Handgrip Strength and Serum Uric Acid Levels are Associated with Dialysis-Malnutrition Scores in Chronic Hemodialysis Patients

El-Sıkma Gücü ve Serum Ürik Asit Seviyeleri, Kronik Hemodiyaliz Hastalarında Diyaliz-Malnütrisyon Skoru ile İlişkilidir

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ABSTRACT

OBJECTIVE: Protein-energy-wasting (PEW) is common and contributes to increased mortality in hemodialysis (HD) patients. Herein we aimed to investigate the relationships between the parameters of malnutrition including dialysis malnutrition score (DMS), bioimpedance analysis (BIA), handgrip strength (HGS) in chronic HD patients.

MATERIAL and METHODS: Forty chronic HD patients (mean age:58±18 years; males:22) were enrolled. Mid-arm circumference (MAC) measurements and BIA were performed. HGS was measured by a Jamar hydraulic hand dynamometer.

RESULTS: HGS, MAC and uric acid levels were higher in patients with mild malnutrition compared to severe malnutrition group. Postdialysis creatinine was associated with lean body ratio (LBR) (r=0.56, p=0.002), DMS (r=-0.57, p=<0.001), HGS (r=0.73, p<0.001) and MAC (r=0.51, p=0.001). DMS was inversely correlated with HGS (r= -0.63, p<0.001), MAC (r= -0.48, p=0.002), total protein (r=-0.36, p=0.02) and uric acid levels (r=-0.54, p<0.001). In linear regression analysis (R^2=0.58; p<0.001), HGS and uric acid were found to independently predict DMS. HGS was associated with MAC, LBR, uric acid and post-HD urea. HGS was negatively correlated with age, DMS, fat tissue ratio (FTR) and Kt/V. In linear regression analysis (R^2=0.71; p<0.001), gender, DMS and MAC were found to independently predict HGS.

CONCLUSION: HGS and uric acid were significantly associated with dialysis-malnutrition scores. HGS is an easy and reliable test for the evaluation of malnutrition in HD patients.

KEY WORDS: Malnutrition, Hemodialysis, Handgrip strength, Dialysis malnutrition score, Uric acid

ÖZ

AMAÇ: Protein-enerji tükenmesi sendromu, hemodiyaliz (HD) hastalarında sıktır ve artmış mortalite ile ilişkilidir. Burada, el-sıkma gücünün (ESG); diyaliz malnütrisyon skoru (DMS) ve biyoimpedans analizi (BİA) gibi diğer malnütrisyon parametreleri ile ilişkisinin araştırılması amaçlanmıştır.

GEREÇ ve YÖNTEMLER: Kırk kronik HD hastası (ortalama yaş: 58±18 yıl; erkek :22) çalışmaya katıldı. Orta-kol çevresi (OKÇ) ve BİA ölçümleri yapıldı. ESG, Jamar hidrolik el dinamometresi ile ölçüldü.

BULGULAR: ESG, OKÇ ve ürik asit seviyeleri, hafif malnütrisyon grubunda, ciddi malnütrisyon grubuna göre daha yüksek saptandı. Postdiyaliz kreatinin seviyeleri, yağsız vücut oranı (YVO) (r=0,56, p=0,002), DMS(r= -0,57, p=<0,001), ESG(r=0,73, p<0,001) ve OKÇ(r=0,51, p=0,001) ile anlamlı olarak ilişkili bulundu. DMS ise ESG (r= -0,63, p<0,001), OKÇ(r= -0,48, p=0,002), total protein(r=-0,36, p=0,02) ve ürik asit seviyeleri (r=-0,54, p<0,001) ile ters-ilişkili bulundu. Lineer regresyon analizinde (R^2=0,58; p<0,001), ESG ve ürik asitin DMS'nin bağımsız öngörücüleri olduğu bulundu. ESG ile OKÇ, YVO, ürik asit ve post-HD üre değerleri ilişkiliydi. Buna karşın ESG; yaş, DMS, yağ doku oranı ve Kt/V ile ters ilişkili bulundu. Lineer regresyon analizinde (R^2=0,71; p<0,001), cinsiyet, DMS ve OKÇ'nin ESG'nin bağımsız öngörücüleri oldukları gösterildi.

SONUÇ: ESG ve ürik asit seviyeleri, diyaliz-malnütrisyon skorlarıyla anlamlı olarak ilişkilidir. ESG, HD hastalarında malnütrisyonun değerlendirilmesi için kolay ve güvenilir bir test olabilir.

ANAHTAR SÖZCÜKLER: Malnütrisyon, Hemodiyaliz, El sıkma gücü, Diyaliz malnütrisyon skoru, Ürik asit

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INTRODUCTION

Protein-energy wasting (PEW) is described as the reduction in protein and energy reserves and it contributes to extremely increased morbidity and mortality in patients with CKD (1). PEW is commonly observed in CKD patients, and its prevalence ranges from 23% to 76% (2). However, the diagnosis of PEW may be difficult. Various clinical, anthropometric and biochemical parameters have been determined as the criteria of PEW such as nutritional scoring systems (such as dialysis malnutrition score- DMS), low body mass index (BMI), muscle mass, decreased serum albumin, and transthyretin and cholesterol levels (1). In CKD patients, measurements of BMI are commonly interfered with by hypervolemia and thus determination of lean body mass and muscle mass is not easy. Body composition measurements using bioimpedance analysis (BIA) are therefore preferred to evaluate loss of lean body and muscle mass, which are considered reliable indicators of PEW (3). Besides these parameters, functional evaluation of the muscle mass is also important. The handgrip strength test (HGS) which is an indicator of the maximal voluntary force of the hand, is a noninvasive, objective and rapid test to evaluate muscle function (4). HGS has been found to reflect the nutritional status of various patient groups including CKD patients (5-7). Herein we aimed to investigate the relationships between the various parameters of malnutrition including DMS, body composition measurements with BIA, functional evaluation of muscle mass with HGS and adequacy of dialysis in chronic hemodialysis (HD) patients.

MATERIALS and METHODS

Study Population and Data Collection

A total of 40 chronic HD patients (mean age:58 ± 18 years; male:22/female:18) were enrolled. Median time (IQR) on dialysis was 82(22-135) months. Etiologies of chronic kidney disease were as follows: diabetes mellitus, 7 (17.5%); hypertension, 7 (17.5%); glomerulonephritis, 5 (12.5%); polycystic kidney disease, 3 (7.5%); others, 5 (12.5%) and unknown, 13 (32.5%). Patients were receiving thrice weekly dialysis for 4-hour periods with a single-use, hollow-fiber, high-flux HD membrane (Nipro-ELISIO, Osaka, Japan). Blood flow rates ranged from 250 to 300 mL/min, while the dialysate flow rate was kept constant at 500 mL/min. The standard dialysate solution was composed of glucose 1 g/L, bicarbonate: 32 mmol/L, sodium 140 mmol/L, potassium 2 mmol/L; chloride: 111 mmol/L, calcium 1.25 mmol/L and magnesium 0.5 mmol/L. Mean eKt/V was found to be 1.61 ± 0.47. Mean urea reduction rate (URR) was 75 ± 10%.

The exclusion criteria were determined as follows; age older than 90 and younger than 18 years, presence of pregnancy, active malignancy, infection, advanced heart failure, inflammatory diseases including inflammatory bowel disease. Also patients with cardiac pacemaker and a history of amputation were excluded.

This study was reviewed and approved by the local ethical commitee (No: 2015/0149). This study was performed according to good medical and laboratory practices and the recommendations of the Declaration of Helsinki on Biomedical Research Involving Human Subjects. Informed consents were obtained from all participants of the study.

Laboratory Analysis

Fasting blood samples were collected before the midweek HD session. Laboratory values such as complete blood cell counts, electrolytes, uric acid, calcium, phosphorus, total protein, albumin, total cholesterol, triglycerides, iron, ferritin, C-reactive protein and intact parathyroid hormone (PTH) were measured. Serum levels of urea and creatinine were measured before and after dialysis. Accordingly urea reduction rate and equilibrated Kt/V parameters were calculated.

Anthropometric Measurements

Body mass index was calculated as weight/ $(\text{height})^2$ of the patient. Mid-arm circumference (MAC) was measured. HGS was measured at least 3 times by a Jamar hydraulic hand dynamometer (Patterson Medical, IL, US) with the shoulder adducted and elbow flexed at 90^o and the highest value was accepted as the HGS of the patient.

Bioelectrical Impedance Analysis (BIA) Measurements

Bioelectrical impedance analysis was performed to determine the body composition including fat tissue ratio (FTR) and lean body ratio (LBR). FTR and LBR measurements were done after the HD sessions during the "dry-weight" period to avoid the possible confounding effects of inter-variability of volume status between the patients in the pre-dialysis period.

Dialysis Malnutrition Score

The malnutrition degree was evaluated with subjective global assessment (SGA) as described by Kalantar-Zadeh et al. (8). Accordingly, DMS consists of seven features: weight change, dietary intake, gastrointestinal symptoms, functional capacity, comorbidity, subcutaneous fat and signs of muscle wasting. Each component has a score from 1 (no change) to 5 (very severe malnutrition). The DMS is defined as a number between 7 (normal) and 35 (severely malnourished). Patients were divided into two groups according to DMS such as the no malnutrition to mild malnutrition group (DMS: 7-13) and the moderate to severe malnutrition group (14-35).

Statistical Analysis

Statistical analysis was performed with the Statistical Package for Social Sciences for Windows version 16.0 (SPSS Inc, Chicago, IL, USA). Results of the data with normal distribution were expressed as mean ± standard deviation. Data with non-normal distribution were presented as median (interquartile range: 25-75%). Comparisons of the groups were performed using the t test or Mann-Whitney U test. Correlation analysis was performed by Pearson's test and Spearman's test where appropriate. Linear regression analysis was performed to evaluate the variables predicting DMS and HGS. Two-tailed p value of <0.05 was defined as statistically significant.

RESULTS

Biochemical and malnutrition parameters of the patients are presented in Table I. Comparison of male and female patients in terms of biochemical and malnutrition parameters is presented in Table II. Accordingly, HGS (Figure 1), LBR and serum uric acid levels were significantly higher in males compared to female patients. Conversely, FTR, Kt/V, URR, total cholesterol and HDL levels were found to be significantly higher in females. Age and DMS tended to be higher in female patients (p=0.09 and p=0.06 respectively). BMI and MAC were found to be similar in male and female patients.

Patients were divided into two groups according to DMS scores such as the no malnutrition to mild malnutrition group (DMS: 7-13) and the moderate to severe malnutrition group (DMS: 14-35). Comparison of the groups is presented in Table III. BMI, HGS, MAC and serum uric acid levels were found to be significantly higher in patients with mild malnutrition compared to severe malnutrition. On the other hand, patients were older and they had higher Kt/V and URR values in the severe malnutrition group compared to the mild malnutrition group.

Predialysis serum creatinine levels were significantly associated with LBR (r=0.48, p=0.008), DMS (r= -0.39, p=0.01), HGS (r=0.44, p=0.005), hemoglobin (r=0.45, p=0.004), uric acid (r=0.46, p=0.003), total protein (r=0.40, p=0.01) and

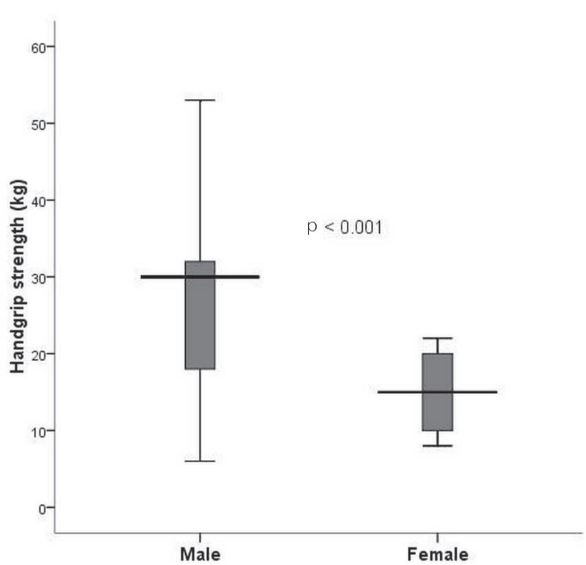

Figure 1: *Handgrip strength was significantly higher in male patients compared to female patients (p<0.001).*

Table I: Biochemical and malnutrition parameters of the patients.

Parameters	Mean (±SD) / median (IQR)
Age (years)	58 ± 18
Dx vintage (months)	82 (22-135)
BMI (kg/m^2)	24 ± 5
DMS	13 ± 4
MAC (cm)	26.75 ± 4.38
Handgrip strength (kg)	22.6 ± 11.34
Lean body ratio (%)	37 ± 9
Fat tissue ratio (%)	27 ± 13
Total leukocyte (/mm^3)	6692 ± 1709
Lymphocyte count (/mm^3)	1626 ± 486
Hemoglobin (g/dl)	11.1 ± 1.36
Iron (μg/dL)	62.98 ± 20.31
Ferritin (ng/mL)	554 ± 281
Parathormone (pg/mL)	606 (386-771)
CRP (mg/dL)	0.95 (0.40-1.67)
Kt/V (equilibrated)	1.61 ± 0.47
URR (%)	75 ± 10
Urea (Pre-dx) (mg/dL)	131 ± 39
Urea (Post-dx) (mg/dL)	34 ± 17
Creatinine (Pre-dx) (mg/dL)	8.98 ± 2.84
Creatinine (Post-dx) (mg/dL)	3.14 ± 1.47
Uric acid (mg/dL)	5.93 ± 1.38
Calcium (mg/dL)	8.38 ± 1.09
Phosphorus (mg/dL)	5.48 ± 1.31
Total Protein (g/dL)	6.61 ± 0.59
Albumin (g/dL)	3.58 ± 0.32
Total cholesterol (mg/dL)	168 ± 39
Triglyceride (mg/dL)	144 ± 64
LDL (mg/dL)	103 ± 31
HDL (mg/dL)	36 ± 12

Dx: Dialysis, **BMI:** Body mass index, **DMS:** Dialysis malnutrition score, **MAC:** Mid-arm circumference, **CRP:** C-reactive protein, **URR:** Urea reduction rate, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein albumin (r=0.44, p=0.005). However, they were not associated with BMI (r=0.16, p=0.32). Postdialysis serum creatinine levels were significantly associated with age (r= -0.38, p=0.01), LBR (r=0.56, p=0.002) (Figure 2), DMS (r= -0.57, p=<0.001), HGS (r=0.73, p<0.001) (Figure 3), MAC (r= 0.51, p=0.001), hemoglobin (r=0.35, p=0.03) and uric acid (r=0.57, p<0.001).

Postdialysis urea levels were associated with DMS (r= -0.37, p=0.01), MAC (r=0.49, p=0.001), HGS (r=0.51, p=0.001), and BMI (r=0.37, p=0.02) but predialysis urea levels were not related to the mentioned parameters.

Correlation analysis between DMS and various anthropometric and biochemical parameters is presented in Table IV. Accordingly, DMS was significantly associated with age (r=0.43, p=0.005) and Kt/V (r=0.39, p=0.01). In contrast, DMS was inversely correlated with HGS (r= -0.63, p<0.001) (Figure 4), MAC (r= -0.48, p=0.002), serum total protein (r= -0.36, p=0.02) and uric acid levels (r= -0.54, p<0.001) (Figure 5).

Linear regression analysis (Adjusted $R^2 = 0.58$; p<0.001) was performed to determine factors independently predicting DMS (Table V). Age, gender, HGS, MAC, LBR, total protein, uric acid and Kt/V were included in the analysis as variables. HGS and serum uric acid levels were found to be the independent variables significantly predicting DMS.

HGS was significantly associated with MAC, LBR (Figure 6), serum uric acid and post HD serum urea levels. It tended to be related to serum phosphorus levels (p=0.05). In contrast, HGS was negatively correlated with age, DMS, FTR, Kt/V, URR and serum HDL concentrations (Table VI).

Linear regression analysis (Adjusted $R^2 =0.71$; p<0.001) was performed to determine the factors independently predicting HGS (Table VII). Age, gender, DMS, MAC, LBR, FTR, Kt/V, uric acid, HDL and ferritin were included in the analysis. Gender, DMS and MAC were found to be the independent variables significantly predicting HGS.

Table II: Comparison of male and female patients in terms of biochemical and malnutrition parameters.

	Male (n=22)	Female (n=18)	p
Age (years)	53 ± 17	63 ± 18	0.09
Dx vintage (months)	83 (41-141)	60 (20-155)	0.73
BMI (kg/m^2)	24 ± 5	24 ± 6	0.89
DMS	12 ± 4	15 ± 4	0.06
Handgrip strength (kg)	28.36 ± 10.95	15.55 ± 7.18	<0.001
MAC (cm)	27.09 ± 3.95	26.33 ± 4.95	0.59
Lean body ratio (%)	42 ± 7	31 ± 7	<0.01
Fat tissue ratio (%)	20 ± 10	34 ± 11	0.002
KT/V	1.42 ± 0.32	1.84 ± 0.53	0.007
URR (%)	71 ± 8	79 ± 11	0.02
Lymphocyte count (/mm^3)	1648 ± 414	1601 ± 575	0.77
Urea (Pre-dx) (mg/dL)	139 ± 46	120 ± 25	0.10
Creatinine (Pre-dx) (mg/dL)	10.43 ± 1.94	7.18 ± 2.78	<0.001
Hemoglobin (g/dL)	11.41 ± 1.39	10.75 ± 1.27	0.12
Uric acid (mg/dL)	6.34 ± 1.17	5.42 ± 1.48	0.03
Albumin (g/dL)	3.61 ± 0.27	3.52 ± 0.38	0.36
Total cholesterol (mg/dL)	157 ± 30	182 ± 46	0.04
Triglyceride (mg/dL)	146 ± 66	142 ± 64	0.84
LDL (mg/dL)	99 ± 29	109 ± 34	0.29
HDL (mg/dL)	31 ± 7	42 ± 14	0.002
CRP (mg/dL)	1.10 (0.57-1.55)	0.80 (0.32-1.72)	0.58

Dx: Dialysis, **BMI:** Body mass index, **DMS:** Dialysis malnutrition score, **MAC:** Mid-arm circumference, **URR:** Urea reduction rate, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein, **CRP:** C-reactive protein.

Table III: Comparison of groups with no malnutrition-to-mild malnutrition (DMS: 7-13) and moderate-to-severe malnutrition (DMS: 14-35).

DMS Groups	No change- mild malnutrition (n=22)	Moderate-severe malnutrition (n=18)	p value
Age (years)	51 ± 16	65 ± 17	0.009
Dx vintage (months)	81 (21-117)	93 (22-216)	0.35
BMI (kg/m^2)	26 ± 5	21 ± 4	0.008
Handgrip strength (kg)	28.18 ± 10.21	15.77 ± 8.77	<0.001
MAC (cm)	28.50 ± 4.09	24.61 ± 3.83	0.004
Lean body ratio (%)	38 ± 10	34 ± 8	0.22
Fat tissue ratio (%)	28 ± 14	27 ± 12	0.88
Kt/V	1.44 ± 0.40	1.82 ± 0.48	0.01
URR (%)	71 ± 11	78 ± 8	0.02
Urea (Pre-dx) (mg/dL)	135 ± 38	126 ± 41	0.50
Urea (Post-dx) (mg/dL)	39 ± 17	27 ± 15	0.02
Creatinine (Pre-dx) (mg/dL)	9.90 ± 3.36	7.84 ± 1.43	0.01
Creatinine (Post-dx) (mg/dL)	3.85 ± 1.50	2.31 ± 0.93	0.001
Lymphocyte count (/mm^3)	1677 ± 402	1565 ± 579	0.49
Hemoglobin (g/dL)	11.05 ± 1.30	11.18 ± 1.47	0.77
Uric acid (mg/dL)	6.45 ± 1.38	5.28 ± 1.12	0.006
Albumin (g/dL)	3.61 ± 0.34	3.52 ± 0.30	0.41
T cholesterol (mg/dL)	158 ± 35	181 ± 42	0.06
Triglyceride (mg/dL)	143 ± 71	145 ± 57	0.95
CRP (mg/dL)	0.75 (0.35-1.50)	1.15 (0.55-1.82)	0.18

DMS: Dialysis malnutrition score, **Dx:** Dialysis, **BMI:** Body mass index, **MAC:** Mid-arm circumference, **URR:** Urea reduction rate, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein, **CRP:** C-reactive protein.

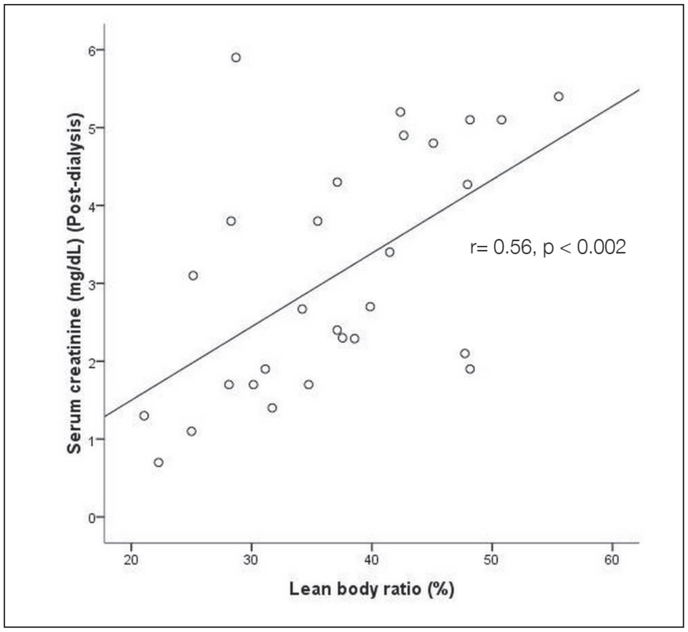

Figure 2: *Post-dialysis serum creatinine levels were significantly associated with LBR (r=0.56, p=0.002).*

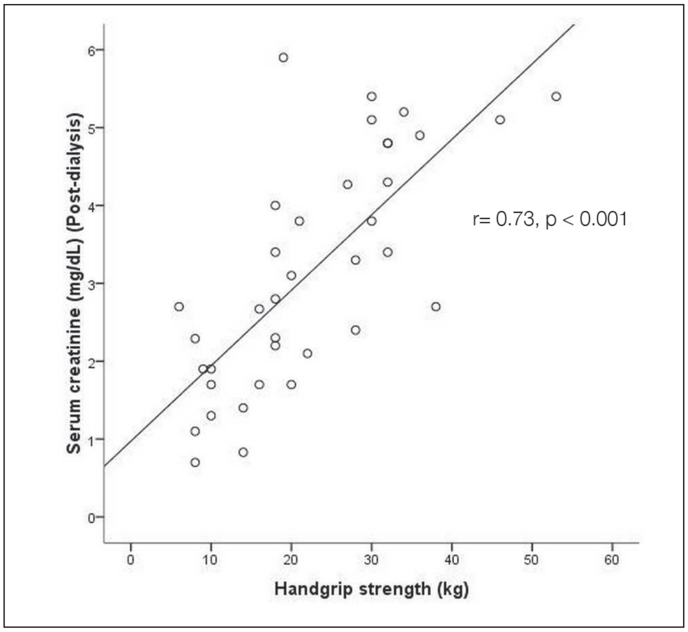

Figure 3: *Post-dialysis serum creatinine levels were significantly associated with HGS (r=0.73, p<0.001).*

Table IV: Correlation analysis between DMS and various anthropometric and biochemical parameters.

Parameters	Correlation coefficient (r)	p value
Age	**0.43**	**0.005**
Dx vintage	0.20	0.24
BMI	-0.28	0.08
Handgrip strength	**-0.63**	**<0.001**
MAC	**-0.48**	**0.002**
Lean body ratio (%)	-0.31	0.09
Fat tissue ratio (%)	0.15	0.39
Kt/V	**0.39**	**0.01**
URR	**0.37**	**0.01**
Urea (Pre-dx)	-0.07	0.62
Urea (Post-dx)	**-0.37**	**0.01**
Creatinine (Pre-dx)	**-0.39**	**0.01**
Creatinine (Post-dx)	**-0.57**	**<0.001**
Uric acid	**-0.54**	**<0.001**
Total protein	**-0.36**	**0.02**
Albumin	-0.24	0.12
Total cholesterol	0.18	0.26
Triglyceride	0.03	0.85
CRP	0.22	0.16

Dx: Dialysis, **BMI:** Body mass index, **MAC:** Mid-arm circumference, **URR:** Urea reduction rate, **CRP:** C-reactive protein.

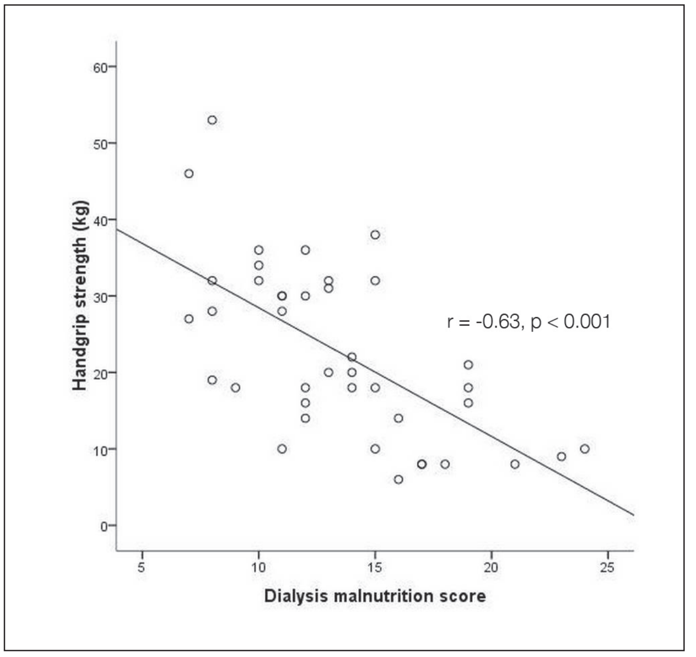

Figure 4: *Handgrip strength was significantly negatively correlated with DMS (r= -0.63, p<0.001).*

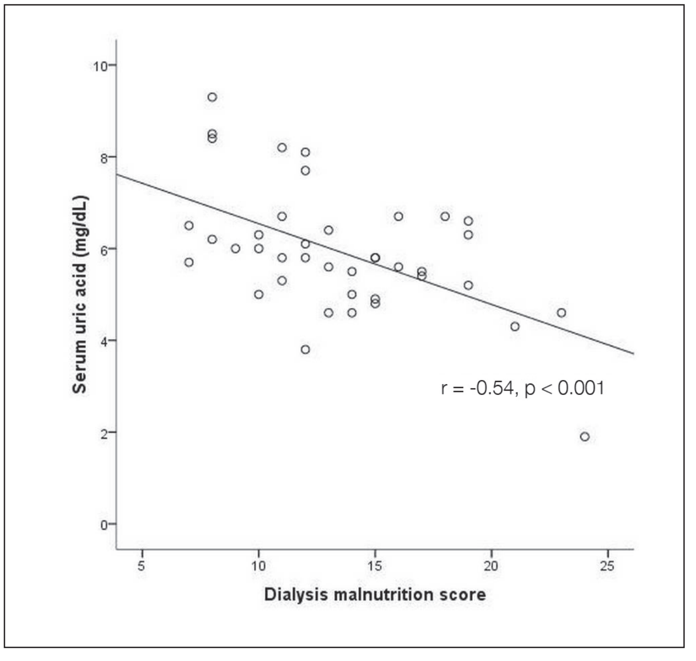

Figure 5: *DMS was significantly negatively associated with serum uric acid levels (r= -0.54, p<0.001).*

DISCUSSION

The DMS (SGA) is a practical test of clinical nutritional assessment which is advised for the evaluation of the malnutrition in dialysis patients by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (9,10). According to DMS, in our study, 22 patients had mild malnutrition and 18 patients had moderate to severe malnutrition. Patients with severe malnutrition were older and they were found to have lower BMI, HGS, MAC and serum uric acid levels. Pre and post-dialysis creatinine levels and only post-dialysis urea levels were lower in the group with severe malnutrition. Interestingly, post-dialysis creatinine and urea levels seemed to be more related to parameters of malnutrition including lean body mass defined by LBR and muscle functions depicted by HGS. Actually, serum creatinine levels are considered to be unreliable as an indicator of muscle mass because they are dialysis dependent. However, in several studies, serum creatinine levels were found to be associated with lean body mass, confirming our findings (3,11,12). In the univariate correlation analysis, DMS was found to be strongly associated with both anthropometric measurements such as MAC and functions of the muscle mass defined by HGS. However in multivariate analysis, only HGS was found to be associated with DMS.

Table V: Linear regression analysis (Adjusted $R^2 = 0.58$; $p<0.001$) to determine factors independently predicting DMS.

Variables	β	Standardized β	%95 CI		p values
			Lower bound	Upper bound	
Age	0.06	0.22	-0.01	0.13	0.10
Gender	0.92	0.10	-2.26	4.10	0.55
Handgrip strength	-0.19	-0.52	-0.35	-0.03	0.02
MAC	-0.19	-0.19	-0.56	0.18	0.30
LBR	0.02	0.05	-0.15	0.20	0.75
Total protein	-1.41	-0.18	-3.46	0.63	0.16
Uric acid	-0.93	-0.32	-1.77	-0.09	0.03
Kt/V	-1.55	-0.17	-5	1.89	0.35

MAC: Mid-arm circumference, **LBR:** Lean body ratio.

Table VI: Correlation analysis between handgrip strength and various anthropometric and biochemical parameters.

Parameters	Correlation coefficient (r)	p value
Age	-0.32	0.04
Dx vintage	-0.05	0.74
BMI	0.16	0.32
DMS	-0.63	<0.001
MAC	0.48	0.002
LBR (%)	0.53	0.002
FTR (%)	-0.35	0.04
Kt/V	-0.54	<0.001
URR	-0.56	<0.001
Urea (pre-dx)	0.16	0.31
Urea (post-dx)	0.51	0.001
Creatinine (pre-dx)	0.44	0.005
Creatinine (post-dx)	0.73	<0.001
Uric acid	0.44	0.004
Total protein	0.20	0.21
Albumin	0.05	0.75
Phosphorus	0.30	0.05
Total cholesterol	-0.28	0.07
Triglyceride	0.06	0.69
HDL	-0.33	0.03
LDL	-0.21	0.17
CRP	0.17	0.29
Hemoglobin	0.26	0.10
Ferritin	-0.38	0.01

Dx: Dialysis, **BMI:** Body mass index, **MAC:** Mid-arm circumference, **LBR:** Lean body ratio, **FTR:** Fat tissue ratio, **URR:** Urea reduction rate, **HDL:** High density lipoprotein, **LDL:** Low density lipoprotein, **CRP:** C-reactive protein

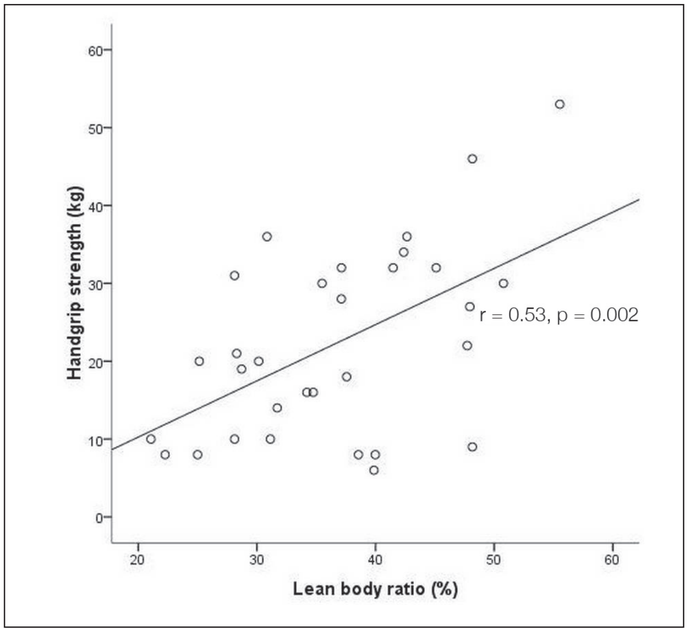

Figure 6: *Handgrip strength was significantly associated with lean body ratio (r= 0.53, p=0.002).*

HGS is a simple bedside test that reliably indicates the nutritional status of various patient groups including CKD and dialysis patients (5-7). HGS is known to decrease in patients with CKD. Uremic toxins such as β2-microglobulin, deficiency of carnitine, disturbances of electrolyte metabolisms, hemodynamic factors related to dialysis procedure, increased inflammation and acidosis may all cause lower values of HGS in HD patients (5,7). Low values of HGS were found to predict mortality in both non-uremic and uremic patients (15,16). Furthermore HGS was also found to predict renal outcomes in non-dialysis CKD patients (17).

Table VII: Linear regression analysis (Adjusted R^2 =0.71; p<0.001) to determine factors independently predicting handgrip strength.

Variables	β	Standardized β	%95 CI		P values
			Lower bound	Upper bound	
Age	-0.005	-0.006	-0.18	0.17	0.95
Gender	**7.93**	**0.33**	**0.56**	**15.29**	**0.03**
DMS	**-0.91**	**-0.33**	**-1.80**	**-0.02**	**0.04**
MAC	**1.51**	**0.56**	**0.48**	**2.54**	**0.006**
LBR	-0.12	-0.08	-0.81	0.57	0.72
FTR	-0.39	-0.41	-0.88	0.09	0.10
Kt/V	0.75	0.03	-9.91	8.41	0.86
Uric acid	-0.75	-0.09	-3.00	1.50	0.49
HDL	0.20	0.21	-0.06	0.46	0.12
Ferritin	-0.005	-0.12	-0.01	0.005	0.31

DMS: Dialysis malnutrition score, **MAC:** Mid-arm circumference, **LBR:** Lean body ratio, **FTR:** Fat tissue ratio, **HDL:** High density lipoprotein).

In our study, HGS was significantly lower in female patients compared to males as expected and it was found to be significantly associated with MAC, LBR, serum uric acid and post-dialysis serum urea levels. HGS was negatively correlated with age and FTR. In multivariate analysis, the gender, DMS and MAC were found to be significant independent predictors of HGS. Confirming our findings, HGS was found to be negatively associated with DMS scores in several studies (17-19). In several other studies, HGS was directly correlated to LBM in CKD patients in parallel to our findings (15,19-21).

Furthermore, we also found that HGS was negatively associated with FTR but no relationship was present between HGS and BMI. Confirming our findings, in the study by Leal et al., HGS was negatively correlated with body fat ratio and it was not associated with BMI (22). This issue may be explained by the fact that BMI is not a reliable indicator of body composition, in other words it cannot differentiate muscle mass from hypervolemia or fat mass (23). Patients may have normal or high BMI but at the same time they may have decreasing muscle mass and be suffering from PEW. In our study, the negative relationship between HGS and FTR in univariate analysis disappeared in multivariate analysis suggesting a gender-related effect.

Recently, iron accumulation in HD patients (mostly iatrogenic) has been reported to have a negative impact on muscle strength. In the study by Nakagawa et al., serum ferritin levels were found to be independently negatively associated with HGS (24). In a study performed on HD patients with severe proximal myopathy, muscle biopsies showed iron deposition in macrophages and muscle fibers (25). It is hypothesized that accumulated iron in myoglobin causes free radical formation in muscle leading to impaired muscle functions. Similarly we also found a significant negative association between serum ferritin levels and HGS in univariate analysis. However this effect disappeared in multivariate analysis. Iatrogenic iron overload should be avoided to prevent the possible harmful effects of iron on muscles in HD patients.

In this study, we found that serum uric acid levels were negatively associated with DMS. In multivariate analysis, serum uric acid levels were still significantly predicting DMS independent of Kt/V values. Similarly in the study by Beberashvili et al., serum uric acid levels were negatively correlated with the malnutrition-inflammation score (26). In our study, serum uric acid levels were also correlated with HGS in univariate analysis but this correlation disappeared in multivariate analysis. In the study by Beberashvili et al., serum uric acid levels were found to be positively associated with body composition parameters such as BMI, MAC, fat mass, lean body mass and HGS (26). Uric acid is the end product of purine metabolism. Increased serum uric acid levels are known to be associated with an increased risk for CKD (27,28), and cardiovascular disease in the general population (29,30). However, in HD patients, low uric acid levels have been found to be associated with higher risk of mortality (31-33). Higher serum uric acid levels have been suggested to reflect a better nutritional status in HD patients.

Adequacy of dialysis, defined by Kt/V and URR, was found to be higher in patients with more severe malnutrition determined by DMS. Kt/V and URR were negatively associated with HGS in univariate analysis. However, parameters of dialysis adequacy did not independently predict HGS in multivariate regression analysis. Confirming our findings, single pool Kt/V was found to be negatively correlated with both skeletal muscle index and HGS in the study by Morishita et al. (34). The sole determinant of Kt/V is not only the dialysis efficacy and the muscle mass of the patients also affects the Kt/V values. HD patients with high muscle mass have been reported to have low Kt/V regardless of dialysis efficacy (35,36). There are also controversies in terms of the relationship between Kt/V and HGS; Qureshi et al. (6) could not find an association between HGS and Kt/V.

The observational and cross-sectional design of the study and a relatively low sample size may be considered as the limitations of this study. Further studies with long-term follow-up data will contribute to our knowledge of malnutrition in HD patients.

In conclusion, HGS and serum uric acid levels were significantly associated with dialysis malnutrition scores. HGS is an easy and reliable test for the evaluation of malnutrition in HD patients. BMI may be misleading as a parameter of malnutrition in HD patients and body composition analysis with BIA is therefore crucial for follow-up of LBR. Evaluation of the effects of dialysis adequacy on malnutrition by the use of Kt/V may be difficult and misleading.

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