North Clin Istanb 2024;11(6):560–568
doi: 10.14744/nci.2023.66503

Original Article NUTRITION & DIETETICS

Determination of nutritional status and protein-energy wasting in patients with diabetic nephropathy

Elif Karakas,[1] Hatice Colak,[2] Fatma Esra Gunes,[3] Berna Karakoyun[4]

[1]Department of Nutrition and Dietetics, Marmara University Institute of Health Sciences, Istanbul, Turkiye
[2]Department of Nutrition and Dietetics, Uskudar University Faculty of Health Sciences, Istanbul, Turkiye
[3]Department of Nutrition and Dietetics, Istanbul Medeniyet University Faculty of Health Sciences, Istanbul, Turkiye
[4]Department of Physiology, University of Health Sciences Hamidiye Faculty of Medicine, Istanbul, Turkiye

ABSTRACT

OBJECTIVE: This study aims to evaluate the nutritional status of patients with stage 3 and 4 diabetic nephropathy (DN; DN-3 and DN-4) and to explain the effect of DN stages on the prognosis of protein-energy wasting (PEW).

METHODS: Data from demographic characteristics, anthropometric measurements, biochemical findings, food consumption records, and the Subjective Global Assessment (SGA) screening tool of 49 patients (25 DN-3; 24 DN-4) who were followed at the nephrology department were collected. The criteria of the International Society of Renal Nutrition and Metabolism (ISRNM) were used to determine PEW.

RESULTS: 56% of DN-3 and 66.7% of DN-4 have been diagnosed with diabetes for over 15 years. The groups differed in total body weight, body-muscle weight, creatinine, microalbuminuria, and eGFR values ($p<0.05$). Protein (g/kg) intake was only different between the groups ($p<0.05$). 18.4% of patients had SGA-B score, and 26.5% had PEW.

CONCLUSION: Our study provides a general impression about the presence of PEW in DN patients not receiving dialysis in Turkiye. In patients with DN-3 and DN-4, daily energy and macronutrient intakes are adequate by recommendation. According to ISRNM criteria, the prevalence of PEW increased with advancing disease stage. PEW was observed to be more effective than SGA in assessing malnutrition.

Keywords: Diabetic kidney disease; malnutrition; nephropathy; nutrition; protein energy wasting.

Cite this article as: *Karakas E, Colak H, Gunes FE, Karakoyun B. Determination of nutritional status and protein-energy wasting in patients with diabetic nephropathy. North Clin Istanb 2024;11(6):560–568.*

Diabetes mellitus (DM) is a chronic, progressive disease characterized by hyperglycemia leading to various problems such as neuropathy, nephropathy, skin changes and ulceration, and cardiovascular complications [1, 2]. Diabetic nephropathy (DN) occurs with progressive deterioration of renal function due to hypertension and decreased glomerular filtration rate (GFR). DN is a persistent microvascular complication of DM, defined as high levels of albumin excretion in the urine and impaired renal activity [3, 4].

Chronic kidney disease (CKD) patients have depleted protein and energy stores and accompanying inflammation [5]. The International Society of Renal Nutrition and Metabolism (ISRNM) defines protein-

This study was presented at Joint Congress of FEPS and Turkish Society of Physiological Sciences, and published in abstract form in Acta Physiologica 2023; Vol. 237 (Suppl. 727): 64–65.

Received: July 13, 2023 *Revised:* October 20, 2023 *Accepted:* November 19, 2023 *Online:* November 19, 2024

Correspondence: Hatice COLAK, MD. Uskudar Universitesi Saglik Bilimleri Fakultesi, Beslenme ve Diyetetik Bolumu, Istanbul, Turkiye.
Tel: +90 216 400 22 22 e-mail: hatice.colak@uskudar.edu.tr / colakhatice5@gmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

energy wasting (PEW) as the combination of muscle loss, fat loss, malnutrition, and inflammation associated with kidney disease that can occur without insufficient dietary intake [5]. Patients with stage 3 DN (DN-3) and stage 4 DN (DN-4) have been reported to have an increased risk of PEW and a higher PEW rate than non-diabetics [6].

Stage 3 is defined as microalbuminuria and usually occurs 6–15 years after the onset of diabetes. The risk of DN and cardiovascular disease is increased at this stage. Stage 4 is referred to as macroalbuminuria and is characterized by a decrease in GFR of 10–12 ml/min per year. When appropriate treatment is not commenced, it results in end-stage renal disease over the years [7].

Studies on the prevalence of PEW have shown that when the Subjective Global Assessment (SGA) screening tool is used, the prevalence of PEW in stage 3 and 4 CKD patients is 12–18%; this prevalence appears to reach 70% in dialysis patients [8–10]. In this study, we aimed to evaluate the nutritional status of patients with DN-3 and DN-4 and to examine PEW. It is also aimed to explain the effect of nutritional status and DN stages on the prognosis of PEW.

Highlight key points

- It was demonstrated that 26.5% of the non-dialysis patients with DN had PEW. The existence of PEW was found to be higher in patients with stage 4 DN than stage 3.
- Patients diagnosed with PEW were found to have significantly lower body weight, body muscle weight, and waist circumference measurements than non-PEW patients. In addition, patients diagnosed with PEW have higher microalbuminuria and lower eGFR.
- It is important that PEW criteria are routinely used to prevent the progression of DN to end-stage renal disease or to detect DN in its early stages.

MATERIALS AND METHODS

Ethics Committee Approval

Ethical approval for this study was obtained from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (date: 04.01.2019, decision no: 09.2018.800). All patients signed the "informed consent form" and "consent form". All procedures were carried out in accordance with the Declaration of Helsinki.

Study Design and Subjects

This descriptive cross-sectional study was conducted in Marmara University Faculty of Medicine, Department of Nephrology, between January 2019 and June 2019. All patients who applied to the nephrology department and were diagnosed with DN were contacted within these dates, and 49 patients diagnosed with DN-3 (n=25) and DN-4 (n=24) patients who met the research criteria and volunteered to participate in the study were included. When the sample size was calculated using the sample article in the G-power analysis with a 95% CI, 5% error, both groups were found to have 13 people each [11].

Patients diagnosed with DN-3 and DN-4 without any chronic disease other than DN (except diabetes and hypertension) were enrolled in the study. Patients aged 25–75 years were selected for the study because DN is reported to be more common in older adults and those with diabetes duration between 15 and 30 years [12, 13]. Individuals who did not meet the inclusion criteria and who had a major illness that would affect their ability to record food consumption using the 3-day recall method were excluded from the study.

Data Collection Tool

In the study, patients were provided with a questionnaire via face-to-face interview. The questionnaire includes individuals' demographic and anthropometric characteristics, biochemical findings and 3-day food records. The SGA screening tool was used to assess patients' nutritional status, and the ISRNM criteria were utilized for determining PEW.

Anthropometric Measurements

The patient's weight, body fat percentage, body mass index (BMI), fat mass, and muscle mass were obtained using the bioelectrical impedance analysis technique with the Inbody 120 brand scale. A seca mechanical height was used to gauge the patients' height and waist circumference was measured with a tape measure. The individuals' height (m) and body weight (kg) values were used to calculate their BMI.

Food Consumption Record

Food consumption records of the patients were taken for 3 consecutive days, including 2-weekdays and 1-weekend day. Energy and macronutrient analyses of food consumption records were evaluated in the BeBis 8.1 program. The percentages of energy and macronutrients

in the food consumption records were calculated based on the Recommended Daily Allowance (RDA). Energy and macronutrient intakes by RDA are considered "inadequate intake" for <66%, "adequate intake" for 67–133%, and "excessive intake" for >133% [14].

Subjective Global Assessment (SGA) Screening Tool

SGA is a tool that assesses nutritional status by using both objective and subjective components. It consists of three sections, including the patient's history, physical examination, and SGA score. The history section includes questions related to weight change, change in food intake, gastrointestinal symptoms, functional capacity, illness, and nutritional needs. The physical examination section evaluates subcutaneous fat loss (triceps, chest), loss of muscle mass, edema, and ascites. The scores of these assessments are classified into the following categories: SGA-A (well-nourished), SGA-B (moderately-malnourished) and SGA-C (severely-malnourished) [15].

Biochemical Parameters

Blood glucose, serum albumin, microalbuminuria, total cholesterol, creatinine, GFR, and C-reactive protein (CRP) levels were retrospectively obtained from the biochemical findings of the patients within the last three months.

Protein-Energy Wasting (PEW) Diagnostic Criteria

Following the ISRNM, four basic parameters (serum biochemistry, body mass, muscle mass, and dietary intake) are evaluated as diagnostic criteria for PEW. Clinical diagnostic criteria of PEW in CKD require serum biochemistry (low serum albumin or low serum prealbumin or low serum cholesterol), body mass (BMI <23 kg/m^2 or unintentional weight loss over time or total body fat percentage), muscle mass (muscle loss or decreased upper middle arm muscle circumference), and dietary intake (unintentional low protein intake or undesirable low dietary energy intake). At least three of the four categories (and at least one test in each of the selected categories) must be met for a diagnosis of PEW due to kidney disease [16].

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) 22.0 software (IBM Corp.; Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were calculated for demographic data. Independent Sample T-test, Mann-Whitney U, Chi-square, and Spearman tests were used to analyze the data. The p-value <0.05 was considered statistically significant.

RESULTS

Our study involved 49 patients diagnosed with DN; 40.8% of the participants were >65 years of age and 61.2% were men. In our study, the body weight and muscle weight of DN-3 patients were higher than DN-4 patients, and this difference was significant (p=0.007; p<0.001, respectively). At the same time, no muscle wasting was observed in DN-3 patients, whereas muscle wasting was found in DN-4 patients (p=0.019). PEW was found in 26.5% of all patients, and 12 of 13 patients with PEW were in the DN-4 group (p=0.001). SGA-B was found in 18.4% of all patients. It was found that the year of kidney disease was negatively correlated with body weight (kg), BMI (kg/m^2), and waist circumference (cm) in DN-3 patients and it was also negatively correlated with body fat weight (kg), body fat percentage (%), waist circumference (cm) in DN-4 patients. (p<0.05; Table 1).

According to the biochemical parameters of the patients, CRP, glucose, and albumin values were higher than the reference values, but there was no difference by the disease stage (Table 2). Creatinine and microalbuminuria levels were lower (p<0.001) and eGFR values were higher (p<0.001) in patients with DN-3 compared to DN-4.

Table 3 shows energy, carbohydrate, and fat intakes did not differ between the groups, while protein intakes per weight were higher in DN-4 patients (p<0.05).

Although age, years of renal disease and diabetes were higher in patients with SGA-B, no significant difference was found (p>0.05). There was a statistically significant difference in body and muscle weight, muscle loss, and eGFR values by SGA scores (p<0.05). The eGFR values, body and muscle weight were more elevated in patients with SGA-A than those with SBA-B, and muscle loss was lower (Table 4).

Table 5 states that body weight, body muscle weight, and waist circumference decreased in patients with PEW (p=0.009, 0.002, 0.044, respectively). In addition, these patients had higher microalbuminuria levels and lower eGFR values (p=0.002, 0.005, respectively).

TABLE 1. Demographic and anthropometric characteristics of the patients and the relationship between anthropometric measurements and year of kidney disease in patients

Variables	Stage of disease				
	Stage 3 DN (n=25) %	Stage 4 DN (n=24) %	Total (n=49) %	χ^2	p
Gender				15.414	<**0.001***
Male	88	33.3	61.2		
Female	12	66.7	38.8		
Age				0.214	0.773
<65 years	56	62.5	59.2		
≥65 years	44	37.5	40.8		
Type of diabetes				0.271	0.667
Type 1 DM	8	12.5	10.2		
Type 2 DM	92	87.5	89.8		
Age at kidney disease diagnosis				0.698	0.538
<9 years	64	75	69.4		
≥9 years	36	25	30.6		
Age at diabetes diagnosis				0.587	0.561
≤15 years	44	33.3	38.8		
>15 years	56	66.7	61.2		
PEW				13.293	**0.001***
PEW exists	4	50	26.5		
PEW not exists	96	50	73.5		
SGA score				3.659	0.074
SGA-A	92	70.8	81.6		
SGA-B	8	29.2	18.4		

Anthropometric measurements	Median (Q1–Q3)		U	Z	p
	Stage 3 DN (n=25)	Stage 4 DN (n=24)			
Body weight (kg)	84.1 (76.8–95.7)	73.0 (67.1–86.3)	164.5	-2.710	**0.007***
BMI (kg/m²)	29.2 (26.4–34.1)	27.6 (24.5–35.7)	264.5	-0.710	0.478
Body fat weight (kg)	24.0 (20.1–33.1)	26.3 (14.3–39.8)	280.5	-0.390	0.697
Body fat percentage (%)	29.2 (25.5–37.4)	38.9 (23.5–46.2)	267.5	-0.650	0.516
Body muscle weight (kg)	34.5 (29.3–37.7)	26.0 (23.0–29.8)	102.5	-3.951	<**0.001***
Waist circumference (cm)	103.0 (97.0–112.5)	100.0 (88.0–111.0)	223.0	-1.541	0.123
Muscle loss (%)	0.0 (0.0–0.0)	0.0 (0.0–4.1)	209.0	-2.343	**0.019***

Anthropometric measurements	Year of kidney disease			
	Stage 3 DN (n=25)		Stage 4 DN (n=24)	
	r	p	r	p
Body weight (kg)	-0.444	**0.026***	-0.386	0.062
BMI (kg/m²)	-0.424	**0.035***	-0.371	0.074
Body muscle weight (kg)	-0.192	0.358	0.140	0.515
Body fat weight (kg)	-0.288	0.163	-0.453	**0.026****
Body fat percentage (%)	-0.119	0.570	-0.437	**0.033****
Waist circumference (cm)	-0.526	**0.007***	-0.456	**0.025****
Muscle loss (%)	0.221	0.288	-0.058	0.786

DN: Diabetic nephropathy; DM: Diabetes mellitus; SGA: Subjective global assessment; BMI: Body mass index; *: Fisher's exact chi-square p<0.05; Mann-Whitney U test; Asym p. Sig. (2-tailed); **: Spearman correlation; Sig. (2-tailed) p<0.05.

Table 2. Biochemical parameters of the patients

Biochemical parameters	Stage of disease, Median (Q1–Q3)		U	Z	p
	Stage 3 DN (n=25)	Stage 4 DN (n=24)			
CRP (mg/L)	5.51 (3.13–16.2)	5.9 (3.1–15.0)	284.5	-0.310	0.756
Glucose (mg/dl)	148.0 (126.5–182.0)	134.0 (115.5–189.2)	243.5	-1.130	0.258
Albumin (g/dl)	3.9 (3.7–4.2)	3.8 (3.6–3.9)	218.0	-1.650	0.099
Creatinine (mg/dl)	2.5 (2.0–2.7)	3.2 (2.6–3.5)	115.5	93.692	<**0.001***
Cholesterol (mg/dl)	183.0 (154.5–209.5)	185.0 (163.5–223.2)	258.5	-0.830	0.406
Microalbuminuria (mg/dl)	58.0 (35.5–207.5)	794.5 (426.8–2295.5)	0.0	-6.001	<**0.001***
eGFR (ml/min/1.73 m^2)	37.8 (30.2–49.9)	23.2 (15–45.4)	18.0	-5.641	<**0.001***

DN: Diabetic nephropathy; CRP: C-Reactive protein; eGFR: Estimated glomerular filtration rate; *: Mann-Whitney U test; Asym p. Sig (2-tailed) p<0.05. Reference values: CRP, 0–5.5 mg/L; Glucose, 70–100 mg/dl; Albumin, 3.5–5.5 g/dl; Creatinine, 0.5–1.2 mg/dl; Cholesterol, <200 mg/dl; Microalbuminuria, <30 mg/dl normal 30–300 mg/dl microalbuminuria >300 mg/dl macroalbuminuria; eGFR (ml/min/1.73 m^2), ≥90 Stage 1, 50–89 Stage 2, 30–49 Stage 3, 15–29 Stage 4, <15 Stage 5.

Table 3. Patients' daily energy and nutrient intakes according to the RDA

Energy and nutrient intake	Stage of disease				U	Z	p
	Stage 3 DN (n=25)		Stage 4 DN (n=24)				
	Median (Q1–Q3)	RDA (%)	Median (Q1–Q3)	RDA (%)			
Energy (kcal/day)	1414.5 (836–2238.3)	74.4	1457.1 (930–2000.2)	76.7	263.0	-0.740	0.459
Carbohydrate (g/day)	147.7 (74.8–227.8)	113.6	159.5 (85.2–228.8)	122.7	238.0	-1.240	0.215
Carbohydrate (%TE)	41.3 (32.4–57.8)	77	43.5 (32.6–53.2)	79	224.5	-1.510	0.131
Protein (g/day)	56 (34.3–84.5)	88.1	53.2 (34.5–88.2)	83.7	286.5	-0.270	0.787
Protein (g/kg)	0.63 (0.26–0.88)	75.9	0.79 (0.28–2.15)	95.2	198.5	-2.031	**0.042***
Fat (g/day)	65.2 (41.1–111.1)	100.3	64.5 (42.7–94.8)	99.2	284.0	-0.320	0.749

DN: Diabetic nephropathy; RDA: Recommended daily allowance; %TE: Total energy percentage; *: Mann-Whitney U test; Asym p. Sig (2-tailed); PEW: Protein-energy waste; DN: Diabetic nephropathy; BMI: Body mass index; SGA: Subjective global assessment; **: Fisher's Exact chi-square. p<0.05.

DISCUSSION

Diabetic nephropathy is a major cause of morbidity and mortality in patients with DM and increases the risk of renal disease progression. Therefore, DN should be diagnosed early, and its progression should be prevented and/or slowed down with appropriate interventions [17].

In our study, over half of patients with DN have been diagnosed with DM for >15 years. It is known that patients with type 1 or type 2 DM have a high risk of developing nephropathy within 15 years after the onset of the disease. [18]. Patients with diabetes duration between 15 and 30 years had a higher prevalence of DN diagnosis [13]. The fact that the year of diabetes diagnosis was more than 15 years in the majority of patients, and this was higher in DN-4, may increase the existence of PEW and consequently progress to end-stage renal disease.

In patients with CKD, it is first recommended to assess body composition for nutritional evaluation [19]. In our study, the total body weight and muscle weight of patients with DN-3 were higher, and muscle loss was increased in patients with DN-4. It was also found that body weight, waist circumference, and BMI in DN-3 and body fat weight, body fat percentage and waist circumference in DN-4 decreased with increasing years of renal disease. Similarly, diabetic CKD patients had re-

Table 4. The relationship between patients' SGA scores and variables

Variables	SGA score, Median (Q1–Q3)		U	Z	p
	SGA-A (n=40)	SGA-B (n=9)			
Age	63 (57.0–68.7)	65 (45.0–71.0)	179.5	-0.013	0.990
Year of kidney disease	5 (3.2–10.0)	6 (4.5–9.0)	166.0	-0.364	0.716
Duration of diabetes	17 (12.2–25.0)	18 (13.5–20.0)	172.5	-0.195	0.846
Anthropometric measurements					
Body weight (kg)	83.7 (74.8–93.7)	66.6 (49.9–80.6)	81.5	-2.543	**0.011***
BMI (kg/m²)	29.4 (26.0–34.7)	27.5 (20.7–33.5)	125.5	-1.407	0.159
Body fat weight (kg)	25.8 (19.0–35.9)	19.0 (10.9–33.7)	135.0	-1.162	0.245
Body fat percentage (%)	29.9 (24.6–43.8)	28.9 (23.5–43.6)	169.5	-0.271	0.786
Body muscle weight (kg)	31.3 (26.3–35.9)	24.1 (21.3–26.1)	56.0	-3.202	**0.001***
Waist circumference (cm)	103.0 (96.2–111.0)	98.0 (81.5–109.5)	117.5	-1.615	0.106
Muscle loss (%)	0.0 (0.0–0.0)	4.7 (3.8–5.7)	6.5	-5.766	**0.001***
Energy and nutrient intake					
Energy (kcal/day)	1502.3 (1229.9–1594.2)	1274.7 (1097.6–1794.9)	162.0	-0.465	0.642
Carbohydrate (g/day)	157.9 (136.4–180.3)	121.8 (98.9–208.1)	167.0	-0.336	0.737
Fat (g/day)	62.6 (52.3–75.2)	64.3 (52.3–70.0)	172.5	-0.194	0.846
Biochemical parameters					
Albumin (g/dl)	3.9 (3.7–4.1)	3.7 (3.1–4.0)	120.0	-1.558	0.119
Glucose (mg/dl)	139.0 (118.0–177.0)	138.0 (118.5–216.5)	154.5	-0.658	0.510
Creatinine (mg/dl)	2.65 (2.3–3.1)	3.0 (2.0–3.6)	170.5	-0.245	0.806
Cholesterol (mg/dl)	183.5 (156.5–210.2)	198.0 (164.0–300.5)	138.5	-1.072	0.284
CRP (mg/L)	5.7 (3.1–15.5)	5.9 (3.1–12.7)	161.5	-0.478	0.632
Microalbuminuria (mg/dl)	250.5 (50.5–559.5)	689.0 (198.5–1574.0)	124.0	-1.446	0.148
eGFR (ml/min/1.73 m²)	32.2 (15.2–49.9)	23.6 (15.1–33.5)	100.0	-2.066	**0.039***

SGA: Subjective global assessment; BMI: Body mass index; CRP: C-Reactive protein; eGFR: Estimated glomerular filtration rate; *: Mann-Whitney U test; Asymp. Sig. (2-tailed) p<0.05.

duced body muscle mass, elevated fat mass, and a lower BMI compared to non-diabetic CKD patients [20]. Changes in body weight, muscle mass, and fat mass are expected as a result of increased exposure to inflammation, increased anorexia and susceptibility to malnutrition as the renal disease year increases.

Our study detected lower eGFR values and higher levels of microalbuminuria and serum creatinine in patients with DN-4 compared to DN-3. CKD patients with DN have been found to lower eGFR levels compared to those without DN [21]. CKD patients with PEW have low albumin levels, total lymphocyte count, fat and muscle mass, high proteinuria, and Na/K ratio [22]. Our outcomes are similar to those in the literature, as the eGFR level decreases and the microalbuminuria level increases as the disease stage progresses.

In non-dialyzed CKD stage 3–5 patients, energy intake is 25–35 kcal/ideal kg/day for ideal weight, while protein intake is recommended as 0.8–0.9 g/kg/day for diabetics. It is generally expected to obtain 50–60% of their total energy intake from carbohydrates and 30% from fat [23]. Our study showed no significant difference in daily energy and protein intake between DN-3 and DN-4. However, patients with DN-4 had a higher protein intake (g/kg) than DN-3. Both groups' daily energy and macronutrient intakes were also adequate by RDA. A study reported a significant reduction in urinary albumin excretion in individuals with type 2 DM and microalbuminuria after restricting carbohydrate intake to 38% of total energy for 12 months [24]. Other studies have demonstrated that energy and macronutrient intake are significantly reduced in patients diagnosed with PEW [22, 25]. Although the anthropometric parameters of

Table 5. Relationship of PEW status with biochemical parameters and anthropometric measurements

Variables	PEW status, Median (Q1–Q3)		U	Z	p
	Exists (n=13)	Not exists (n=36)			
Age	64 (53–67)	62.5 (56.2–69)	228.0	-0.139	0.892
Year of kidney disease	6 (3.5–10)	5.5 (3.2–9.7)	212.0	-0.502	0.616
Duration of diabetes	20 (16.5–21)	16 (12–25)	197.0	-0.842	0.400
Biochemical Parameters					
Glucose (mg/dl)	136.0 (117.0–201.5)	140.0 (119.0–178.7)	228.0	-0.136	0.892
Microalbuminuria (mg/dl)	689.0 (445.0–1811.0)	207.5 (41.2–398.5)	100.0	-3.035	**0.002***
eGFR (ml/min/1.73 m^2)	20.7 (16.8–29.7)	30.4 (27.9–43.7)	111.0	-2.786	**0.005***
Creatinine (mg/dl)	2.5 (1.9–3.2)	2.2 (1.6–2.4)	149.0	-1.925	0.054
CRP (mg/dl)	6.3 (3.19–15.1)	5.7 (3.1–15.2)	230.5	-0.079	0.937
Anthropometric measurements					
Body weight (kg)	70.6 (61.1–81.8)	84 (74.8–94.6)	118.0	-2.627	**0.009***
Body muscle weight (kg)	25.3 (22.7–27.6)	31.9 (26.5–36.1)	98.0	-3.080	**0.002***
Body fat weight (kg)	19.0 (13.7–36.8)	26.1 (19.8–35.9)	171.1	-1.427	0.154
Waist circumference (cm)	99 (86–106.5)	103 (97–113.2)	145.0	-2.017	**0.044***

PEW: Protein-energy wasting; eGFR: Estimated glomerular filtration rate; CRP: C-Reactive protein; *: Mann Whitney U test; Asymp. Sig. (2-tailed) p<0.05.

the patients with DN-3 in our study were better, the daily energy intake and protein intake of the patients with DN-4 were relatively higher. This may indicate enhanced catabolism in patients with DN-4. Inadequate energy and macronutrient intake in renal patients with PEW may lead to malnutrition and the inability to compensate for catabolism in DN.

SGA is a valid tool for assessing malnutrition in CKD [15]. In this study, the majority of the patients were well-nourished, and only 18.4% were moderately malnourished on the SGA score. A study stated that 56.3% had moderate malnutrition and 8.1% had severe malnutrition in hemodialysis patients [26]. In our study, moderately-malnourished patients had lower body weight, less muscle weight, higher muscle loss, and fewer eGFR levels. It was observed that the energy and carbohydrate intakes of moderately-malnourished individuals were lower, although no significant difference was found. In addition, the body weights of patients with SGA-B were statistically lower than patients with SGA-A, and this finding is consistent with other studies in the literature [15, 27]. A study evaluating malnutrition with SGA reported that the incidence of malnutrition increased gradually with the progression of kidney disease and the presence of malnutrition was associated with lower body weight, hemoglobin, total protein, albumin, pre-albumin, and reduced food intake. This study reported the need for a more detailed and sensitive scale for the assessment of malnutrition, especially in stage 3–5 CKD patients [28].

PEW is a valuable tool for early diagnosis of alterations in nutrient intake which includes a combination of several SGA parameters [15]. We determined that 26.5% of the patients had PEW by ISRNM diagnostic criteria and PEW was higher in DN-4 than DN-3. In non-diabetic nephropathy patients, PEW was more common in stage 4 nephropathy than stage 3 [15]. In patients with DN receiving dialysis, the PEW rate was 21–23% based on ISRNM criteria [29]. In another study, the prevalence of PEW among pre-dialysis CKD patients was 33.3% [30]. Pérez-Torres et al. [22] found the prevalence of PEW to be 30.1% and SGA-B to be 27.9% in advanced CKD patients, and there was no difference between the two methods. Meanwhile, another study demonstrated that PEW was more effective than SGA. Using an albumin cut-off value of 3.8 mg/dl instead of 3.5 mg/dl in PEW criteria provides superiority over SGA because PEW successfully predicts and is more sensitive to detect malnutrition [8]. Furthermore, Ho et al. [8] demonstrated that obligatory BMI assessment, in addition to the original PEW criteria, provided a better measure of mortality rate. These PEW rates may differ due to patients with CKD at different stages, dialysis and diabetic status.

Low serum albumin, microalbuminuria, high GFR levels, low BMI and unintentional weight loss, and low muscle and/or fat mass are indicators of PEW [25]. In this study, albumin levels were lower in DN-4 and patients with SGA-B, although not statistically significant. Microalbuminuria was observed in DN-3 patients, macroalbuminuria was noted in DN-4 patients and patients with PEW had more albuminuria than those without PEW. In research in Turkiye, 36% of CKD patients receiving dialysis had albumin levels below 3.8 mg/dl [11]. In the majority of hemodialysis patients, serum albumin levels are below 3.7 mg/dl [31]. Studies have confirmed that the albumin levels of patients with PEW were lower than the patients without PEW [8, 11, 22]. Oral energy supplementation for 2 months among hemodialysis patients with PEW has improved hemoglobin, albumin and nutrient intake [32]. In non-dialysis CKD patients who followed up for 2 years, oral nutritional support resulted in improvements in BMI, serum albumin and inflammatory markers [33]. It is critical to screen for PEW in patients who have had diabetes for many years and in patients with early-stage CKD and to provide appropriate nutritional support to patients with PEW.

Our study found that the body weight, body muscle weight and waist circumference measurements of patients with PEW were significantly lower than those without PEW. Vanden Wyngaert et al. [34] stated that PEW is a predictor of increased fall risk and impaired exercise capacity in hemodialysis patients. Changes such as insufficient nutrient intake due to appetite loss and dietary factors, increased energy expenditure, acidosis, multi-catabolic endocrine disorders, and continuous inflammation lead to excessive muscle and adipose loss [6]. Therefore, it is expected that the deterioration of nutritional status in patients with PEW is accompanied by inflammation [16]. In our study, CRP values were found to be higher in patients with PEW, although not statistically significant. At the same time, CRP values were above the reference values in both groups, indicating inflammation in patients. PEW, which uses total cholesterol, serum albumin and BMI values for diagnostic criteria, reflects malnutrition and inflammation, and PEW values are associated with morbidity and mortality [16]. In a large cohort study by Ho et al. [8], PEW was associated with a higher risk of mortality at 3 months and 1 year. It was also stated that a modest decrease in BMI, serum albumin and total cholesterol levels based on PEW criteria caused by malnutrition results in worse survival.

The limitations of our study include the single-center design of the study and the small population. The evaluation and comparison of malnutrition in DN patients according to the PEW criteria defined by ISRNM and using the SGA screening tool is a strength of this study. Our study determined that the presence of PEW in non-dialysis patients with diabetic nephropathy is at significant levels while PEW studies in the literature have generally focused on renal patients receiving dialysis. Therefore, it is considered that PEW assessment may predict malnutrition in this patient group.

Conclusion

This study presents an overview of the PEW assessment in diabetic nephropathy non-dialysis patients in Turkiye with the aim of enhancing awareness of malnutrition and encouraging early intervention. This study evaluated the nutritional status of patients with DN, and all patients had adequate daily energy and macronutrient intakes by RDA. It was reported that 26.5% of the patients had PEW. Furthermore, in a comparison of SGA and PEW used to evaluate malnutrition, PEW was assessed to be more effective. PEW was observed to affect albuminuria, GFR, body weight, body muscle weight, and waist circumference. PEW, related to mortality and morbidity risk, is an important tool that reflects inflammation and malnutrition as assessed by serum albumin, total cholesterol, CRP, GFR, BMI, and muscle mass. Therefore, it is important to use PEW criteria routinely to prevent the progression of DN to end-stage renal disease or to detect DN in the early stages. There should be longitudinal cohort studies on the effectiveness of PEW to predict malnutrition in this patient group.

Ethics Committee Approval: The Marmara University Clinical Research Ethics Committee granted approval for this study (date: 04.01.2019, number: 09.2018.800).

Authorship Contributions: Concept – EK; Design – EK, FEG; Supervision – BK; Fundings – EK; Materials – EK, HC; Data collection and/or processing – EK, HC, FEG, BK; Analysis and/or interpretation – EK, HC; Literature review – EK, HC; Writing – EK, HC; Critical review – HC, FEG, BK.

Conflict of Interest: No conflict of interest was declared by the authors.

Use of AI for Writing Assistance: This article does not include any work by artificial intelligence – assisted technologies.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Mekala KC, Bertoni AG. Epidemiology of diabetes mellitus. In: Orlando G, Piemonti L, Ricordi C, Stratta RJ, Gruessner RWG, editors. Transplantation, Bioengineering, and Regeneration of the Endocrine Pancreas. Cambridge: Academic Press; 2020. p. 49–58. [CrossRef]
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37:S81–90. [CrossRef]
3. Dagar N, Das P, Bisht P, Taraphdar AK, Velayutham R, Arumugam S. Diabetic nephropathy: a twisted thread to unravel. Life Sci 2021;278:119635. [CrossRef]
4. Cai T, Yang J. Diabetic kidney disease. In: Yang J, He W, editors. Chronic Kidney Disease: Diagnosis and Treatment. Singapore: Springer; 2020. pp. 33–43. [CrossRef]
5. Carrero JJ, Stenvinkel P, Cuppari L, Ikizler TA, Kalantar-Zadeh K, Kaysen G, et al. Etiology of the protein-energy wasting syndrome in chronic kidney disease: a consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM). J Ren Nutr 2013;23:77–90. [CrossRef]
6. Hyun YY, Lee KB, Han SH, Kim YH, Kim YS, Lee SW, et al. Nutritional status in adults with predialysis chronic kidney disease: KNOW-CKD study J Korean Med Sci 2017;32:257–63. [CrossRef]
7. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. Kidney Int 2020;98:S1–115. [CrossRef]
8. Ho LC, Wang HK, Chiu LT, Wang HH, Lee YC, Hung SY, et al; Taiwan Stroke Registry Investigators. Protein energy wasting-based nutritional assessment predicts outcomes of acute ischemic stroke and solves the epidemiologic paradox. Nutrition 2022;93:111431. [CrossRef]
9. Cordeiro AC, Qureshi AR, Stenvinkel P, Heimbürger O, Axelsson J, Bárány P, et al. Abdominal fat deposition is associated with increased inflammation, protein-energy wasting and worse outcome in patients undergoing haemodialysis. Nephrol Dial Transplant 2010;25:562–8. [CrossRef]
10. Kovesdy CP, Kopple JD, Kalantar-Zadeh K. Management of protein-energy wasting in non-dialysis-dependent chronic kidney disease: reconciling low protein intake with nutritional therapy. Am J Clin Nutr 2013;97:1163–77. [CrossRef]
11. Yurtdaş G, Karabudak E, Mandıroğlu F. Assessment of nutritional status of haemodialysis patients with protein energy wasting diagnostic criteria. [Article in Turkish]. J Nutr Diet 2017;45:35–43.
12. Satirapoj B, Adler SG. Comprehensive approach to diabetic nephropathy. Kidney Res Clin Pract 2014;33:121–31. [CrossRef]
13. Al-Rubeaan K, Bawazeer N, Al Farsi Y, Youssef AM, Al-Yahya AA, AlQumaidi H, et al. Prevalence of metabolic syndrome in Saudi Arabia - a cross sectional study. BMC Endocr Disord 2018;18:16. [CrossRef]
14. Trumbo P, Schlicker S, Yates AA, Poos M; Food and Nutrition Board of the Institute of Medicine, The National Academies. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. J Am Diet Assoc 2002;102:1621–30. [CrossRef]
15. Cuppari L, Meireles MS, Ramos CI, Kamimura MA. Subjective global assessment for the diagnosis of protein-energy wasting in nondialysis-dependent chronic kidney disease patients. J Ren Nutr 2014;24:385–9. [CrossRef]
16. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney Int 2008;73:391–8. [CrossRef]
17. Warren AM, Knudsen ST, Cooper ME. Diabetic nephropathy: an insight into molecular mechanisms and emerging therapies. Expert Opin Ther Targets 2019;23:579–91. [CrossRef]
18. Varghese RT, Jialal I. Diabetic nephropathy. Available at: https://www.ncbi.nlm.nih.gov/books/NBK534200/. Accessed Sept 13, 2024.
19. Teo BW, Chua HR, Wong WK, Haroon S, Subramanian S, Loh PT, et al. Blood pressure and antihypertensive medication profile in a multiethnic Asian population of stable chronic kidney disease patients. Singapore Med J 2016;57:267–73. [CrossRef]
20. D'Alessandro C, Barsotti M, Cianchi C, Mannucci C, Morganti R, Tassi S, et al. Nutritional aspects in diabetic CKD patients on tertiary care. Medicina (Kaunas) 2019;55:427. [CrossRef]
21. Liang H, Lu T, Liu H, Tan L, Li L, Tang X. Significance of renal perfusion angiography and biochemical indicators in early diagnosis of type 2 diabetic nephropathy. Pathol Lab Med 2018;3:5–9. [CrossRef]
22. Pérez-Torres A, González Garcia ME, San José-Valiente B, Bajo Rubio MA, Celadilla Diez O, López-Sobaler AM, et al. Protein-energy wasting syndrome in advanced chronic kidney disease: prevalence and specific clinical characteristics. Nefrologia (Engl Ed) 2018;38:141–51. [CrossRef]
23. Ikizler TA, Burrowes JD, Byham-Gray LD, Campbell KL, Carrero JJ, Chan W, et al. KDOQI clinical practice guideline for nutrition in CKD: 2020 update. Am J Kidney Dis 2020;76:S1–S107. [CrossRef]
24. Haimoto H, Sasakabe T, Umegaki H, Wakai K. Reduction in urinary albumin excretion with a moderate low-carbohydrate diet in patients with type 2 diabetes: a 12-month intervention. Diabetes Metab Syndr Obes 2012;5:283–91. [CrossRef]
25. Beddhu S, Chen X, Wei G, Raj D, Raphael KL, Boucher R, et al. Associations of protein-energy wasting syndrome criteria with body composition and mortality in the general and moderate chronic kidney disease populations in the United States. Kidney Int Rep 2017;2:390–9. [CrossRef]
26. Mun CY, Shariff ZM, Seong CLT, Leong GB. Factors associated with poor nutritional status among hemodialysis patients in Malaysia. Malays J Med Health Sci 2019;15:77–83.
27. Essadik R, Msaad R, Lebrazi H, Taki H, Tahri EH, Kettani A, et al. Assessing the prevalence of protein-energy wasting in haemodialysis patients: a cross-sectional monocentric study. Nephrol Ther 2017;13:537–43. [CrossRef]
28. Xi WZ, Wu C, Liang YL, Wang LL, Cao YH. Analysis of malnutrition factors for inpatients with chronic kidney disease. Front Nutr 2023;9:1002498. [CrossRef]
29. Ruperto M, Sánchez-Muniz FJ, Barril G. Predictors of protein-energy wasting in haemodialysis patients: a cross-sectional study. J Hum Nutr Diet 2016;29:38–47. [CrossRef]
30. Osunbor OA, Unuigbe EI, Okaka EI, Adejumo OA. Protein energy wasting in pre-dialysis chronic kidney disease patients in Benin City, Nigeria: a cross-sectional study. PLoS One 2023;18:e0286075. [CrossRef]
31. Arias-Guillén M, Collado S, Coll E, Carreras J, Betancourt L, Romano B, et al. Prevalence of protein-energy wasting in dialysis patients using a practical online tool to compare with other nutritional scores: results of the nutrendial study. Nutrients 2022;14:3375. [CrossRef]
32. Qin A, Tan J, Hu W, Liu Y, Chen L, Tang Y, et al. Oral energy supplementation improves nutritional status in hemodialysis patients with protein-energy wasting: a pilot study. Front Pharmacol 2022;13:839803. [CrossRef]
33. Wong MMY, Zheng Y, Renouf D, Sheriff Z, Levin A. Trajectories of nutritional parameters before and after prescribed oral nutritional supplements: a longitudinal cohort study of patients with chronic kidney disease not requiring dialysis. Can J Kidney Health Dis 2022;9:20543581211069008. [CrossRef]
34. Vanden Wyngaert K, Celie B, Calders P, Eloot S, Holvoet E, Van Biesen W, et al. Markers of protein-energy wasting and physical performance in haemodialysis patients: a cross-sectional study. PLoS One 2020;15:e0236816. [CrossRef]