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Risk Stratification of Hemodialysis Patients with Protein-Energy Wasting Using Hand Grip Strength and Malnutrition-Inflammation Score: are Two Indices Better than One?

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Abstract

Background: We aimed to detect whether risk stratification of hemodialysis (HD) patients with a combination of both malnutrition-inflammation score (MIS) and hand grip strength (HGS) indices identified more precisely patients at increased risk of protein-energy wasting (PEW).

Methods: This was a deductive-analytical cross-sectional study. We determined the HGS and MIS of 83 HD patients who were randomly selected from the dialysis centers in Kerman. Data were analyzed using *t*-tests and One-way ANOVA. Multinomial logistic regression and receiver operating characteristic (ROC) curve analysis were performed accordingly.

Results: There were significant differences between normal and high risk MIS regarding gender, having diabetes mellitus (DM), duration of dialysis, serum albumin, and C-reactive protein (P= 0.021, 0.049, 0.003, 0.038, and 0.027, respectively). There were also significant differences between normal and high risk HGS groups regarding age, having DM, cause of kidney disease (DM and/or hypertension), creatinine level, total cholesterol, weight, height, and mid upper arm circumference (P= 0.000, 0.006, 0.024, 0.011, 0.044, 0.026, 0.014, and 0.029, respectively). The ROC curves of the MIS and HGS indices showed sensitivity and specificity of 89.7% and 93.8%; 78.0% and 72.5%; respectively.

Conclusions: Our findings reveal that patients, defined as "normal by both", "normal by either", and/or "high risk by both" based on the diagnostic tools, exhibit different markers compared to patients categorized by either index separately. The cutoff of MIS for the occurrence of PEW varied depending on the procedure used. The sensitivity and specificity of MIS and HGS indices were excellent.

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Introduction

Many methods have been used to evaluate the occurrence of protein-energy wasting (PEW) in hemodialysis (HD) patients. There are several clinical, nutritional, and biochemical indicators such as Subjective Global Assessment (SGA), Malnutrition-Inflammation Score (MIS), hand grip strength (HGS), serum albumin, dietary intake assessment, and nutritional anthropometry assessment that may be indicative of PEW in HD patients (1, 2). The SGA has been recently confirmed as a simple, inexpensive and validated method for evaluating the nutritional status of HD patients (3). Unless a gold standard method for detecting and diagnosing malnutrition in population is established, the SGA seems to be the method capable of detecting the highest number of patients with PEW. The low sensitivity of the SGA to detect small changes in the nutritional status is a known limitation which gives room to more research in order to longitudinally improve its nutritional status assessment power (4). Due to the high prevalence of PEW and its association with morbidity and mortality as well as the paucity of a reliable single method to detect nutritional problems in these patients, the use of multiple indicators is a matter of attention (5). Kalantar-Zadeh et al. proposed a new combined method called MIS which was composed of SGA method and other indicators such as serum albumin, total iron binding capacity (TIBC), and body mass index (BMI) (6). It seems that MIS has adequate reliability and validity for detecting and diagnosing PEW in the HD patients. It is also important to note that MIS takes into account all the criteria set by the International Society of Renal Nutrition and Metabolism (ISRNM) for diagnosing PEW (7). The HGS, in particular, has been shown to be an inexpensive, reliable and easily performed parameter of nutritional status (8). It is a useful marker of nutritional status in HD patients. It can independently predict variations in nutritional status (9). We previously revealed that, the HGS was significantly associated with nutritional assessment indicators on the basis of the MIS. As a result, the HGS can be incorporated as a reliable tool for assessing nutritional status in clinical practice (10). On the other hand, we believe that it is necessary to apply several parameters to properly evaluate the nutritional status of HD patients and to overcome the limitations of each of the methods when used in separation.

Hence, the aim of this study was to examine a range of clinical, biochemical, and anthropometry markers in a random sample of 83 HD patients that were classified as normal or high risk to detect whether risk stratification with a combination of both indices (MIS and HGS) could more precisely identify patients at increased PEW risk.

Study Design and Methods

Patients

In this deductive-analytical cross-sectional study, 90 HD patients were randomly selected from 175 HD patients in Kerman HD centers. Randomization was performed by the statistics counselor using Microsoft Excel software. The sample size was estimated to be 10%. This size was more than the computed sample as some participants might refrain from participating in the study. As the baseline protocol has been previously described in detail (10), the inclusion criteria for recruitment were patients who underwent HD for at least 2 months before the initiation of the study. The exclusion criteria were participants with a degenerative disease or acute illness such as malignancies, AIDS, liver cirrhosis, any abnormalities of the upper extremities, osteoarthritis, and amputation.

In our study, all patients signed an informed consent form. This study was approved by review panels and the ethics committee of the Deputy of Research at Kerman University of Medical Sciences (Ref. Num. K/92/399).

Clinical and Biochemical Measurements

As previously described (10), the blood samples of HD patients were collected in order to measure biochemical and inflammatory biomarkers such as serum albumin, creatinine, blood urea nitrogen (BUN), total cholesterol, C-reactive protein (CRP), and TIBC after an overnight fasting before the dialysis session. Blood samples were centrifuged for 5 min at 3000 rpm and stored at -21°C until analysis. Serum albumin and TIBC were measured by Pars Azmoon Kit with the use of an automated analyzer (Selektra XL). Biomarkers such as the urea reduction ratio (URR) and Kt/V (dialysis efficiency) were used to evaluate dialysis adequacy. Some patients' biomedical history was obtained from their hospital records or they were interviewed and recorded.

HGS was measured on the non-fistula side before the dialysis session using Jamarhydraulic dynamometer (Sammons Preston Rolyan, Made in America) with a precision of 0.5 kg and ranged from 0 to 90 kg. The American Society of Hand Therapists suggested a standard testing protocol for HGS in which the subject is seated with his/her shoulder adducted and neutrally rotated. Also, the elbow is flexed at 90º, forearm in neutral and the wrist between 0 and 30 degrees extension and between 0 and 15 degrees ulnar deviation. A pretest was done allowing the patients to become familiar with the device and technique. Three trials were performed with a rest period of at least 1 min between trials and the highest HGS value was used in the analysis.

Anthropometry Assessment

The dry weight and height of each patient were measured to the nearest 0.1 kg and 0.5 cm respectively. Dry weight measurement was assessed within 10-20 minutes after a dialysis session using Seca scale. BMI was calculated as the end-dialysis body weight (dry weight) in kilograms divided by the square of height in meters (kg/m^2). Patients' waist circumference (WC) and mid upper arm circumferences (MUAC) were measured using a Seca measuring tape. The waist to hip ratio (WHR) was calculated as WC divided by hip circumferences.

Classification and grouping of MIS and HGS

As previously described (10), the MIS markers were SGA components together with three additional parameters such as BMI, serum albumin and TIBC, which were recorded in a questionnaire. Afterwards, participants were considered as mild, moderate and severe wasting if MIS scores were between 0-10, 11-20, and 21-30, respectively. The HGS of participants was measured before the dialysis session using Jamar hydraulic dynamometer for three times.

Both HGS and MIS were divided into equal dichotomous items. Patients were categorized on the basis of their HGS percentiles as high risk HGS (≤50%) and normal HGS (>50%). In our patients, these cut points corresponded to ≤26.330 and >26.330 for HGS in males and ≤13.500 and >13.500 for HGS in females. Median of 26.330 for HGS was nearly corresponding to the mean of 26.762 in males and the median of 13.500 for HGS was nearly corresponding to the mean of 13.964 in females. On the other hand, Patients were categorized on the basis of their MIS percentiles as normal MIS (≤50%) and high risk MIS (>50%). In both gender, these

cut points corresponded to ≤7.1 and >7.1 for MIS. The median and the mean were corresponding to each other and were equals to 7.1 and 7.4, respectively. The HGS and MIS groups were combined to form a 3-category variable. We integrated normal MIS and normal HGS in the first group as "normal by both" and normal MIS or normal HGS with high risk MIS or HGS in the second group as "normal by either" and high risk MIS and high risk HGS in the third group as "high risk by both".

Variables, Logistic Regression and ROC Curve

Clinical, biomedical, and nutritional anthropometry variables such as serum albumin, BUN, creatinine level, total cholesterol, CRP, Kt/V, URR, having diabetes mellitus (DM), family history of DM, family history of kidney disease, cause of kidney disease (DM and/or hypertension), duration of dialysis, age, weight, height, BMI, WC, WHR, MUAC were predictors (nineteen variables) in logistic regression models in which the dependent variable was MIS=1 for 35 high risk patients and MIS=0 for 48 patients with normal MIS as well as another dependent variable was HGS=1 for 43 high risk patients and HGS=0 for 40 patients with normal HGS. Hence, the classification cutoffs in the option box of logistic regression based on normal participants divided by total participants for MIS and HGS were precisely computed and the models were accomplished. The predicted probabilities for MIS and HGS were calculated and were coded with 1 and 0 according to earlier dichotomization of MIS and HGS in order to determine sensitivity and specificity. The cross tabulation of MIS (0/1) and recoded predicted probability of MIS (0/1) determined the sensitivity and specificity for MIS index. In addition, the cross tabulation of HGS (0/1) and recoded predicted probability of HGS (0/1) determined the sensitivity and specificity for HGS index. The receiver operating characteristic (ROC) method was implemented for MIS and HGS indices. The area under the curve (AUC) was also used to evaluate the discriminatory ability of both models.

Statistical analysis

Data analysis was conducted using IBM SPSS Statistics software, version 22.0. Significance was considered at $P < 0.05$. Results were expressed as mean ± standard deviation, or percent. The *t*-tests and one-way ANOVA were used to examine the difference between the means of the groups. Clinical, biochemical, and nutritional anthropometry measurements were examined according to normal and high risk defined by HGS and MIS dichotomous items. Dichotomous features are presented as percentages and continuous variables are shown as a mean ± SD. Binary logistic regression models were designed to determine the predicted probability of MIS and HGS in order to calculate the sensitivity and specificity for MIS and HGS indices. The ROC curve analysis was used to calculate the discriminatory ability index. Multinomial logistic regression was performed to determine the probability of protein-energy wasting on HGS and MIS groupings. Patients were classified as normal by both MIS and HGS (group 1) (the reference category), normal by either MIS or HGS (group 2), and high risk by both MIS and HGS (group 3). Therefore, multinomial logistic regression was a predictive analysis to explain the relationship between one dependent variable such as HGS and MIS groupings (three groups) and independent variables. The odds ratios (OR) with 95% confidence interval (CI) for all markers were computed.

Results

Forty five (65.2%) and five (35.7%) patients from 83 participated HD patients were males with mild PEW and moderate PEW, respectively. Baseline characteristics of HD patients with mild and moderate PEW are shown in table 1. There were significant differences between mild and moderate PEW in serum albumin, weight, WC in males, and WHR (*P*= 0.009, 0.048, 0.007, and 0.021, respectively) (Table 1). The dialysis efficiency, the HGS, and MUAC in patients with mild PEW were higher than moderate PEW. However, there was no significant difference between both PEW groups.

Table 1. Baseline characteristics of hemodialysis patients based on protein-energy wasting (PEW)

Variables	Mild PEW (n=69)	Moderate PEW (n=14)	*P* Value
Gender (Male)	45 (65.2%)	5 (35.7%)	0.040
Diabetic Patients	37 (53.6%)	9 (64.3%)	0.464
Family History of Diabetes	29 (42.0%)	8 (57.1%)	0.300
Family History of Kidney Disease	14 (20.3%)	2 (14.3%)	0.604
Cause of Kidney Disease (Diabetes and or Hypertension)	57 (82.6%)	13 (92.9%)	0.336
Duration of Dialysis (month)	28.65 ± 23.21	35.71 ± 33.14	0.458
Num. of Dialysis in Week	2.97 ± 0.38	2.93 ± 0.27	0.694
Length of Dialysis Session (hr)	3.96 ± 0.14	3.93 ± 0.27	0.573
Kt/V (Dialysis Efficiency)	1.17 ± 0.22	1.14 ± 0.40	0.794
Kt/V≥ 1.2	33 (47.8%)	7 (50.0%)	0.882
Urine Reduction Ratio	0.62 ± 0.09	0.60 ± 0.12	0.644
URR> 0.65	29 (42.0%)	5 (35.7%)	0.661
Serum Albumin	3.86 ± 0.41	3.39 ± 0.56	0.009
Blood Urea Nitrogen	107.36 ± 28.18	113.36 ± 34.76	0.488
CRP *	1.48 ± 0.93	2.21 ± 1.37	0.073
Creatinine Level	8.87 ± 2.69	9.27 ± 1.92	0.597
Tot. Cholesterol	146.68 ± 30.49	149.93 ± 38.83	0.730
Weight (Kg)	70.27 ± 14.79	61.57 ± 14.65	0.048
Height (Cm)	161.94 ± 8.73	157.61 ± 7.34	0.087
BMI ¶(Kg/M^2)	26.82 ± 5.41	24.83 ± 5.69	0.217
Waist Circum. (Cm)			
Men	99.03 ± 12.81	82.40 ± 9.15	0.007
Women	102.21 ± 16.03	101.44 ± 11.26	0.527
Men > 90 & Women > 80	58 (84.1%)	9 (64.3%)	0.087
Hip Circum. (Cm)	101.24 ± 10.94	99.79 ± 11.87	0.656
Waist to Hip ratio			
Men	0.98 ± 0.07	0.90 ± 0.10	0.021
Women	0.99 ± 0.07	0.97 ± 0.06	0.897
Men ≥ 0.90 & Women ≥ 0.85	62 (89.9%)	12 (85.7%)	0.650
MUAC # (Cm)	29.26 ± 4.16	28.36 ± 6.50	0.624
HGS ‡ before			
Men	27.27 ± 8.30	22.23 ± 6.99	0.199
Women	13.99 ± 4.89	13.90 ± 5.32	0.965
HGS after			
Men	25.39 ± 8.07	22.73 ± 6.73	0.483
Women	14.37 ± 4.10	13.28 ± 5.55	0.542
Malnutrition Inflammation Score	6.19 ± 2.66	13.37 ± 1.65	0.000

* C-reactive protein; ¶ body mass index; # mid upper arm circumference; ‡ hand grip strength.

The difference between patients with normal and high risk MIS and patients with normal and high risk HGS are shown in table 2. There were significant differences between normal and high risk MIS regarding gender, family history of DM, duration of dialysis, serum albumin, and CRP (*P*= 0.021, 0.049, 0.003, 0.038, and 0.027, respectively). There were also significant differences between normal and high risk HGS regarding age, having DM, cause of kidney disease (DM and/or hypertension), creatinine level, total cholesterol, weight, height, and MUAC (*P*= 0.000, 0.006, 0.024, 0.011, 0.044, 0.026, 0.014, and 0.029, respectively) (Table 2).

Table 2. Characteristics of hemodialysis patients based on normal and high risk MIS and HGS

Variables	Normal MIS (n=48)	high Risk MIS (n=35)	*P* value	Normal HGS (n=40)	high Risk HGS (n=43)	*P* value
Gender (Male)	34 (70.8%)	16 (45.7%)	0.021	25 (62.5%)	25 (58.1%)	0.685
Age	55.81 ± 14.24	60.91 ± 9.95	0.580	51.35 ± 13.58	64.12 ± 8.25	0.000
Diabetic Patients	25 (52.1%)	21 (60.0%)	0.474	16 (40.0%)	30 (69.8%)	0.006
Family History of Diabetes	17 (35.4%)	20 (57.1%)	0.049	16 (40.0%)	21 (48.8%)	0.481
Family History of Kidney Disease	7 (14.6%)	9 (25.7%)	0.204	7 (17.5%)	9 (20.9%)	0.692
Cause of Kidney Disease (Diabetes and or Hypertension)	38 (79.6%)	32 (91.4%)	0.129	30 (75.0%)	40 (93.0%)	0.024
Duration of Dialysis (month)	22.35 ± 15.98	40.11 ± 31.21	0.003	31.98 ± 25.97	27.86 ± 24.32	0.458
Num. of Dialysis in Week	2.96 ± 0.41	2.97 ± 0.30	0.873	3.03 ± 0.42	2.91 ± 0.29	0.141
Length of Dialysis Session (hr)	3.94 ± 0.17	3.97 ± 0.17	0.573	3.95 ± 0.15	3.95 ± 0.18	0.925
Kt/V (Dialysis Efficiency)	1.17 ± 0.24	1.16 ± 0.28	0.860	1.17 ± 0.21	1.15 ± 0.29	0.751
Kt/V≥ 1.2	23 (47.9%)	17 (48.6%)	0.953	20 (50.0%)	20 (46.3%)	0.751
Urine Reduction Ratio	0.62 ± 0.09	0.61 ± 0.10	0.443	0.62 ± 0.09	0.61 ± 0.11	0.442
URR> 0.65	21 (43.8%)	13 (37.1%)	0.546	19 (47.5%)	15 (34.8%)	0.442
Serum Albumin	3.87 ± 0.41	3.65 ± 0.51	0.038	3.73 ± 0.46	3.82 ± 0.48	0.353
Blood Urea Nitrogen	105.15 ± 26.37	112.80 ± 32.66	0.241	114.55 ± 26.50	102.63 ± 30.78	0.063
CRP *	1.38 ± 0.87	1.91 ± 1.20	0.027	1.75 ± 1.17	1.47 ± 0.91	0.222
Creatinine Level	8.58 ± 2.74	9.43 ± 2.26	0.133	9.67 ± 2.59	8.26 ± 2.38	0.011
Tot. Cholesterol	148.00 ± 31.57	146.17 ± 32.57	0.798	139.98 ± 28.09	153.98 ± 33.84	0.044
Weight (Kg)	69.97 ± 14.56	67.20 ± 15.75	0.411	72.65 ± 17.21	65.22 ± 11.80	0.026
Height (Cm)	162.75 ± 8.63	159.09 ± 8.29	0.087	163.60 ± 8.79	158.98 ± 7.94	0.014
BMI ¶(Kg/M^2)	26.46 ± 5.32	26.51 ± 5.76	0.967	27.23 ± 6.53	25.79 ± 4.23	0.240
Waist Circum. (Cm)						
Men	97.82 ± 12.68	96.41 ± 15.22	0.731	9.16 ± 14.81	96.58 ± 12.09	0.681
Women	103.50 ± 16.56	100.90 ± 13.56	0.623	104.43 ± 19.67	99.97 ± 8.92	0.427
Men > 90 & Women > 80	40 (83.3%)	27 (77.1%)	0.480	33 (82.5%)	34 (79.1%)	0.692
Hip Circum. (Cm)	100.63 ± 11.19	101.50 ± 10.97	0.724	102.83 ± 13.24	99.29 ± 8.31	0.146
Waist to Hip ratio						
Men	0.98 ± 0.07	0.97 ± 0.10	0.914	0.97 ± 0.08	0.98 ± 0.02	0.767
Women	1.01 ± 0.06	0.97 ± 0.07	0.085	0.98 ± 0.07	1.00 ± 0.07	0.378
Men ≥ 0.90 & Women ≥ 0.85	42 (87.5%)	32 (91.4%)	0.570	34 (85.0%)	40 (93.0%)	0.240
MUAC # (Cm)	29.31 ± 4.28	28.83 ± 5.06	0.639	30.26 ± 5.20	28.04 ± 3.71	0.029
HGS ‡ before						
Men	27.69 ± 8.53	24.80 ± 7.51	0.253	34.00 ± 4.25	19.52 ± 3.45	0.000
Women	13.94 ± 5.19	13.98 ± 4.87	0.965	18.43 ± 2.78	10.25 ± 2.67	0.000
HGS after						
Men	25.87 ± 8.45	23.53 ± 6.66	0.335	31.52 ± 5.37	18.73 ± 3.77	0.000
Women	14.63 ± 4.57	13.66 ± 4.48	0.546	17.64 ± 2.63	11.09 ± 3.37	0.000
Malnutrition Inflammation Score	3.31 ± 1.19	7.74 ± 1.56	0.000	4.98 ± 2.25	5.37 ± 2.87	0.483

* C-reactive protein; ¶ body mass index; # mid upper arm circumference; ‡ hand grip strength.

Table 3 indicates three groups that were described in "classification and grouping of MIS and HGS" section. The results of ANOVA analysis indicated that there were significant differences among the three groups concerning age, cause of kidney disease (DM and/or hypertension), and height (*P*= 0.000, 0.023, and 0.011, respectively) (Table 3). Other indicators such as having DM, weight, and MUAC were close to be significant (Table 3).

Table 3. Biochemical, biomedical and anthropometry profiles according to the classification of normal and the high risk status of patients defined by either MIS, HGS or both

Variables	Normal by both (n=25)	Normal by either (n=38)	high Risk By both (n=20)	*P* value
Gender (Male)	18 (72.0%)	23 (60.5%)	9 (45.0%)	0.184
Age	49.68 ± 15.34	59.18 ± 10.29	66.00 ± 6.49	0.000
Diabetic Patients	10 (40.0%)	21 (55.3%)	15 (75.0%)	0.064
Family History of Diabetes	9 (36.0%)	15 (39.5%)	13 (65.0%)	0.104
Family History of Kidney Disease	4 (16.0%)	6 (15.8%)	6 (30.0%)	0.378
Cause of Kidney Disease (Diabetes and or Hypertension)	17 (68.0%)	34 (89.5%)	19 (95.0%)	0.023
Duration of Dialysis (month)	23.96 ± 16.99	30.37 ± 26.30	36.20 ± 30.17	0.265
Num. of Dialysis in Week	3.00 ± 0.50	2.97 ± 0.28	2.90 ± 0.31	0.647
Length of Dialysis Session (hr)	3.92 ± 0.19	3.97 ± 0.11	3.95 ± 0.22	0.467
Kt/V (Dialysis Efficiency)	1.19 ± 0.20	1.15 ± 0.25	1.16 ± 0.33	0.833
Kt/V≥ 1.2	13 (52.0%)	17 (44.7%)	10 (50.0%)	0.838
Urine Reduction Ratio	0.63 ± 0.07	0.61 ± 0.10	0.60 ± 0.11	0.583
URR> 0.65	12 (48.0%)	16 (42.1%)	6 (30.0%)	0.466
Serum Albumin	3.82 ± 0.43	3.79 ± 0.45	3.71 ± 0.55	0.708
Blood Urea Nitrogen	110.68 ± 26.41	107.76 ± 27.67	106.65 ± 36.16	0.889
CRP *(Negative)	19 (76.0%)	28 (73.7%)	12 (60.0%)	0.446
Creatinine Level	9.18 ± 2.77	8.93 ± 2.71	8.65 ± 2.10	0.790
Tot. Cholesterol	139.48 ± 28.76	150.76 ± 31.44	150.20 ± 35.80	0.349
Weight (Kg)	71.60 ± 18.26	70.65 ± 12.36	61.80 ± 13.74	0.054
Height (Cm)	164.54 ± 9.58	161.29 ± 7.17	156.88 ± 8.43	0.011
BMI ¶(Kg/M^2)	26.57 ± 6.88	27.13 ± 4.43	25.14 ± 5.35	0.426
Waist Circum. (Cm)				
Men	97.06 ± 15.61	99.39 ± 10.04	92.83 ± 16.45	0.467
Women	104.79 ± 23.27	103.23 ± 13.28	98.55 ± 10.01	0.633
Men > 90 & Women > 80	20 (80.0%)	30 (86.8%)	14 (70.0%)	0.301
Hip Circum. (Cm)	101.80 ± 14.76	101.40 ± 7.99	99.23 ± 11.04	0.711
Waist to Hip ratio				
Men	0.97 ± 0.08	0.98 ± 0.07	0.97 ± 0.11	0.813
Women	0.97 ± 0.05	1.01 ± 0.07	0.96 ± 0.06	0.201
Men ≥ 0.90 & Women ≥ 0.85	20 (80.0%)	36 (94.7%)	18 (90.0%)	0.182
MUAC #(Cm)	29.68 ± 5.30	29.83 ± 3.99	27.03 ± 4.35	0.065
HGS ‡ before				
Men	34.61 ± 4.76	23.72 ± 6.66	18.85 ± 3.43	0.000
Women	17.90 ± 3.19	14.73 ± 5.41	10.42 ± 2.26	0.003
HGS after				
Men	32.37 ± 5.81	21.84 ± 6.04	19.02 ± 4.66	0.000
Women	17.71 ± 2.88	14.77 ± 4.41	10.80 ± 3.19	0.002
Malnutrition Inflammation Score	3.52 ± 1.16	4.79 ± 2.46	8.00 ± 1.72	0.000

* C-reactive protein; ¶ body mass index; # mid upper arm circumference;

‡ hand grip strength

Table 4 indicates the results of the multinomial logistic regression analysis for all biomarkers in various groupings. "Normal by either" and "high risk by both" groups were significantly associated with age (OR = 1.06, 95% CI: 1.02–1.11, *P* = 0.008; OR = 1.18, 95% CI: 1.07-1.30, *P* = 0.024; respectively). The ORs of not having DM, weight, height, and MUAC in "high risk by both" group were compared with "normal by both" (OR = 0.22, 95% CI: 0.06–0.81, *P* = 0.022; OR = 0.95, 95% CI: 0.91-0.99, *P* = 0.028; OR = 0.89, 95% CI: 0.82–0.97, *P* = 0.004; OR = 0.86, 95% CI: 0.74-0.99, *P* = 0.048; respectively) (Table 4).

Table 4. Results of Multinomial Logistic Regression of Biochemical, biomedical and anthropometry markers which affect the probability protein-energy wasting

Markers	Compared to normal by Both §			
	Normal by either MIS or HGS		high Risk by both MIS and HGS	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age	1.06 (1.02-1.11)	.008	1.18 (1.07-1.30)	.001
Duration of Dialysis (mo)	1.01 (0.99-1.04)	.291	1.02 (0.99-1.05)	.109
Non-Diabetic Patients	0.54 (0.19-1.50)	.238	0.22 (0.06-0.81)	.022
Not having a Family History of Diabetes	0.86 (0.30-2.45)	.781	0.30 (0.09-1.04)	.057
Not having a Family History of Kidney Disease	1.02 (0.26-4.04)	.982	0.44 (0.11-1.87)	.268
Weight (Kg)	0.99 (0.96-1.03)	.806	0.95 (0.91-0.99)	.028
Height (Cm)	0.95 (0.89-1.02)	.135	0.89 (0.82-0.97)	.004
BMI ¶(Kg/M^2)	1.02 (0.93-1.12)	.693	0.95 (0.84-1.07)	.363
Waist Circum. (Cm)	1.01 (0.97-1.05)	.641	0.98 (0.94-1.03)	.426
MUAC #(Cm)	1.01 (0.90-1.13)	.899	0.86 (0.74-0.99)	.048
Serum Albumin	0.85 (0.27-2.63)	.775	0.59 (0.17-2.09)	.416
Blood Urea Nitrogen	0.99 (0.98-1.01)	.698	0.99 (0.98-1.02)	.645
CRP *(Negative)	0.88 (0.28-2.84)	.836	0.47 (0.13-1.71)	.253
Creatinine Level	0.96 (0.79-1.17)	.706	0.92 (0.73-1.16)	.487
Tot. Cholesterol	1.01 (0.99-1.03)	.169	1.01 (0.99-1.03)	.253
Kt/V (Dialysis Efficiency)	0.53 (0.07-3.99)	.540	0.70 (0.07-7.22)	.764

§ Reference category: normal by both malnutrition-inflammation score and hand grip strength.

* C-reactive protein; ¶ body mass index; # mid upper arm circumference;

The ROC curve of the MIS index (The AUC= 0.865, *P* < 0.001) with the sensitivity and specificity of 89.7% and 93.8%, respectively, and the ROC curve of the HGS index (The AUC= 0.829, *P* < 0.001) with the sensitivity and specificity of 78.0% and 72.5%, respectively were illustrated as different diagnostic markers for the diagnosis of PEW in HD patients (Figure 1). The sensitivity and the specificity of both MIS and HGS indices were excellent.

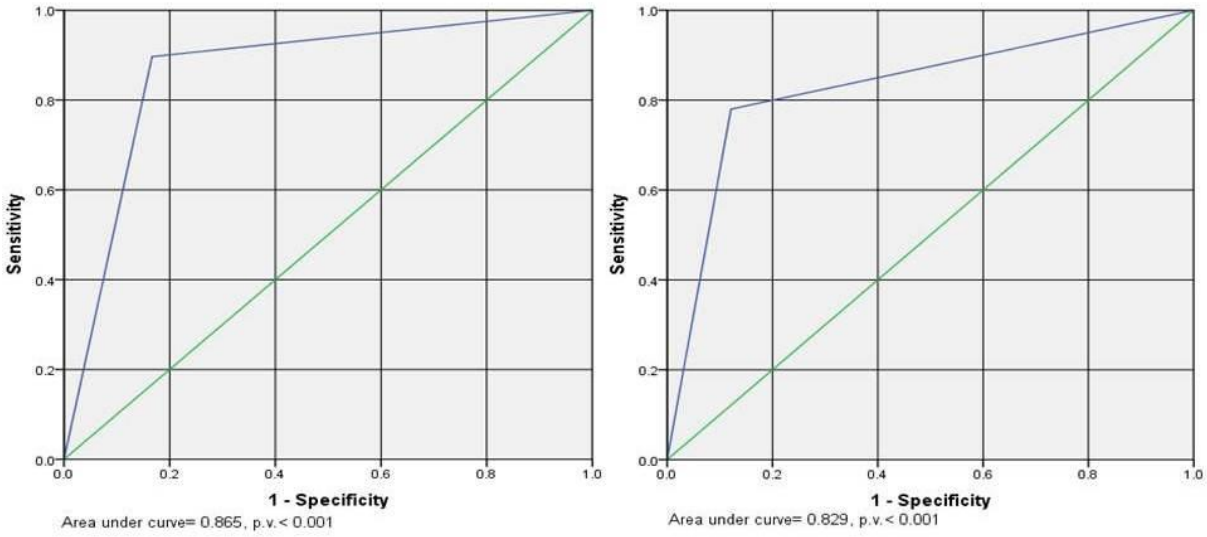

Figure 1. Receiver operation characteristic curves of malnutrition-inflammation score (left) [sensitively and specificity, 89.7% and 93.8%, respectively] and hand grip strength (right) [sensitively and specificity, 78.0% and 72.5%, respectively] as different diagnostic markers for diagnosis of protein-energy wasting in hemodialysis patients

Discussion

In this study, our aim was to detect whether risk stratification with a combination of both MIS and HGS indices identified more precisely patients at increased PEW risk. Klantar-Zadeh et al. proposed that applying MIS, as an inclusive scoring system with its significant associations for nutritional status, inflammation, prospective hospitalization and mortality, has superiority to the conventional SGA (6). Hence, MIS has acceptable consistency and validity for diagnosing PEW in HD patients (7). Due to the need for predicting clinical consequences, the accurate diagnosis of PEW is really vital. As MIS index incorporates SGA method and indicators such as serum albumin, TIBC, and BMI, it can better detect and diagnose PEW in HD patients in comparison to SGA method. In the first step, we compared all of the selected markers between HD patients with mild and moderate PEW. We found significant differences between mild and moderate PEW for serum albumin, weight, WC in males, and WHR. Also, we observed a close significance for CRP and height. Therefore, these indicators have more impact on the capability of MIS index in detecting and diagnosing PEW. The serum albumin, weight, height, WC, and WHR were negatively correlated with CRP (Data not shown). The prediction power of serum albumin is high and this variable alone or together with MIS in comparison with other nutrition-related tests could predict comorbidity and mortality in malnourished HD patients (11,12). The prevalence of moderate PEW was higher in female than male patients. Therefore, similar to another study, gender could act as an inconsistent factor between markers and in the occurrence of non-communicable diseases (13). Briefly, in our study, the significant difference between MIS in two groups of mild and moderate PEW led to other changes in clinical, biochemical, and nutritional anthropometry variables. Similarly, in another research, variations in MIS were associated with variations in

most anthropometries, muscle strength, serum albumin (only for male), and creatinine level (only for female) (14).

When MIS and HGS indexes were dichotomized individually to normal and high risk, risk stratifications slightly varied with each other. Significant differences between normal MIS and high risk MIS as well as normal HGS and high risk HGS in some indicators showed that those variable indicators had more influence on the capability of MIS and HGS indices in detecting and diagnosing PEW. With respect to MIS index, in addition to serum albumin and CRP, gender, family history of DM, and duration of dialysis could better predict the diagnosis of PEW than other indicators. There was an important fact that significant difference and the cutoff in MIS indicator between normal and high risk MIS groups (Table 2) was closer to certainty than significant difference and cutoff in MIS indicator between mild and moderate PEW groups (Table 1). The cutoff of MIS indicator in mild PEW was higher than the cutoff of normal MIS. Kara et al. revealed that the 1-year mortality rate in HD patients was significantly higher in MIS > 6.5 group compared to the MIS ≤ 6.5 group and additional risk indicators associated with mortality (15). With respect to HGS index, age, having DM, cause of kidney disease (DM and/or hypertension) BUN, creatinine, total cholesterol, weight, height, and MUAC could better predict the diagnosis of PEW than other indicators. Unfortunately, there was no significant difference between normal HGS and high risk HGS regarding MIS score. It seems that MIS could not have a specific effect on high risk HGS (Table 2). We conclude that worsening of HGS score may independently have a key role in PEW other than MIS index. The use of HGS as a single-item index in order to diagnose PEW in HD patients, confirm its clinical efficiency.

Interestingly, when HD patients were classified into "normal by both", "normal by either", and "high risk by both" (classification and grouping of MIS and HGS in the method section), risk stratification was considerably (Table 3) similar to dichotomized HGS (Table 2). However, there were significant differences between groups concerning MIS and HGS scores. Unfortunately, due to the low number of HD patients, we were not able to classify our patients into quartile or quintile. As it is seen from the cutoff MIS and HGS scores for each group presented in table 3, increase of MIS and decrease of HGS could predict the risk of PEW. Ho et al. indicated that the likelihood of death for a hemodialysis patient whose MIS was 3, 4, and 5 was 10, 40, and 80%, respectively (16). Evidence shows that HD patients with MIS score of more than 4-5 have a significant risk of 1-year mortality (15-16).

In our study, the sensitivity and specificity of MIS and HGS indices were excellent and corroborated with other studies. In another study, the sensitivity and specificity of MIS with the optimal cutoff point of MIS>6.5 for predicting death was 85.7% and 62.4%, respectively (15). As'habi et al. indicated that the sensitivity, specificity, and area under ROC curve for MIS were 87%, 96%, and 91% in comparison with SGA, respectively (17). Silva et al. showed that the optimized cutoff point of HGS for MIS ≥6 for male and female were 28.3 kg (sensitivity = 70.0%; specificity = 66.0%) and 23.4 kg (sensitivity = 87.0%; specificity = 43.0%), respectively. Lower HGS values were independently associated with higher MIS among patients on MHD across several subgroups (18). However, in our study, unlike the Silva's study, the mean of HGS in females was half of the mean of HGS in males. Our

study was unique in determining the sensitivity and specificity of HGS and MIS in comparison with other studies.

Conclusion

This study demonstrates that MIS index alone or together with HGS index is a valuable tool for risk stratification of HD patients. Besides, it can identify those at increased risk of malnutrition and inflammation. Our findings reveal that patients defined as "normal by both", "normal by either", and/or "high risk by both" based on diagnostic tools, exhibit different indicators compared to patients categorized by either index separately. We conclude that worsening of HGS score may independently have a key role in PEW other than MIS index. The use of HGS as a single-item index in order to diagnose PEW in HD patients, confirm its clinical efficiency. The sensitivity and specificity of MIS and HGS indices were excellent. The cutoff of MIS for the occurrence of PEW varied depending on the procedure used.

Authors' Contributions

Mohammad Reza Mahmoodi contributed to the conception of the original idea, conducting the study design, analysis, interpretation of the data, drafting, revising and the final approval of the manuscript. Naser Hasheminejad contributed to the conception of the original idea and approval of the final version of the manuscript. Abbas Bahrampour contributed to the analysis and offering models, and approval of the final version of the manuscript. Jalal Azmandian contributed to the acquisition of biochemical data, random selection of HD patients, and approval of the final version of the manuscript. Mina Namdari contributed to the acquisition of clinical, biochemical, and nutritional anthropometry data and approval of the final version of the manuscript.

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Consent for publication and Ethical approval

This study was approved by review panels and ethics committee of Deputy of Research at Kerman University of Medical Sciences (Ref. Num. K/92/399). In this study, all patients signed an informed consent form.

Conflict of interest statement

Authors declare no potential conflicts of interest.

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