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Can the serum Creatine Kinase (CK) level be a malnutrition parameter in patients with end-stage kidney failure?

Son Dönem Böbrek Yetmezliği Hastalarında Serum Kreatin Kinaz (Ck) Düzeyi Malnutrisyon Parametresi Olabilir Mi?

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ABSTRACT

Aim: The aim of this study was to investigate the relationship between serum CK levels and malnutrition parameters in patients undergoing hemodialysis (HD) and peritoneal dialysis (PD) for end stage renal disease (ESRD).
Methods: In this prospective study, 60 patients receiving HD and 30 patients receiving PD for ESRD were evaluated. The relationship between serum CK levels and Mini Nutritional Assessment (MNA) Test scores, albumin, C-Reactive Protein (CRP), arterial blood gas parameters, KT / V ratio, total body water, muscle mass, body mass index (BMI) and lean body mass (determined by Bioelectrical Impedance Analysis (BIA) were examined.
Results: No correlation was found between CK levels and age, dialysis duration and Ca values in HD and PD patients (p> 0.05). A positive correlation was found between CK levels and MNA scores and triceps skinfold thickness, lean body mass, body muscle mass and BMI values of PD and HD patients, and a significant negative correlation between total body water values (p <0.001).
Conclusions: It was determined that serum CK level was compatible with other parameters used in the determination and follow-up of nutritional disorder and sarcopenia in ESRD patients.

Key Words: End-Stage Renal Disease, Bioelectrical Impedance, Creatine Kinase, Sarcopenia, Malnutrition

ÖZ

Amaç: Bu çalışmanın amacı; Son Dönem Böbrek Yetmezliği (SDBY) nedeniyle hemodiyaliz (HD) ve periton diyalizi (PD) tedavisi alan hastalarda serum CK düzeyleri ile malnutrisyon parametreleri arasındaki ilişkiyi incelemektir.
Gereç ve Yöntem: Prospektif olarak yürütülen bu çalışmada, Türkiye' nin Ege bölgesinde hizmet veren bir hastanede SDBY nedeniyle HD tedavisi alan 60 hasta ve PD tedavisi alan 30 hasta değerlendirildi. Hastaların serum CK düzeyi ile Mini Nutrisyonel Değerlendirme Testi (MND)' nden aldıkları puanlar, albumin ve C-Reaktif Protein (CRP) gibi biokimyasal parametreler, arteriyel kan gazı değerleri, KT/V oranı, Biyoelektriksel İmpedans Analiz (BİA) yöntemiyle bakılan total vücut suyu, kas kütlesi, vücut kitle indeksi (VKİ) yağsız vücut kütlesi ve VYO (vücut yağ oranı) gibi değişkenler arasındaki ilişki incelendi.
Bulgular: HD ve PD hastalarında CK düzeyleri ile yaş, diyaliz süresi ve Ca değerleri arasında ilişki saptanmadı (p>0,05). HD ve PD hastalarının CK düzeyleri ve MND puanları ile BİA parametrelerinden yağsız vücut kütlesi, vücut kas kütlesi ve VKİ değerleri arasında pozitif yönde, TVS değerleri arasında negatif ilişki saptandı (p<0,001).
Sonuç: SDBY hastalarında serum CK düzeyinin, beslenme bozukluğu ve sarkopeninin belirlenmesi ve takibinde kullanılan diğer parametreler ile uyumlu olduğu görülmektedir.

Anahtar Kelimeler: Son Dönem Böbrek Hastalığı, Biyoelektriksel Empedans, Kreatin Kinaz, Sarkopeni, Malnütrisyon

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INTRODUCTION

Chronic renal failure (CRF) is an increasingly important public health problem in our country and in the world, and is defined as a pathological condition characterized by chronic, progressive and irreversible nephron loss due to various diseases (1). End-stage renal failure (ESRD) develops as a result of persistent kidney damage in patients followed up with the diagnosis of CRF. In this period, renal replacement treatment (RRT) is needed and the conservative approach consists of hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation (2). After starting dialysis treatment in patients with CRF, susceptibility to malnutrition occurs through factors such as the metabolic effects caused by dialysis in the body, chronic acidemia, chronic inflammation and oxidative stress (3).

Malnutrition means both poor nutrition and over nutrition and expresses the intake deficiency that will not meet the need and thereupon the developing pathological condition (4); it is an important problem leading to mortality and morbidity in CRF patients. Many biochemical and anthropometric measurements are used for the diagnosis of malnutrition (5). Bio-impedance Analysis (BIA) is the body composition analysis method which is used in the follow-up of malnutrition and the main principle of which is to measure the resistance of the tissues against the passage of the electrical current through the body tissues. Through the BIA method, various body components can be examined such as the body mass index (BMI), the lean body mass, the basal metabolic rate, the body fat ratio (BFR), and the total body water (TBW) (6). The Mini Nutritional Assessment (MNA) test is a fast, reliable, cheap and practical method used to determine the nutritional status of the elderly population and outpatients, which includes questions about the patient's lifestyle, mobilization and diet, as well as anthropometric measurements. It consists of four sections that provide the opportunity to determine the nutritional status in a subjective and general manner. These sections include questions about the patient's lifestyle, mobility, nutritional content and order, and anthropometric measurements (7).

Serum creatine kinase (CK) level is used in clinical practice in the diagnosis and follow-up of muscle-related diseases such as rhabdomyolysis, myocardial infarction, myositis and muscular dystrophy (8). CK enzyme that keeps the cell energy balance and have a key role in energy flow is closely associated with the parameters, reflecting the muscle mass directly, such as BMI and lean body mass, which are the known indicators of muscle mass in an organism (9). The aim of this study was to examine whether or not there is a correlation between the serum CK levels and other parameters (anthropometric measurements, biochemical values, MNA test, BIA) used in the follow-up of malnutrition in the patients receiving HD and PD treatment due to ESRD.

MATERIAL-METHOD

Study Model

This prospective study was conducted in a training and research hospital in the Aegean Region of Turkey, between April 2017 and April 2018, with 60 patients followed-up as a result of a diagnosis of ESRD and included in the routine HD program, and 30 patients in the PD program. We received the written, Informed Volunteer Consent Form (IVCF) of all patients and those who did not complete the IVCF, provided an inadequate answer to their anamnesis questions, were illiterate, had an additional psychiatric disease, were pregnant, were diagnosed with coronary artery disease, rhabdomyolysis and myopathy, had gone through a recent physical trauma, or were using statin drugs for hyperlipidemia, were excluded from the study. Approval to conduct the study was received from the clinical trials ethics committee of the hospital where the study was conducted (Date: 07.03.2017, Decision number: 10).

Data Collection

The laboratory findings specific to malnutrition measured in the last 3 months synchronously with CK were reached through the hospital information system, thanks to the routine follow-ups of the HD and PD patients, in order to assess the laboratory data for the nutritional condition of the patients. In the biochemistry laboratory of the hospital where the research was conducted,

laboratory examination data were obtained using the enzymatic method in the Olympus AO 5800 autoanalyzer. The patients were subjected to a four-part MNA check including 18 questions and were divided into three groups based on their MNA scores. The anthropometric evaluations (height, middle arm and calf circumference) in the first section were made using a tape measure with a sensitivity of 0.01 cm. The measurements were taken with the head upright, the soles of the feet flat on the ground, the knees stretched, the heels adjacent and the body taken upright. BMI values of the patients were calculated. The answers to the questions in the other three sections were filled in as a separate questionnaire for each patient and the scores were collected. Results were evaluated over 30 points and divided into three groups according to MND scores. It was considered that the nutritional status of patients obtaining the scores of > 24.0 in MNA was good, whereas patients obtaining a score between 17.0-23.5 were considered at risk for protein energy malnutrition (PEM); the presence of PEM was considered for patients obtaining a MNA score of 17.0.

BİA measurements were done with the Tanita-Body Composition Analyzer BC-420MA device. Patients were asked to stand on bare feet on the metal surface of the device and to release their arms parallel to the body. The measurement results were output from the device and the process required approximately 1-2 minutes for each subject.

Triceps skin fold thicknesses were measured with Holtain Skinfold Caliper device. With the patient standing upright, bending the left arm 90˚ from the elbow, the middle point between the acromion and olecranon protrusions was found, the arm was released and the layer was held with the left marker and thumb, and the right hands were measured from the place marked with the caliper.

Statistical Analyses

SPSS 25.0 packaged software was used in the analysis of variables. While the compatibility of the data with normal distribution was assessed with the Shapiro-Wilk test, the homogeneity of variances was evaluated using Levene's test. In the comparison of two independent groups based on qualitative data, Independent-Samples T test was used together with Bootstrap results and the Mann-Whitney U test was used using the Monte Carlo simulation technique. The correlations of the variables with each other were assessed using Pearson Correlation and Kendall's tau-b tests. In the comparison of the categorical variables, the Pearson Chi-Square and Fisher-Fisher Exact tests were performed using Exact results and the Fisher-Freeman-Holton test was performed using the Monte Carlo Simulation technique. The quantitative variables were shown as mean±SD (Standard Deviation) and median (Minimum / Maximum) and the categorical variables were shown as n (%) in the tables. The variables were examined at confidence level of 95% and the results with $p<0.05$ were determined to be significant.

RESULTS

The average age of the PD patients included in the study was 46.5 (28-73)/ years and was statistically significantly lower compared to the HD patients (58.0 (26-78) / years) ($p<0.001$). There was no significant difference between the groups in terms of gender and the presence of comorbid diseases ($p>0.05$) (Table 1).

Phosphor median value was 3.8 (1.8 - 5.7) mg/dl in HD patients and 4.8 (3.5 - 5.3) mg/dl in PD patients and it was observed to be statistically significantly lower in HD patients ($z=-4.022$, $p<0.001$). The Ca median value was 9.0 (7.7 - 11.0) mg/dl in HD patients and 10.0 (8.7 - 10.9) mg/dl in PD patients and it was statistically significantly lower in HD patients ($z=-5.300$, $p<0.001$). Mean pH value of venous blood was 7.3±0.1 in HD patients and 7.4±0.0 in PD patients and it was observed to be statistically significantly lower in HD patients ($t=-2.789$, $p=0.004$). Mean value of KT/V ratio was 1.5±0.1 in HD patients and 1.7±0.1 in PD patients and it was statistically and significantly lower in HD patients ($t=-11.993$, $p=0.001$). No statistically significant difference was determined between HD and PD patients in terms of albumin, HCO3, total cholesterol, LDL cholesterol and transferrin saturation percentage medians and CK, creatinine and CRP median values ($p>0.05$)(Table 2).

Median MNA score was determined to be 21.0 (15.0 - 28.0) and in HD patient group and 22.0

(15.0-26.0) in PD patient group and no statistically significant difference was determined between HD and PD patients in terms of MNA scores (z=-1.367; p=0.218). Based on MNA test scores, it was determined that there was malnutrition in 21.7% (n=13) of the HD patients, 60% (n=36) of them had risk in terms of malnutrition and 18.3% (n=11) had a normal nutrition status. It was determined that 13.3% (n=4) of the PD patients had malnutrition, 53.3% (n=16) were at risk of malnutrition, and 33.3% (n=10) had a normal nutrition status. In the intergroup comparison performed based on MNA test scores of HD and PD patients, no statistically significant difference was determined (p=0.218; X 2 =2.701) (Table 2).

Table 1. Sociodemographic characteristics of the patients undergoing hemodialysis and peritoneal dialysis

		Dialysis Type			
		Hemodialysis (n=60)	Peritoneal (n=30)		
		Median (Min.-Max.)	Median (Min.-Max.)	z-X2-t	p
Age		58.0 (26.0 - 78.0)	46.5 (28.0 - 73.0)	-4.507	<0.001a
		n (%)	n (%)		
Gender	Female	30.0 (50.0)	16.0 (53.3)	0.089	0.825 b
	Male	30.0 (50.0)	14.0 (46.7)		
Presence of Comorbid Disease	Yes	8.0 (13.3)	5.0 (16.7)	0.180	0.753 c
	No	52.0 (86.7)	25.0 (83.3)		
Comorbid Disease	Other	16.0 (30.8)	7.0 (28.0)	0.681	0.900 d
	DM	19.0 (36.5)	9.0 (36.0)		
	HT	13.0 (25.0)	8.0 (32.0)		
	PKD	4.0 (7.7)	1.0 (4.0)		
Time / year		Mean±SD	Mean±SD		
		5.4±1.9	4.9±1.2	1.275	0.209 e

a: Mann Whitney U test (Monte Carlo), b: Pearson Chi-Square Test (Exact), c: Fisher Exact Test (Exact), d: Fisher Freeman Halton Test (Monte Carlo), e: Independent Samples T test (Bootstrap), Min: Minimum, Max: Maximum, SD: Standard deviation, DM: Diabetes Mellitus, HT: Hypertension , PKD: Polycystic Kidney Disease

In the comparison of BIA values of HD and PD patients, no statistically significant difference was determined between the two groups in terms of body muscle index, BMI and TBW median values (p>0.05). The BFR median value was 26.3 (16.7 - 30.4) in HD patients and 27.2 (22.5 - 29.8) in PD patients and was statistically significantly lower in HD group (p=0.016; z=-2.594). While the mean value of lean body mass was 35.4 ± 4.1 in HD patients, it was 37.7±2.3 and statistically significantly higher in PD patients (p=0.001; t=-3.466) (Table 2). No statistically significant correlation was determined between CK levels and age, duration of dialysis, and Ca variables in HD and PD patients (p>0.05). While CK levels had a statistically significant positive correlation with albumin, phosphor, HCO3, HGB, total cholesterol, LDL, transferrin saturation, pH of arterial blood gas, KT/V ratio and creatinine values in HD and PD patients, they had a statistically significant negative correlation with CRP values (p<0.05) (Table 3).

There was a positive statistically significant correlation between CK levels and MNA scores, triceps skinfold thickness, lean body mass, body muscle mass and BMI values in HD and PD patients, and a negative statistically significant correlation between CK levels and TBW values (p<0.001) (Table 3).

DISCUSSION

When the correlation of serum CK levels with BIA data in HD and PD patient group was examined in the present study, it was determined that they had a positive statistically significant correlation with the variables such as BMI, BFR, lean body mass and body muscle mass (p<0.001) and a negative statistically significant correlation with TBW (p<0.001) in both patient populations. In the literature, Flahault et al., (2016) assessed retrospectively 1801 chronic kidney patients not undergoing dialysis in their study, where they stated that serum CK level had a significant correlation with BMI and muscle mass and that it may reflect the nutritional situation (8). In the present study, it was revealed that serum CK level was correlated with the parameters in BIA method that has been increasingly used recently, which is compatible with the literature.

MNA test is a method widely used in determination of malnutrition and it is recommended in determination and follow-up of malnutrition by international guidelines. A statistically significant correlation was determined between serum CK levels and MNA scores both in HD and PD patients (p<0.001). In the literature review, it was observed that there was a statistically significant correlation

Table 2. Comparison of the laboratory findings, MNA scores and bioimpedance analyses of patients undergoing hemodialysis and peritoneal dialysis.

		Dialysis Type			
		Hemodialysis(n=60)	Peritoneal (n=30)		
		Median(Min-Max)	Median(Min-Max)	z/t	p
Laboratory Findings	Albumin (g/dl)	3.5 (2.6 - 4.9)	3.8 (2.8 - 4.7)	-1.749	0.068 a
	Phosphor (mg/dl)	3.8 (1.8 - 5.7)	4.8 (3.5 - 5.3)	-4.022	<0.001 a
	HCO3 (mmol/L)	22.0 (17.0 - 28.0)	22.1 (17.9 - 25.8)	-0.433	0.649 a
	HGB (g/dl)	11.3 (8.6 - 12.7)	10.7 (9.8 - 11.9)	-2.241	0.018 a
	Ca (mg/dl)	9.0 (7.7 - 11.0)	10.0 (8.7 - 10.9)	-5.300	<0.001a
	Total Cholesterol (mg/dl)	126.5 (48.0 - 178.0)	124.0 (59.0 - 168.0)	-0.539	0.602 a
	LDL (mg/dl)	95.0 (52.0 - 128.0)	88.5 (64.0 - 130.0)	-1.426	0.153 a
	Transferrin sat (%)	18.9 (8.5 - 25.9)	20.5 (13.2 - 26.9)	-1.190	0.240 a
		Mean±SD	Mean±SD		
	CK (U/L)	75.1±36.5	88.1±31.5	-1.666	0.078 b
	pH	7.3±0.1	7.4±0.0	-2.789	0.004 b
	KT/V	1.5±0.1	1.7±0.1	-11.993	0.001 b
	Creatinine (mg/dl)	5.1±0.7	4.9±0.5	0.732	0.410 b
	CRP (mg/dl)	10.6±2.3	10.3±1.83	0.469	0.636 b
		n (%)	n (%)	x2 / Z	p
MNA Scores	Impaired	13.0 (21.7)	4.0 (13.3)	2.701	0.218 c
	Risky	36.0 (60.0)	16.0 (53.3)		
	Normal	11.0 (18.3)	10.0 (33.3)		
		Median(Min-Max)	Median(Min-Max)		
	MNA	21.0 (15.0- 28.0)	22.0 (15.0 – 26.0)	-1.367	0.166 d
		Mean±SD	Mean±SD	z/t	p
Bioimpedance Analyses	Lean body Mass	35.4±4.1	37.7±2.3	-3.466	0.001 b
		Median(Min-Max)	Median(Min-Max)		
	Body Muscle Mass	33.0 (20.1 - 41.8)	35.2 (27.8 - 41.9)	-1.793	0.076 a
	BMI	25.5 (19.7 - 30.7)	24.7 (21.3 - 28.9)	-1.875	0.056 a
	BFR	26.3 (16.7 - 30.4)	27.2 (22.5 - 29.8)	-2.594	0.016a
		27.8 (25.3 - 44.5)	27.4 (26.0 - 43.9)	-1.610	0.100a

a: Mann Whitney U test (Monte Carlo), b: Independent Samples T test (Bootstrap), c: Fisher Freeman Halton Test (Monte Carlo), d: Mann Whitney U test (Monte Carlo), SD: Standard deviation, Min: Minimum, Max: Maximum, MNA, Mini Nutritional Assessment, BMI: Body Mass Index, BFR: Body Fat Rate, TBW: Total Body Water

between MNA test and the other nutritional parameters, such as albumin and CRP (10,11). Similar to the literature, it was also revealed in the present study that the improvement in the nutritional situation in HD and PD patient groups was compatible with an increased serum CK level, which was considered to be an indicator of muscle mass and nutrition in the group of patients with ESRD.

In the present study, a positive statistically significant correlation was determined between serum CK levels and albumin in HD and PD patient groups (p<0.001). Similar to the present study, in their study Flahault et al., (2016) determined the existence of a positive statistically significant correlation between serum CK levels and albumin (8).

In addition to the use of CRP as acute phase reactant in the clinic, it was reported that it may be used in the follow-up of malnutrition in CRF (11). A previous study conducted in HD patient group revealed that CRP value was negatively associated with the reduced loss of muscle mass (12). In the present study, a negative significant correlation was determined between serum CK levels and CRP in HD and PD patient groups (p<0.001). This situation may be explained by the loss of muscle mass occurring after the inflammatory process was observed increasing in ESRD patients, resulting potentially from

decreased cytokine clearance, atherosclerosis, cardiac failure or a stubborn infection.

Table 3. The correlation between CK levels with sociodemographic characteristics, laboratory values, MNA scores and bioimpedance analyses of the patients undergoing hemodialysis and peritoneal dialysis

Correlation with CK						
	r	p	r	p	r	p
Age	-0.160	0.077	-0.037	0.846	-0.201	0.058
Duration of Dialysis	-0.036	0.786	0.051	0.790	-0.020	0.785
Albumin	0.737	<0.001	0.938	<0.001	0.758	<0.001
Phosphor	0.626	<0.001	0.708	<0.001	0.592	<0.001
HCO3	0.557	<0.001	0.750	<0.001	0.583	<0.001
HGB	0.625	<0.001	0.791	<0.001	0.511	<0.001
Ca	0.117	0.371	0.189	0.159	0.151	0.039
Total Cholesterol	0.697	<0.001	0.560	<0.001	0.660	<0.001
LDL	0.759	<0.001	0.760	<0.001	0.776	<0.001
Transferrin saturation	0.633	<0.001	0.615	<0.001	0.625	<0.001
pH	0.814	<0.001	0.834	<0.001	0.822	<0.001
KT/V	0.838	<0.001	0.885	<0.001	0.535	<0.001
Creatinine	0.811	<0.001	0.945	<0.001	0.811	<0.001
CRP	-0.837	<0.001	-0.820	<0.001	-0.827	<0.001
MNA	0.867	<0.001	0.767	<0.001	0.831	<0.001
Triceps skinfold thickness	0.755	<0.001	0.829	<0.001	0.716	<0.001
Lean body Mass	0.918	<0.001	0.853	<0.001	0.744	<0.001
Body Muscle Mass	0.710	<0.001	0.509	0.004	0.630	<0.001
BMI	0.786	<0.001	0.931	<0.001	0.611	<0.001
BFR	0.672	<0.001	0.615	<0.001	0.639	<0.001
TBW	-0.781	<0.001	-0.731	<0.001	-0.764	<0.001

Pearson Correlation Test, Kendall's tau-b Test r: Correlation Coefficient, CK: Creatine Kinase, HCO3: Bicarbonate, HGB: Hemoglobin, Ca: Calcium, LDL: Low density cholesterol, pH: potential hydrogen, CRP: C-reactive protein, MNA: Mini Nutritional Assessment, BMI: Body Mass İndex, BFR: Body Fate Ratio, TBW: Total Body Water

In the patients followed-up due to ESRD, serum creatinine levels have a very important place in the determination of the nutritional situation and muscle mass. It has been stated that the level of creatinine produced in skeletal muscle reflects muscle mass and is associated with survival (13). In the previous studies, it was revealed that low serum creatinine level was associated with malnutrition, showed low muscle mass, and was associated with increased mortality (14). In the present study, a positive statistically significant correlation was determined between serum CK levels and creatinine level in both of HD and PD patient groups ($p<0.001$). In a previous study, a positive statistically significant correlation was also determined between serum CK levels and creatinine level in patients with CRF not undergoing dialysis (8).

Limitations of the study

This research was conducted in a single-center study, therefore our results may not yet be applied universally.

CONCLUSION

Consequently, it is thought that measurement of serum CK level is compatible with other parameters used for the determination and follow-up of malnutrition and sarcopenia, in patients with ESRD. Since it is an inexpensive and reliable method that can be easily applied in clinical practice, there is a need for conducting more comprehensive studies with larger patient groups.

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