Photography Catalog[15]. The daily average intake levels of energy and nutrients in the diet were determined, and these values were analyzed using the "Nutrition Information Systems Package Program" developed for Turkey.

Evaluation of Biochemical Findings

The biochemical parameters of the patients (blood glucose, total cholesterol/TC, low density lipoprotein cholesterol/LDL-C, high density lipoprotein cholesterol/HDL-C, triglyceride, total protein, albumin, urea, uric acid, creatinine, iron, total iron binding capacity/TIBC, ferritin, sodium, potassium, calcium, phosphorus, magnesium, C-reactive protein/CRP, glomerular filtration rate/GFR) were obtained by analyzing blood samples taken by nephrology nurses in the hospital laboratory.

Subjective Global Assessment

The Subjective Global Assessment (SGA) is a clinical assessment test that combines the subjective and objective aspects (BW change, dietary intake change, gastrointestinal symptoms and changes in functional capacity) of medical history with physical examination data (subcutaneous fat loss, muscle wastage, ankle or sacral edema). After evaluating the patients, their nutritional status was classified into three groups: well-nourished (SGA-A), moderately malnourished (SGA-B) and severely malnourished (SGA-C)[16].

Statistical Evaluation of Data

The data were analyzed with SPSS statistical package program. Descriptive statistics were shown as mean±standard deviation (SD) for variables with normal distribution and median and interquartile range (IQR) values for variables with non-normal distribution number of cases (n) and percentage (%) for nominal variables. The relationship between two categorical variables was determined by the Chi-Square test. Statistically significant difference situation between the categories of quantitative variables with ≥3 categories was evaluated with One Way ANOVA test if normal distribution assumptions were provided; if not Kruskal Wallis test was used. The relationship between two quantitative variables was determined using the Pearson Correlation Coefficient when both of the variables met the normal distribution assumptions and the Spearman Correlation Coefficient if at least one of the variables did not satisfy the normal distribution assumptions. In all statistical tests, the confidence interval was accepted as 95.0% and it was evaluated at $p<0.05$ significance level.

Results

The study was conducted with 119 individuals with a median age of 64.0 (15.00) years and a mean GFR of 40.1±15.92 mL/min/1.73 m^2. It was determined that, as a result of the SGA 20.2% of the individuals had moderate or severe malnutrition and 8.4% with PEW.

According to Table 1, where the distribution of PEW presence was given according to the stage of CKD and SGA level, the incidence of PEW is higher in individuals in stages 4 and 5 of CKD compared to individuals in other stages ($p>0.05$). At the same time, 19.2% of individuals without PEW and 30.0% of individuals with PEW had moderate and severe malnutrition according to SGA ($p>0.05$).

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Table 1. Distribution of PEW presence according to the stage of CKD and SGA level

	Stage of CKD (n, %)				
PEW presence	**Stage 2 (13, 10.9)**	**Stage 3 (74, 62.2)**	**Stage 4 (20, 16.8)**	**Stage 5 (12, 10.1)**	**χ^2 p**
PEW [N, (%)]	1 (7.7)	6 (8.1)	2 (10.0)	1 (8.3)	6.275
Non-PEW [N, (%)]	12 (92.3)	68 (91.9)	18 (90.0)	11 (91.7)	0.958[a]
	SGA Level (n, %)				
PEW presence	**SGA-A (95, 79.8)**	**SGA-B ve SGA-C (24, 20.2)**			
PEW [N, (%)]	7 (70.0)	3 (30.0)			0.598
Non-PEW [N, (%)]	88 (80.8)	21 (19.2)			0.439[b]

[a] Fisher-exact Chi-square [b]Likelihood Chi-square test was used. $^*p<0.05$

It was determined that the levels of BW, BMI, UMAC, TSFT and BFP decreased significantly according to the number of PEW criteria met by the individuals participating in the study ($p<0.05$) (Table 2).

Table 2. Anthropometric measurements and blood pressure levels according to the number of PEW criteria met by individuals

	Number of PEW criteria met				**F/χ^2**	**p**
	0 (n:15) [a]	**1 (n:64)** [b]	**2 (n:30)** [c]	**≥3 (n:10)** [d]		
Anthropometric measurements and blood pressures						
BW (kg) [a-d, b-d]	85.2 (12.20)	81.1 (19.80)	77.5 (15.17)	67.8 (8.22)	14.252	0.003$^{*\alpha}$
BMI (kg/m^2)[a-c, a-d, b-d]	34.1 (5.05)	29.9 (6.25)	27.4 (5.67)	20.9 (4.24)	34.619	0.000$^{*\alpha}$
UMAC (cm)[a-c, a-d, b-c, b-d]	35.0 (4.00)	33.0 (5.88)	30.0 (4.00)	28.0 (3.50)	38.758	0.000$^{*\alpha}$
TSFT (mm)[a-d, b-d, c-d]	20.0 (10.00)	15.6 (11.00)	15.5 (9.25)	10.0 (4.27)	13.966	0.003$^{*\alpha}$
BFP (%)[a-b, a-c, a-d, b-c, b-d, c-d]	35.5±9.86	30.3±9.07	25.4±8.77	13.6±6.77	14.519	0.000$^{*\beta}$
LBM (kg)	50.8 (18.90)	54.7 (17.67)	54.6 (19.88)	57.8 (10.70)	1.352	0.717$^{\alpha}$
SBP (mmHg)	158.6±13.57	140.5±17.36	155.5±37.17	133.9±40.44	0.107	0.745$^{\beta}$
DBP (mmHg)	79.6±9.29	75.0±13.24	94.2±24.98	84.0±12.40	0.951	0.332$^{\beta}$

Significant differences are indicated as exponent. $^{\alpha}$ Kruskal Wallis test $^{\beta}$ One Way ANOVA test was used. $^*p<0.05$

BW: Body weight, BMI: body mass index, UMAC: upper middle arm circumference, TSFT: triceps skinfold thickness, BFP: body fat percentage, LBM: lean body mass, SBP: sistolic blood presure, DBP: diastolic blood presure

When the biochemical parameters of the individuals were evaluated according to the number of PEW criteria they met, it was observed that the total protein, albumin, calcium and magnesium levels of the individuals decreased with the increase in the PEW criteria met ($p<0.05$) (Table 3).

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Table 3. Biochemical parameters according to the number of PEW criteria met by individuals

Biochemical parameters	Number of PEW criteria met				F/χ²	p
	0 (n:15) [a]	**1 (n:64)** [b]	**2 (n:30)** [c]	**≥3 (n:10)** [d]		
Blood glucose (mg/dL)	110.5 (55.75)	138.1 (47.00)	114.0 (41.50)	90.5 (13.25)	5.968	0.113^{α}
TC (mg/dL)	196.5 (37.75)	188.5 (56.00)	177.0 (48.50)	201.5 (104.5)	3.540	0.316^{α}
LDL-C (mg/dL)	119.5 (37.00)	109.0 (58.00)	101.0 (45.50)	133.5 (55.00)	2.186	0.535^{α}
HDL-C (mg/dL)	44.5 (17.00)	44.5 (13.25)	37.0 (16.00)	37.0 (16.75)	2.454	0.484^{α}
Triglyceride (mg/dL)	158.0 (91.75)	150.5 (102.5)	125.0 (160.0)	156.0 (88.00)	0.917	0.821^{α}
Total Protein (g/dL) [a-b, a-d, b-d, c-d]	7.4 (0.50)	7.0 (0.60)	7.0 (0.60)	5.6 (1.70)	19.333	$0.000^{*\alpha}$
Albumin (g/dL) [a-d, b-d, c-d]	4.5 (0.50)	4.3 (0.40)	4.4 (0.60)	3.4 (0.80)	17.496	$0.001^{*\alpha}$
Urea (ng/dL)	67.5 (36.3)	62.0 (30.5)	62.0 (55.0)	87.0 (70.5)	2.245	0.523^{α}
Uric acid (mg/dL)	7.8 (3.9)	7.4 (2.2)	7.4 (1.9)	7.5 (1.8)	2.316	0.509^{α}
Creatinine (mg/dL)	1.5 (1.1)	1.5 (0.5)	1.8 (2.7)	1.8 (2.0)	2.662	0.447^{α}
Iron (µg/dL)	53.0 (37.0)	50.0 (32.0)	68.0 (49.0)	39.0(-)	4.811	0.186^{α}
TIBC (µg/dL)	327.0 (28.0)	338.0 (72.0)	299.0 (94.0)	325.0 (-)	1.729	0.631^{α}
Ferritin (ng/mL)	42.0 (149.0)	53.0 (54.0)	88.0 (184.0)	51.0 (-)	2.682	0.443^{α}
Sodium (mEq/L)	139.5 (7.8)	141.0 (5.0)	139.0 (2.0)	141.0 (3.0)	2.266	0.519^{α}
Potassium (mEq/L)	4.6±0.70	4.6±0.53	4.4±0.67	4.6±0.60	1.482	0.223^{β}
Calcium (mg/dL) [a-d, b-d, c-d]	9.4±0.49	9.2±0.50	9.3±0.80	8.9±0.71	3.228	$0.025^{*\beta}$
Phosphorus (mg/dL)	4.0±0.63	3.7±0.74	4.1±0.98	4.0±0.87	0.324	0.808^{β}
Magnesium (mg/dL) [a-b]	2.3 (0.4)	1.9 (0.3)	1.8 (0.5)	2.1 (0.5)	8.032	$0.045^{*\alpha}$
CRP (mg/dL)	7,7 (17,26)	5,6 (11,13)	5,6 (17,40)	8,8 (13,24)	1.207	0.751^{α}
GFR (mg/dL)	37,3±15,47	41,3±13,96	36,5±17,49	39,0±20,18	0.128	0.943^{β}

Significant differences are indicated as exponent. $^{\alpha}$ Kruskal Wallis test $^{\beta}$ One Way ANOVA test was used. $^{*}p<0.05$

The intake levels of energy and nutrients according to the number of PEW criteria met by the individuals participating in the research were given in Table 4. It was determined that the intakes of carbohydrates, protein, total fat, MUFA, fiber and many micronutrients (excluding vitamins B12, C and E) decreased significantly with the increase in the number of PEW criteria met ($p<0.05$).

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Table 4. Intake levels of energy and nutrients according to the number of PEW criteria met by individuals

Energy and nutrients	Number of PEW criteria met				F/χ²	p
	0 (n:15) [a]	1 (n:64) [b]	2 (n:30) [c]	≥3 (n:10) [d]		
Energy (kcal) [a-b, a-c, a-d, b-d]	1712.9±521.48	1338.2±537.63	1198.9±331.01	935.9±417.90	6.087	0.001*β
Carbohydrates (g) [a-d]	187.5 (108.51)	125.1 (56.92)	141.9 (51.95)	99.2 (98.89)	10.939	0.012*α
Protein (g) [a-c, a-d]	62.4 (17.88)	47.6 (39.56)	39.3 (9.70)	32.7 (28.18)	18.979	0.000*α
Total fat (g) [a-d]	65.2 (51.45)	52.2 (35.31)	47.5 (22.40)	28.5 (33.85)	10.832	0.013*α
PUFA (g)	10.1 (10.49)	8.1 (9.70)	5.7 (8.01)	5.5 (4.77)	7.123	0.068α
MUFA (g) [a-d]	25.4 (19.09)	19.4 (10.94)	16.9 (10.24)	10.2 (13.66)	10.413	0.015*α
SFA (g)	25.9 (12.40)	17.6 (11.84)	16.8 (6.49)	12.8 (13.69)	7.310	0.063α
Cholesterol (mg)	262.5 (176.46)	224.4 (248.05)	160.7 (161.16)	245.8 (123.08)	6.017	0.111α
Fiber (g) [a-c, a-d]	19.0 (6.08)	14.7 (9.07)	12.1 (6.24)	7.7 (11.15)	17.065	0.001*α
Vitamin A (µg) [a-b, a-c, a-d]	769.5 (545.85)	556.8 (482.1)	506.7 (274.07)	387.4 (289.42)	8.731	0.033*α
Thiamine (mg) [a-b, a-c, a-d, b-d]	0.8 (0.41)	0.5 (0.38)	0.5 (0.23)	0.3 (0.23)	20.470	0.000*α
Riboflavin (mg) [a-b, a-c, a-d]	1.3 (0.74)	0.8 (0.72)	0.7 (0.44)	0.5 (0.35)	21.099	0.000*α
Niacin (mg) [a-d]	9.3 (7.53)	6.4 (5.60)	6.2 (4.16)	4.6 (5.58)	8.365	0.039*α
Pyridoxine (mg) [a-c, a-d]	1.0 (0.52)	0.6 (0.53)	0.5 (0.36)	0.4 (0.66)	14.815	0.002*α
Folate (µg) [a-c, a-d]	322.1 (155.83)	200.9 (148.71)	173.3 (106.06)	137.4 (109.67)	11.448	0.010*α
Vitamin B_{12} (µg)	2.5 (2.37)	2.6 (2.93)	1.7 (1.38)	1.9 (1.93)	5.627	0.131α
Vitamin C (mg)	87.5 (96.50)	55.7 (57.69)	52.2 (58.00)	50.6 (98.06)	3.696	0.296α
Vitamin E (mg)	13.6 (12.71)	10.0 (10.38)	7.4 (9.68)	4.8 (6.90)	7.770	0.051α
Sodium (mg) [a-d, b-d]	3963.1 (1973.85)	2915.4(2095.06)	2460.8(1384.84)	1373.9(1309.17)	15.743	0.001*α
Potassium (mg) [a-b, a-c, a-d, b-d]	2415.1 (1040.60)	1642.4(1013.51)	1418.2 (582.69)	1095.8 (845.98)	19.576	0.000*α
Calcium (mg) [a-c, a-d, b-d]	943.5 (510.44)	752.5 (577.62)	608.7 (383.43)	356.8 (392.20)	15.369	0.002*α
Magnesium (mg) [a-c, a-d, b-d]	240.8 (117.87)	186.7 (102.86)	154.1 (54.78)	98.8 (70.21)	21.754	0.000*α
Phosphorus (mg) [a-c, a-d, b-d]	975.7 (399.67)	751.6 (522.05)	619.1 (218.35)	483.8 (263.00)	20.445	0.000*α
Iron (mg) [a-b, a-c, a-d, b-d]	9.5 (4.62)	6.7 (3.91)	5.6 (2.59)	4.5 (2.64)	25.440	0.000*α
Zinc (mg) [a-c, a-d]	7.8 (3.91)	6.8 (4.92)	5.3 (1.60)	4.2 (3.71)	15.900	0.001*α

Significant differences are indicated as exponent. α Kruskal Wallis test β One Way ANOVA test was used. *p<0.05

PUFA: poly unsaturated fatty acid, MUFA: mono unsaturated fatty acid, SFA: saturated fatty acid

The correlation between the age, the duration of CKD, anthropometric measurements, blood pressures, biochemical parameters, energy and nutrient intakes of the individuals participating in the study, and the number of PEW criteria met by the individuals were given in Table 5. Accordingly, the number of PEW criteria met by individuals; had a negative correlation with BW, BMI, UMAC, TSFT, BFP, total protein and albumin levels ($p<0.05$). In addition, in the evaluation made in terms of energy and nutrients, it was determined that there was a significant correlation between all parameters except cholesterol and vitamin C and the number of PEW criteria that individuals met ($p<0.05$).

Table 5. Correlation of the number of PEW criteria met with various variables

	Number of PEW criteria met			**Number of PEW criteria met**	
Variables	**r**	**p**	**Biochemical parameters**	**r**	**p**
Age (year)	-0.095	0.304	Blood glucose(mg/dL)	-0.150	0.105
Duration of CKD	-0.130	0.159	TC (mg/dL)	-0.164	0.172
			LDL-C (mg/dL)	-0.030	0.803
Energy and nutrients			HDL-C (mg/dL)	-0.156	0.194
Energy (kcal)	-0.340	0.000*	Triglyceride (mg/dL)	0.095	0.433
Carbohydrates (g)	-0.197	0.032*	Total protein (g/dL)	-0.310	0.001*
Protein (g)	-0.394	0.000*	Albumin (g/dL)	-0.307	0.001*
Total fat (g)	-0.292	0.001*	Urea (ng/dL)	0.096	0.300
PUFA (g)	0.236	0.010*	Uric acid (mg/dL)	0.023	0.813
MUFA (g)	-0.291	0.001*	Creatinine (mg/dL)	0.145	0.115
SFA (g)	-0.234	0.010*	Iron (µg/dL)	0.008	0.955
Cholesterol (mg)	-0.151	0.100	TIBC (µg/dL)	-0.031	0.840
Fiber (g)	-0.364	0.000*	Ferritin (ng/mL)	0.189	0.175
Vitamin A (µg)	-0.255	0.005*	PTH (pg/dL)	-0.065	0.651
Thiamine (mg)	-0.239	0.009*	Sodium (mEq/L)	0.015	0.873
Riboflavin (mg)	-0.384	0.000*	Potassium (mEq/L)	-0.113	0.222
Niacin (mg)	-0.404	0.000*	Calcium (mg/dL)	-0.137	0.144
Pyridoxine (mg)	-0.243	0.008*	Phosphorus (mg/dL)	-0.014	0.886
Folate (µg)	-0.340	0.000*	Magnesium (mg/dL)	-0.189	0.075
Vitamin B_{12} (µg)	-0.298	0.001*	CRP (mg/dL)	0.059	0.626
Vitamin C (mg)	-0.213	0.020*	GFR (mL/dk/1.73 m^2)	-0.044	0.637
Vitamin E (mg)	-0.090	0.329	**Anthropometric measurements. blood pressures**		
Sodium (mg)	-0.330	0.000*	BW (kg)	-0.328	0.000*
Potassium (mg)	-0.386	0.000*	BMI (kg/m^2)	-0.523	0.000*
Phosphorus (mg)	-0.410	0.000*	UMAC (cm)	-0.569	0.000*
Calcium (mg)	-0.358	0.000*	TSFT (mm)	-0.279	0.002*
Iron (mg)	-0.443	0.000*	BFP (%)	-0.467	0.000*
Magnesium (mg)	-0.419	0.000*	LBM (kg)	0.053	0.564
Zinc (mg)	-0.364	0000*	SBP (mmHg)	-0.068	0.461
			DBP (mmHg)	-0.012	0.896

Spearman correlation was used. *p<0.05

According to the results of linear regression analysis for parameters with statistically significant correlation in Table 5, it was determined that BMI (26.8%) and BFP (25.5%) from anthropometric measurements, albumin level (18.6%) from biochemical parameters, protein (12.7%) and fiber (14.1%) from macronutrients, and magnesium (15.7%) and thiamine (15.0%) from micronutrients; were the most explain parameters the number of PEW criteria met by individuals (Table 6) (p<0.05).

Table 6. Linear regression with number of PEW criteria met

	B	%95 (CI)	β	R^2	p
BW (kg)	-0.017	-0.027- -0.007	-0.311	0.097	0.001*
BMI (kg/m²)	-0.077	-0.100- -0.053	0.518	0.268	0.000*
UMAC (cm)	-0.034	-0.049- -0.018	-0.368	0.135	0.000*
TSFT (mm)	-0.036	-0.056- -0.015	-0.309	0.095	0.001*
BFP (%)	-0.040	-0.052- -0.027	-0.505	0.255	0.000*
Total protein (g/dL)	-0.047	-0.067- -0.027	-0.410	0.168	0.000*
Albumin (g/dL)	-0.070	-0.097- -0.043	-0.432	0.186	0.000*
Energy (kcal)	-0.001	-0.001- 0.000	-0.360	0.130	0.000*
Carbohydrates (g)	-0.003	-0.006- -0.001	-0.273	0.074	0.003*
Protein (g)	-0.012	-0.017- 0.000	-0.357	0.127	0.000*
Total fat (g)	-0.008	-0.013- - 0.003	-0.295	0.087	0.001*
PUFA (g)	-0.019	-0.037- -0.001	-0.189	0.036	0.039*
MUFA (g)	-0.023	-0.036- -0.011	-0.319	0.102	0.000*
SFA (g)	-0.014	-0.026- -0.002	-0.203	0.041	0.027*
Fiber (g)	-0.049	-0.071- -0.027	-0.375	0.141	0.000*
Vitamin A (μg)	-0.009	0.000-0.000	-0.058	0.003	0.534
Vitamin E (mg)	-0.015	-0.030-0.000	-0.186	0.034	0.043*
Thiamine (mg)	-1.184	-1.699- -0.668	-0.387	0.150	0.000*
Riboflavin (mg)	-0.285	-0.466- -0.105	-0.278	0.077	0.002*
Niacin (mg)	-0.026	-0.045- -0.007	-0.241	0.058	0.008*
Pyridoxine (mg)	-0.587	-0.927- -0.247	-0.301	0.091	0.001*
Folate (μg)	-0.002	-0.003- -0.001	-0.261	0.068	0.004*
Vitamin B_{12} (μg)	-0.007	-0.020-0.007	-0.090	0.008	0.330
Sodium (mg)	0.000	0.000-0.000	-0.355	0.126	0.000*
Potassium (mg)	0.000	-0.001-0.000	-0.360	0.130	0.000*
Phosphorus (mg)	-0.001	-0.001-0.000	-0.383	0.147	0.000*
Calcium (mg)	-0.001	-0.001-0.000	-0.333	0.111	0.000*
Iron (mg)	-0.080	0.116- -0.044	-0.376	0.142	0.000*
Magnesium (mg)	-0.004	-0.006- -0.002	-0.397	0.157	0.000*
Zinc (mg)	-0.077	-0.115- -0.038	-0.341	0.116	0.000*

*p<0.05

Discussion

Malnutrition is a common condition in CKD[3], and it has been determined that the incidence of malnutrition in CKD varies between 28-65%, depending on the criteria used in the diagnosis[4, 17-19]. However, most of the studies have been performed in CKD patients with end-stage renal disease or on dialysis[5, 20-25] and there are limited studies evaluating nutritional status in the early stages of CKD[26-28]. Malnutrition seen in CKD, causes negative consequences such as increased disease severity and the risk of disease-related morbidity and mortality[29] and it has been stated that the use of various methods together is more effective than evaluating the malnutrition status with a single method in individuals with CKD[3]. Nutritional levels of the individuals participating in this study were evaluated with SGA and PEW. SGA, which is an independent predictor of all-cause mortality in CKD, is a practical, non-invasive and inexpensive composite tool that is widely used in clinical practice[30]. PEW is considered an important parameter in CKD because it is associated with increased morbidity and mortality and decreased quality of life[31]. In this study, it was determined that 20.2% of the individuals had moderate/severe malnutrition according to SGA and 8.4% with PEW. At the same time, it was determined that 7.7% of individuals in the 2nd stage of CKD, 8.1% of those in the 3rd stage, 10.0% of those in stage 4, and 8.3% of those in stage 5 had PEW; and the rate of PEW was higher in individuals with moderate and severe malnutrition according to the SGA assessment (Table 1) ($p>0.05$). In studies conducted with individuals with CKD who did not receive dialysis treatment, the incidence of PEW was found to be 11% by Cuppari et al.[32] and 9% by Hyun et al.[27] Also, in the study conducted by Sum et al.[33] with individuals receiving hemodialysis treatment, the frequency of PEW was determined as 21.1%, and in the evaluation made according to SGA, it was stated that the risk of PEW was found in 48.9% of the patients. According to studies in which PEW was evaluated based on CKD stages, in the study conducted by Hyun et al.[27] with individuals with predialysis CKD, the incidence of PEW was 4.4% in stage 2 of CKD, 8.3% in stage 3a, 6.2% in stage 3b, 15.6% in the 4th stage and 24.6% in the 5th stage; in the study conducted by Dai et al.[30] it was found that among individuals who did not receive dialysis treatment, it was 2% in those with CKD in stages 1 and 2, 16% in those in 3 and 4 stages, 31% in those in 5th stage, and 44% in those who received dialysis treatment; in the systematic review study conducted by Milovanova et al.[34] with individuals with predialysis CKD, 4.2% in stage 3b of CKD; 21.3% in stage 4; 74.5% in stage 5, but PEW was not seen in stages 2 and 3a. These data indicate that the risk of malnutrition as determined by PEW increases with increasing CKD stage. Therefore, it is thought that evaluating the nutritional status of individuals with CKD from the early stages and implementing necessary interventions will have a positive impact on disease prognosis. Assessing nutrition using tools such as PEW in the early stages and taking appropriate actions can help prevent muscle mass loss, decline in physical function, immune suppression, increased infection risk, and prolonged hospitalization. This approach can improve quality of life and reduce mortality risk in individuals with CKD.

While obesity is associated with high mortality in the general population, this relationship has not been clearly demonstrated in individuals with CKD who do not receive dialysis treatment[35]. In this context, in a study conducted with approximately 454 thousand individuals, it was stated that BMI showed a U-shaped relationship with CKD prognosis. BMI <25 kg/m^2 has been associated with poor prognosis regardless of CKD severity. Additionally, it has been reported that adverse outcomes can be seen in the early stages of CKD in individuals with BMI ≥35 kg/m^2, and this relationship is weak in individuals with GFR <30 mL/min. Therefore, it was stated that the BW management of individuals with CKD should be carefully evaluated[36]. Also, since BMI is insufficient to distinguish between fat mass and lean body mass, it was stated that various anthropometric measurements such as TSFT[2,37] and UMAC should also be evaluated[2]. In this study, it was found that the number of PEW criteria met and BW, BMI, UMAC, TSFT and BFP levels changed significantly (Table 2), had a negative correlation (Table 5) and among these parameters, BMI (26.8%) and BFP (25.5%) were the parameters that most explained the number of PEW criteria met by individuals (Table 6) ($p<0.05$). Parallel to this study, in various studies conducted with individuals with CKD who did not receive dialysis treatment, it was stated that the number of PEW criteria met by the individuals and the levels of BW[26], BMI[11,26,27] BFP and UMAC[11] showed statistically significant differences. In a study conducted by Windahl et al.[38] with individuals in the 4th and 5th CKD stages, it was determined that PEW was seen at a rate of 29.3% and the BMI level of individuals with PEW was lower. Considering all these results, it was determined that anthropometric measurements are an effective parameter in the evaluation of PEW in individuals with CKD. For this reason, it is important and necessary to evaluate the anthropometric measurements of individuals with CKD at regular intervals and to take the necessary precautions depending on the results in the management of the disease and in increasing the quality of life of the patients.

PEW, which is characterized by a decrease in body protein mass and energy reserve, including muscle and fat mass and visceral protein pool, is a condition that is seen at a significantly in CKD and causes negative consequences[39]. Due to the activation of proinflammatory cytokines together with hypercatabolic mechanisms, the incidence of PEW increases as CKD progresses, and the nutritional status of individuals deteriorates with decreased appetite. This situation causes inadequate protein and energy intake as well as get worse in uremic parameters. Uremic metabolites causes complications such as oxidative stress, endothelial dysfunction, deterioration of nitric oxide homeostasis, renal interstitial fibrosis, sarcopenia, increased proteinuria and kidney dysfunction[9]. In this context, it is stated that the early evaluation of CKD patients who do not receive dialysis treatment for malnutrition is effective in fixing various metabolic disorders and reducing morbidity and mortality rates[3]. In this study, it was found that with the increase in the number of PEW criteria met, the serum total protein, albumin, calcium and magnesium levels decreased (Table 3); the PEW criteria number of the individuals had a negative correlation with the total protein and albumin levels (Table 5); and the number of PEK criteria met by individuals was explained by serum total protein level 18.6% and albumin level 16.8% (Table 6) ($p<0.05$). In various studies conducted with individuals with predialysis CKD, it was determined that CRP[11,26,27], GFR, albumin[11,26,27,40], TC[11], calcium and phosphorus[40] levels changed significantly according to the number of PEW criteria met. In a study conducted by Windahl et al.[38], with individuals aged 65 and over who did not receive dialysis treatment with a GFR level of ≤20 mL/min/1.73 m^2, it was stated that individuals with PEW had lower sodium and albumin levels ($p<0.05$). These

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similar results support that there is a relationship between biochemical parameters, which are indicators of nutritional status, and PEW in CKD, and therefore PEW is a marker that can be used in the evaluation of nutritional status.

In individuals with CKD, holistic treatment has goals such as reducing the negative symptoms of uremia, prolonging the transition to dialysis treatment and improving quality of life[41]. In this context, it is stated that the nutritional interventions to be implemented are an important attempt to optimize the clinical outcomes of individuals with CKD[39], however the number of studies evaluating the nutritional status of individuals in the predialysis period is quite limited in the literature[41]. In addition, studies on food consumption of individuals with CKD who do not receive dialysis treatment generally evaluated energy and protein intake[26,27,42-44]. In a study, it was determined that there was a negative correlation between protein intake and creatinine and phosphate levels in individuals with CKD who do not receive dialysis treatment[41]. In the studies conducted by Hyun et al.[26] and Hyun et al.[27] it was stated that the protein intake of individuals decreased with the increase in the number of PEW criteria met ($p<0.05$). In this study, it was detected that with the increase in the number of PEW criteria met, intake of energy and many macro and micronutrients decreased (Table 4), and the number of PEW criteria and parameters other than PUFA (g) intake had a negative correlation (Table 5) ($p<0,05$). Furthermore, the parameters that most explain the number of PEW criteria met by individuals were protein (12.7%), fiber (14.1%), thiamine (15.0%) and magnesium (15.7%) (Table 6) ($p<0.05$). These results reveal that the number of PEW criteria met in individuals with CKD is related to energy and nutrient intake, and importance of assessing nutritional status and making appropriate interventions in these individuals. In addition, this study differs from others in terms of evaluating the relationship between energy and protein intake and non-protein macronutrients and micronutrients with PEW.

Conclusions

In the literature, studies with individuals with CKD were mostly conducted with patients who received dialysis treatment, and studies on CKD patients who did not receive dialysis treatment are limited. Whereas appropriate interventions to be made with the correct evaluation of the nutritional status of the patients in the period before the dialysis treatment will be effective in prolonging the transition to dialysis treatment, reducing the cost of the disease, and increasing the quality of life. Therefore, using the PEW tool developed for individuals with CKD at regular intervals from the diagnosis of the disease is very practical and effective in the evaluation of malnutrition. In addition, it is important to raise awareness of health professionals such as nurses, dietitians, and doctors about the relationship between the nutritional status of individuals with CKD and the prognosis of the disease, to use practical and effective assessment tools and to take initiatives for this situation in cooperation.

Limitation of the Study

Evaluating one parameter from each PEW criterion category in the PEW evaluation is a limitation of the study.

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Ethical Declarations

Ethical Committee Approval

The study was approved by the Ankara University Ethics Committee (Date: 18.06.2019, Decision No: 231) and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Referee Evaluation Process

Externally peer-reviewed.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Concept and Design: SK, AK; Data collection and processing: SK; Data analysis and interpretation: SK; Literature Review: SK; Writing the article: SK; Critical review: SK, AK.

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