ORIGINAL RESEARCH

Handgrip Strength as a Simple Indicator of Possible Malnutrition and Inflammation in Men and Women on Maintenance Hemodialysis

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Objective: To assess the validity of handgrip strength (HGS) as a simple screening instrument for malnutrition and inflammation in patients on maintenance hemodialysis (MHD) by correlating it with malnutrition-inflammation score (MIS).

Design: Cross-sectional analysis of the Prospective Study of the Prognosis in Chronic Hemodialysis Patients (PROHEMO).

Setting: Satellite dialysis units in the city of Salvador, Brazil.

Patients: The sample included 274 men and 162 women on MHD.

Main Predictor Variable: HGS was chosen as the main predictor variable in this study.

Main Outcome Measure: An MIS ≥6.

Results: As compared with men, women were found to have lower HGS values (19.38 ± 6.48 kg vs. 29.07 ± 8.67 kg; $P < .001$) and higher MIS (6.38 ± 3.84 vs. 5.57 ± 3.39; $P = .032$). HGS was found to be inversely correlated with MIS among women (Spearman's $\rho = -.360$; $P < .001$) as well as men (Spearman's $\rho = -0.384$; $P < .001$); this inverse correlation was observed in patients with and without diabetes, different racial groups, younger and older subjects, incident (<3 months) and prevalent patients, in the case of both genders. Among both men and women, every one standard deviation lower of HGS was associated with more than two-fold higher odds for MIS ≥6, after adjusting for age, race, duration of dialysis, and Kt/V. These associations remained statistically significant after more extensive adjustments. The optimized cutoff point of HGS for MIS ≥6 was 28.3 kg for men (sensitivity = 70.0%; specificity = 66.0%) and 23.4 kg for women (sensitivity = 87.0%; specificity = 43.0%).

Conclusions: Lower HGS values were independently associated with higher MIS among patients on MHD across several subgroups. These results suggest that HGS is a valid screening instrument for malnutrition and inflammation in patients on MHD.

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1051-2276/$36.00

doi:10.1053/j.jrn.2010.07.004

DESPITE IMPROVEMENTS IN the treatment of chronic kidney disease (CKD), patients on maintenance hemodialysis (MHD) continue to face problems that may potentially contribute toward protein-energy malnutrition and inflammation.[1,2] A large amount of evidence has indicated that malnutrition and inflammation are closely linked and frequently present in patients on MHD.[2–4] The malnutrition-inflammation score (MIS) was developed to take into account the close link between malnutrition and inflammation among dialysis patients.[2,5] MIS is a more comprehensive scoring system and a better quantitative assessment tool as compared with its predecessors, that is, the Subjective Global Assessment (SGA) and the Dialysis Malnutrition Score).[5] MIS has been found to be associated with conventional biological markers of inflammation.[6,7] Moreover, there is evidence that the hazard rates of death and hospitalization are higher among patients with higher MIS.[5,8] A previous study involving 257 adult patients on MHD has suggested that 5 is the best cutoff point for MIS to predict risk of mortality in patients on MHD.[8]

Although MIS is a powerful research tool to identify patients who are at a higher risk of adverse outcomes, it may not be practical for systematic and follow-up nutritional evaluation of all patients treated in the clinical setting of a busy dialysis unit. This limitation is because of the fact that the assessment of the 10 items of MIS requires expertise in renal nutrition to ensure accuracy and also because it depends on data that may be unavailable at a certain moment. In contrast, the use of a hand dynamometer to measure handgrip strength (HGS) may be more suitable for clinical practice because it is simple, objective, and can be easily performed at the patient's bedside.[9] The rationale to use HGS as a nutritional screening tool is also supported by evidence that it is strongly correlated with lean body mass,[9–11] and may identify patients who had a significant reduction in nutritional status before the occurrence of any structural changes.[12,13] The existing data suggest that, similar to MIS, HGS can be used to identify those dialysis patients who are at a higher risk of adverse outcomes.[11]

Early identification of dialysis patients with reduced nutritional status through appropriate intervention is pivotal to prevent the development of severe malnutrition. Previous studies have shown associations between HGS and SGA among patients on MHD and among patients with CKD who are about to start renal replacement therapy, thereby suggesting that hand dynamometry is a valid screening nutritional tool for the increasing end-stage renal disease population.[10,11,14] Demonstrating the fact that HGS is also associated with MIS will provide additional support to the systematic use of hand dynamometry in dialysis patients. To demonstrate the validity of HGS as a proxy for MIS among dialysis patients as a whole, it is important to assess whether correlations between these measures are present across the patient's demographic and clinical characteristics that are associated with body composition, for example, gender, age, race, duration of dialysis, and prevalent comorbidities such as diabetes.

Using a sample of patients on MHD treated in 4 dialysis clinics in the city of Salvador, BA, Brazil, the present study assessed the concurrent validity of HGS as a simple screening instrument for malnutrition and inflammation in MHD patients by correlating it with the MIS. To provide insights into the generalizability of the results for the MHD population as a whole, our study also examined gender-specific correlations between HGS and MIS by age and racial groups, diabetic status, and duration of dialysis.

Methods

Study Design and Subjects

A cross-sectional design was made using baseline data from a prospective cohort study, the Prospective Study of the Prognosis in Chronic Hemodialysis Patients (PROHEMO), which was conducted at 4 satellite dialysis units in the city of Salvador, BA, Brazil.[15] The study protocol was approved by the Research Ethics Committee of the School of Medicine of the Federal University of Bahia and all patients provided written informed consent for study participation. All hemodialysis patients aged ≥18 years who were treated in the dialysis units between May 15, 2007 and December 30, 2008 were invited to participate in the study. The acceptance rate was superior to 95%. From an original sample of 489 patients with nutritional data (181 women and 308 men), 436 patients (162 women and 274 men) had data on both hand dynamometry and the variables used to determine the MIS. The data from this particular sample were used for the main analysis of the present study.

Data Collection and Definitions

A census form was used in each of the participating dialysis units to obtain basic data related to all the patients. For the patients who signed the consent form, data on demographic, laboratory, and clinical variables were abstracted from medical records and supplemented with information provided by the patient. Patient race was classified by the interviewer as white, mixed (mulatto), or black. For analysis, patients who were on dialysis for <3 months at the time of data collection were considered as incident. Comorbidities were diagnosed on the basis of medical records and information provided by the attending nephrologists. Blood samples were collected before the dialysis session, after the longest interdialytic period. The laboratory values used for analysis were those from tests performed closest to the patient's entry in the study. Serum albumin concentration was determined by the bromocresol green method.

The data that were used to determine MIS were collected by 2 certified dietitians combined with consultations with the attending nephrologists. HGS was measured with the Takei hand dynamometer (TKK 5401, Takei Scientific Instruments Co., Ltd., Tokyo, Japan). Before the HGS measurements were made, the patients were familiarized with the use of the dynamometer and instructed to apply as much handgrip pressure as possible. The dynamometer was adjusted to fit each subject's grip in the arm. The HGS was measured in the arm without arteriovenous fistula (AVF) to prevent the influence of the patient's concern of applying the maximum handgrip pressure in the arm with the AVF. For patients who did not have an AVF placed, HGS was measured in the dominant arm. HGS was measured 4 times before the initiation of the dialysis session with the dynamometer held close to the patient's body. The mean of the 2 highest values was recorded.

The MIS comprised 7 components of the SGA (weight change, dietary intake, gastrointestinal symptoms, functional capacity, comorbidity, fat store, and muscle wasting) and 3 additional non-SGA components, that is, body mass index (BMI), serum albumin, and total iron-binding capacity. BMI was calculated using the patient's dry weight value by dividing body weight in kilograms by the square of height in meters. Because the associations between years on dialysis and outcomes are complex and highly dependent on the effects of demographics, comorbidities, and treatment factors,[16] MIS was determined by using the more recently proposed method that does not include the number of years that the patient was on dialysis.[7] Each component of MIS has 4 levels of severity ranging from 0 (normal) to 3 (severely abnormal). The sum of all 10 MIS components may range from 0 (normal) to 30 (severely malnourished); a higher score reflects a more severe degree of malnutrition and inflammation.

Variables

The main predictor variable was HGS and the outcome variable was MIS. Baseline characteristics regarding patient's age, race (white, mixed, or black), months on dialysis, dialysis dose by single pool Kt/V, hemoglobin, serum creatinine, heart failure, diabetes mellitus, cerebrovascular disease, and peripheral vascular disease were treated as potential confounders or effect modifiers of the association between HGS and MIS.

Statistical Analyses

The *t*-test for independent samples or the Mann–Whitney test was used for comparing quantitative variables. The χ^2 test or the Fisher's exact test was used to compare categorical variables between groups. Because the MIS values follow a discrete rather than a continuous distribution, the nonparametric Spearman's ρ was used instead of the Pearson's product-moment correlation coefficient for assessing correlations between HGS and MIS, separately for women and men. Correlations among men and women were assessed by strata of age (18 to 39 years, 40 to 59 years, and ≥60 years), diabetic status, and months on dialysis (<3 months and ≥3 months). Gender-specific multivariable linear regression models were used to estimate change in the mean of MIS by one standard deviation of HGS. Gender-specific multivariable logistic regression models were also used to estimate change in the odds for MIS ≥6 by one standard deviation lower of HGS. To make a decision about the inclusion of the covariates in the logistic and linear regression models for obtaining adjusted estimates, we tested for statistical significance of interaction terms between each covariate and HGS. The probability values for the interaction terms were obtained on the basis of the product of the following binary categorical variables with gender-specific median

HGS: age (cutoff point at 60 years), months on dialysis (cutoff point at 3 months), race (white and nonwhite), hemoglobin (cutoff point at 11.0 g/dL), serum creatinine (cutoff point defined by median value), diabetes, heart failure, cerebrovascular disease, and peripheral vascular disease.

For each group of models, different levels of adjustment were tested for their effect on the relationship between HGS and MIS. The associations between HGS and MIS were not adjusted for albumin and BMI because these 2 measures are constituents of the MIS. Comorbidities were included in the models with more extensive adjustments; however, data on the severity of the comorbidity that are required for the comorbidity item of MIS were not included for adjustments in the regression models.

Although the models that were adjusted only for age, race, months on dialysis, and Kt/V may be considered as minimally adjusted, the models with additional covariate adjustments may be viewed as over-adjusted partly because of the inclusion of comorbidities that are used to determine one of the MIS components. To address the issue of unavailability of information on categorical covariates, binary indicator variables (1 = missing, 0 = not missing) were used. Gender-specific mean values were used to replace Kt/V information missing for 5 patients. Receiver operating characteristic (ROC) curves were generated to find the best cutoff value for HGS to predict MIS ≥6 in men and women. The statistical analyses were performed using the SPSS version 16.0 for Windows (SPSS Inc, Chicago, IL), with the exception of the ROC curves which were assessed using StatsDirect version 2.7.3 (StatsDirect Ltd., Cheshire, England).

Results

From an initial sample of 489 patients with nutritional data, 436 patients who had information for both HGS and MIS constituted the sample that was used for the main analysis of this study. The percentage of male subjects was 62.8% among the 436 participants and 64.2% among the 53 nonparticipants (P = .85). Among nonparticipants, hand dynamometry was not performed for 8 patients because of the following reasons: physical impairment (n = 3), death after study entry but before evaluation for HGS and MIS was conducted (n = 3), permission not obtained from the patient because of recent implantable cardiac pacemaker (n = 1), and as a result of transfer to a nonparticipating unit (n = 1). Mean HGS was lower among nonparticipants as compared with participants, for both men (mean HGS: 25.7 ± 8.3 kg vs. 29.1 ± 8.7 kg; P = .048) and women (mean HGS: 16.0 ± 8.0 kg vs. 19.4 ± 6.5 kg; P = .055). Data on MIS were available for 6 of the total 53 nonparticipants. The main reason for unavailability of MIS data was lack of information on previous weight (n = 22), BMI (n = 7), albumin (n = 7), and total iron-binding capacity (n = 7).

As shown in Table 1, mean age was 47.3 ± 14.2 years for the 436 study participants and 50.8 ± 19.2 years for 53 nonparticipants (P = .293). The median of months on dialysis was found to be significantly (P < .001) lower among nonparticipants (median = 3.9 months) as compared with participants (median = 22.0 months). In addition, nonparticipants had significantly lower serum hemoglobin and serum creatinine levels and higher prevalences of heart failure, cerebrovascular disease, and peripheral vascular disease. Table 1 also shows comparisons of the characteristics of 436 participants by gender. As compared with men, women had significantly lower serum albumin and serum creatinine levels and higher neutrophil/lymphocyte ratio and Kt/V.

MIS ≥6 was observed for 53.4% of the 436 participants, 45.7% among men and 58.0% among women (P = .012). Table 2 shows the means of MIS and HGS in men and women by strata of age, racial groups, diabetic status, months on dialysis, and the arm used for hand dynamometry. As compared with men, women were found to have significantly higher mean MIS (6.38 ± 3.84 vs. 5.57 ± 3.39; P < .05) and lower mean HGS (19.38 ± 6.48 vs. 29.07 ± 8.67 kg; P < .001). In men and women, MIS was reported to be significantly higher among patients with diabetes and incident patients as compared with patients without diabetes and prevalent patients. Among men and women, HGS was reported to be significantly lower among patients with diabetes and older patients as compared with patients without diabetes and younger patients. A lower HGS was observed for incident than for prevalent patients, but the difference was statistically significant only among women. Hand dynamometry was performed with the dominant arm by 78.8% (216/274) of men and by 77.2% (125/162) of women. No significant difference in MIS and HGS was

Table 1. Characteristics of All Participants, All Nonparticipants, and Participants by Gender

				Participants (N = 436)		
	Participants (P) N = 436	Nonparticipants (NP) N = 53	*P*-Value P vs. NP	Men (M) N = 274	Women (W) N = 162	*P*-Value M vs. W
Age, years (mean ± SD)	47.33 ± 14.18	50.8 ± 19.2 years	.293	47.38 ± 14.07	47.23 ± 14.39	.915
% 18–39 years	32.8	25.0	.254	32.5	33.3	.855
% 40–59 years	49.3	38.5	.139	49.3	49.4	.982
% ≥60 years	17.9	36.5	.001	18.2	17.3	.800
Race						
% White	10.6	13.2	.557	12.0	8.0	.187
% Mixed race	65.8	52.8	.062	62.8	71.0	.081
% Black	23.6	34.0	.100	25.2	21.0	.319
Body mass index, kg/m^2 (mean ± SD)	22.76 ± 3.96	22.20 ± 3.78	.359	22.83 ± 3.76	22.65 ± 4.31	.653
Albumin, g/dL (mean ± SD)	3.80 ± .52	3.76 ± 0.58	.619	3.84 ± 0.52	3.72 ± 0.52	.022
Hemoglobin, g/dL (mean ± SD)	9.70 ± 1.87	8.81 ± 2.13	.003	9.78 ± 1.87	9.45 ± 1.87	.072
Creatinine, mg/dL (mean ± SD)	10.52 ± 3.55	9.68 ± 3.96	<.001	12.31 ± 3.73	10.59 ± 3.22	<.001
Neutrophil/lymphocyte ratio (mean ± SD)	2.86 ± 2.16	3.09 ± 2.54	.503	2.68 ± 1.83	3.16 ± 2.62	.024
Kt/V (mean ± SD)	1.46 ± 0.26	1.42 ± 0.29	.459	1.42 ± 0.25	1.51 ± 0.26	.001
% Diabetes	23.2	28.3	.410	21.9	24.7	.503
% Heart failure	9.4	25.0	.002	8.1	12.6	.132
% Cerebrovascular disease	3.2	10.4	.034*	3.4	3.1	.865*
% Peripheral vascular disease	2.8	10.4	.022*	1.9	4.4	.225*
Months on dialysis (median)	22.00	3.9	<.001†	16.72	26.05	.312†
% <3 months on dialysis	24.8	41.5	.009	23.7	26.5	.510

Missing data among the 436 participants: heart failure = 17 cases (14 among men and 3 among women); cerebrovascular disease = 11 cases (10 among men and 1 among women); peripheral vascular disease = 16 cases (14 among men and 2 among women); neutrophil/lymphocyte ratio = 8 cases (4 among men and 4 among women); Kt/V = 5 cases (all among men).

*Fisher's exact test.

†Mann–Whitney *U* test.

Table 2. Means of Malnutrition-Inflammation Score and Handgrip Strength in Men and Women, Stratified by Age, Racial Groups, Diabetic Status, Time on Dialysis, and the Arm Used for Hand Dynamometry

	Malnutrition-Inflammation Score		Handgrip Strength	
	Men	Women	Men	Women
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
All patients	5.57 ± 3.38	6.38 ± 3.84*	29.06 ± 8.67	19.38 ± 6.48†
Age groups				
18–39	5.28 ± 2.99	6.09 ± 3.73	33.00 ± 7.73	22.18 ± 6.07†
40–59	5.26 ± 3.33	6.43 ± 3.91*	29.07 ± 8.24	19.17 ± 6.15†
≥60	6.90 ± 3.90	6.79 ± 3.98	22.03 ± 6.88	14.58 ± 5.28†
P-value for age comparison	$P = .024$	$P = .821$	$P < .001$	$P < .001$
Racial groups				
White	5.58 ± 3.78	7.92 ± 4.65	26.42 ± 8.53	16.05 ± 4.56†
Mixed	5.51 ± 3.18	6.16 ± 3.79	29.77 ± 8.57	19.32 ± 6.26†
Black	5.71 ± 3.71	6.53 ± 3.66	28.56 ± 8.83	20.85 ± 7.46†
P-value for race comparison	$P = .976$	$P = .241$	$P = .108$	$P = .074$
Diabetic status				
With diabetes	7.05 ± 3.56	8.36 ± 4.00	23.72 ± 7.39	16.04 ± 6.27†
Without diabetes	5.15 ± 3.22	5.72 ± 3.57	30.56 ± 8.42	20.47 ± 6.19†
P-value for diabetic comparison	$P < .001$	$P < .001$	$P < .001$	$P < .001$
Time on dialysis				
Incident (<3 months)	6.91 ± 3.46	8.21 ± 3.75*	27.35 ± 8.93	17.18 ± 5.13†
Prevalent (≥3 months)	5.15 ± 3.26	5.71 ± 3.67	29.60 ± 8.54	20.17 ± 6.75†
P-value for time on dialysis comparison	$P < .001$	$P < .001$	$P = .068$	$P = .009$
Arm used for hand dynamometry				
Dominant	5.67 ± 3.43	6.62 ± 3.87*	29.45 ± 8.80	19.68 ± 6.93†
Nondominant	5.19 ± 3.19	5.57 ± 3.69	27.61 ± 8.06	18.35 ± 4.57†
P-value for arm comparison	$P = .353$	$P = .117$	$P = .151$	$P = .274$

The *t* test or ANOVA was used for handgrip strength comparisons. Mann–Whitney test or Kruskal–Wallis test was used for malnutrition-inflammation score comparisons.

*P value $<.05$.

†P value $<.001$ for the MIS and HGS comparisons between men and women.

observed between patients who had the HGS performed with the dominant arm and those who performed with the nondominant arm. Lower HGS and higher MIS were also observed for patients with heart failure, hemoglobin levels of <9 g/dL, and serum creatinine levels of <7.5 mg/dL (these data are not shown in the table).

Table 3 shows statistically significant ($P < .001$) inverse correlations between HGS and MIS, both among men (Spearman's $\rho = -0.384$) and women (Spearman's $\rho = -0.360$). The correlations observed for whole groups of men and women followed a similar pattern across age groups, racial groups, diabetes status, time on dialysis (<3 months and ≥3 months), and the arm used for hand dynamometry. In the subgroup analysis, the inverse correlations between HGS and MIS did not reach statistical significance only for the 13 white women and the 37 women who performed the hand dynamometry by using the nondominant arm. We also observed an inverse correlation between HGS and neutrophil/lymphocyte ratio (Spearman's $\rho = -0.157$), but the correlation was significant only among men (data not shown in the table).

Table 4 shows linear and logistic regression results of the associations between HGS and MIS. Before performing adjustments for covariates, we tested for interactions between HGS and each covariate. The associations between HGS and MIS were assessed without including interaction terms in the models because none of the interaction coefficients were statistically significant ($P > .1$). The standard deviation of HGS was 8.67 kg in men and 6.48 kg in women. In the linear regression model with adjustments for age, race, months on dialysis, and Kt/V, the increase in MIS per one standard deviation lower of HGS was approximately 1.41 points ($P < .001$) for men and 1.78 points ($P < .001$) for women. In the logistic regression model with adjustments for the same groups of covariates, each one standard deviation lower of HGS

Table 3. Correlations Between Handgrip Strength and Malnutrition-Inflammation Score in Men and Women, Stratified by Age, Racial Groups, Diabetic Status, Months on Dialysis, and the Arm Used for Hand Dynamometry

	Men		Women	
	N	Spearman's Rho	N	Spearman's Rho
All patients	274	−0.384*	162	−0.360*
Age groups				
18–39 years	89	−0.424*	54	−0.273†
40–59 years	135	−0.326*	80	−0.467*
≥60 years	50	−0.410‡	28	−0.417†
Race				
White	33	−0.537‡	13	−0.218
Mixed	172	−0.376*	115	−0.326*
Black	69	−0.346‡	33	−0.604*
Diabetic status				
With diabetes	60	−0.358‡	40	−0.486‡
Without diabetes	214	−0.325*	122	−0.294‡
Time on dialysis				
Incident (<3 months)	65	−0.436*	43	−0.437‡
Prevalent (≥3 months)	209	−0.341*	119	−0.292‡
Arm used for hand dynamometry				
Dominant	216	−0.390*	125	−0.433*
Nondominant	58	−0.392‡	37	−0.181

*P value <.001.
†P value <.05.
‡P value < .01.

was significantly associated with a two-fold increase in the odds of a MIS ≥6, both among men (odds ratio = 2.25, $P < .001$) and women (odds ratio = 2.53, $P < .001$). The strength of the associations between lower HGS and higher MIS was reduced after performing more extensive and cumulative adjustments for hemoglobin, creatinine, and comorbidities; however, all the associations remained statistically significant after adjusting for the whole set of covariates. We also performed linear and logistic regression analyses with the same level of adjustments of models 6 in a sample restricted to 407 patients (250 men and 157 women) without any data missing for any of the covariates. The results in the restricted sample were very similar to the ones described for models 6 in Table 4. In the restricted sample, the increase in MIS per one standard deviation lower of HGS was approximately 1.28 point ($P < .001$) for women and 0.94 point ($P < .001$) for men. In the logistic regression model, the odds ratio of the association between one standard deviation lower of HGS and the odds of an MIS ≥6 was 2.25 ($P = .001$) for women and 1.76 for men ($P = .004$).These results for the restricted sample of 407 patients are not shown in the table.

A ROC curve analysis was performed to determine the best cutoff point of HGS to identify patients with MIS ≥6. The area under the ROC curve for HGS as a predictor of MIS was 70.0% (95% CI = 57.9% to 82.2%) for men and 68.0% (95% CI = 54.0% to 81.4%) for women. The optimized cutoff point for HGS was 28.3 kg for men (sensitivity = 70.0%; specificity = 66.0%) and 23.4 kg for women (sensitivity = 87.0%; specificity = 43.0%).

Discussion

Among men and women, HGS was inversely correlated with MIS for patients of different racial groups, for patients with and without diabetes, for younger and older subjects, and for incident and prevalent MHD patients. By showing inverse correlations between HGS and MIS across patient's characteristics, the present study gives additional support to the use of HGS as a simple screening nutritional tool for MHD patients. However, on the basis of these results, gender-specific thresholds for HGS should be used to identify patients who may need more comprehensive nutritional evaluation.

Table 4. Increase in the Malnutrition-Inflammation Score in Men and Women by Lower Values of Handgrip Strength

	Men N = 274	Women N = 162
Linear Regression Models	Linear Regression Coefficient of the Increase in the Mean of MIS by One Standard Deviation* Lower of HGS	
Model 1: Unadjusted	1.31 ($P < .001$)	1.62 ($P < .001$)
Model 2: Adjusted for age, race, and months on dialysis	1.41 ($P < .001$)	1.79 ($P < .001$)
Model 3: Model 2 + dialysis dose (Kt/V)	1.41 ($P < .001$)	1.78 ($P < .001$)
Model 4: Model 3 + serum hemoglobin	1.21 ($P < .001$)	1.55 ($P < .001$)
Model 5: Model 4 + serum creatinine	1.16 ($P < .001$)	1.51 ($P < .001$)
Model 6: Model 5 + comorbidities*	0.99 ($P < .001$)	1.27 ($P < .001$)
Logistic Regression Models	Odds Ratio of the Increase in the Odds of MIS ≥6 by One Standard Deviation Lower of HGS	
Model 1: Unadjusted	2.03 ($P < .001$)	2.02 ($P < .001$)
Model 2: Adjusted for age, race, and months on dialysis	2.25 ($P < .001$)	2.53 ($P < .001$)
Model 3: Model 2 + dialysis dose (Kt/V)	2.25 ($P < .001$)	2.53 ($P < .001$)
Model 4: Model 3 + serum hemoglobin	1.96 ($P < .001$)	2.35 ($P < .001$)
Model 5: Model 4 + serum creatinine	1.91 ($P < .001$)	2.40 ($P < .001$)
Model 6: Model 5 + comorbidities†	1.76 ($P = .002$)	2.26 ($P = .001$)

HGS, handgrip strength; MIS, Malnutrition-Inflammation Score.

*Standard deviation of HGS was 8.67 kg for men and 6.48 kg for women. To determine the increase in MIS by 10 kg lower HGS the increase in MIS by one standard deviation should be divided by 0.867 for men and by 0.648 for women.

†Comorbidities = heart failure, cerebrovascular disease, peripheral vascular disease, and diabetes.

There is a strong biological plausibility that malnutrition and inflammation act as mediator factors of the association between lower HGS and higher MIS observed in this study.[4,9,11,14,17] It has been shown, for example, that malnutrition causes muscle fatigability and an altered pattern of muscle contraction and relaxation.[13] Moreover, higher levels of inflammatory biomarkers, such as C-reactive protein and interleukin 6, have been associated with lower HGS, higher MIS, and muscle wasting in CKD patients.[6,7,9,18–20] By showing associations between lower HGS and higher neutrophil/lymphocyte ratio, our study provides additional support to the validity of using HGS as a proxy for inflammation and malnutrition in hemodialysis patients. Previously published data have shown that higher neutrophil/lymphocyte ratio is associated with higher odds of cachexia, lower BMI, and lower serum concentrations of albumin and creatinine among MHD patients.[21,22] MIS was chosen as a research tool for our study because it is a comprehensive measure that considers recommendations of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative of using a panel of measures to assess protein-energy nutritional status.[23] Hand dynamometry was included in the present investigation with the main objective of assessing its value as a simple screening instrument to select patients for a more thorough nutritional status evaluation to prevent adverse outcomes related to malnutrition. The advantage of HGS over more comprehensive nutritional assessment tools is that it does not depend on additional laboratory or clinical data that could be pending or unavailable at a specific moment, particularly for patients who have been recently started on renal replacement therapy.

Separate analyses by gender were performed to assess associations between HGS and MIS in keeping with previous observations suggesting that the associations of HGS with clinical outcomes differ between women and men.[10] Moreover, large variations in HGS have been found both between and within genders which may reflect differences in body composition.[24,25] In our study of MHD patients, the mean HGS in women was approximately 67% of the mean HGS in men. A gender gap in HGS of this magnitude has also been observed in healthy subjects.[26,27] Despite the gender differences in HGS, this simple measure was independently associated with MIS both in men and women enrolled in the present

study. However, the results of the ROC curve analysis indicate that the HGS cutoff to optimize its discriminatory power differs between women and men. The HGS value with the best tradeoff between sensitivity and specificity was 28.3 kg in men and 23.4 kg in women. Studies with larger sample sizes are required to assess ROC curves for HGS as a predictor of MIS that are not only gender-specific but also age-category specific.

Lower HGS and higher MIS were associated with several patient characteristics that have been related to malnutrition and inflammation, such as older age, diabetes, heart failure, and lower serum creatinine and hemoglobin levels.[7,14,21,28] Cumulative adjustments were performed to assess the influence of these patient characteristics on the associations between HGS and MIS. Gender-specific standard deviations of HGS were used to assess associations with MIS by linear regression to take into account the observed differences between women and men in the point estimate and the variation of HGS measures. Additionally, logistic regression was used to assess the association between HGS and MIS. It should be noted that, both in the linear and the logistic regression analyses, lower HGS was independently and significantly associated with higher MIS, even for models with extensive adjustments for covariates, including selected comorbidities. The gender-specific models with minimal adjustments, that is, the one that included only age, months on dialysis, and Kt/V, are perhaps the most suitable for inferences related to the association between HGS and MIS, as the models with more extensive adjustments may contain variables that represent intermediate steps in the pathogenic process that links HGS and MIS.

Methodological limitations of the present study and generalizability of the findings should be considered to draw definitive conclusions regarding the validity of hand dynamometry as a useful nutritional screening tool for MHD patients. One such methodological limitation is the observational and cross-sectional design of the study, which does not permit to assess the actual effect that earlier identification of patients who are at a higher risk of severe malnutrition by HGS will have on adverse hemodialysis outcomes. A project for the phase II of the PROHEMO is underway to examine whether reduction in HGS, as assessed by repeated measures of hand dynamometry across the follow-up, correlates with reduction in nutrition status, biological markers of inflammation, survival, and hospitalization among MHD patients. Missing data should also be viewed as a potential methodological limitation. It was not possible to assess associations of approximately 11% of the patients because of missing data, which was more often because of lack of information on determining the MIS. As compared with the 436 participants, the 53 nonparticipants were more often incident patients with evidence of poorer health status. In contrast to MIS, HGS could be performed for large fraction of nonparticipants. Both for men and women, the mean HGS was much lower for nonparticipants, which suggests that they have a poorer nutritional status as compared with the participants. Another methodological limitation is the absence of a universally acceptable reference standard for MIS. We used an MIS ≥ 6 as a theoretical standard by taking into account previous observations that MIS >5 are strongly associated with higher mortality risk among hemodialysis patients.[8] However, it was not possible to assess the possibility of within-patient differences in the association between HGS and MIS, on the basis of the arm used for hand dynamometry. We decided to use the arm without the AVF, taking into account the possibility that the patient might avoid applying the maximum handgrip pressure in the arm with the vascular access, which more often was the dominant arm. However, as not all patients had the AVF in the nondominant arm, we could observe that the mean of HGS was only slightly higher among those who have used the dominant arm as compared with those who have used the nondominant arm for hand dynamometry. The results suggest that HGS correlates inversely with MIS independently of the arm used for hand dynamometry.

Because the study was developed in dialysis units from a single geographic region, we should be cautious of the generalizability of the finding to other hemodialysis populations. The population of hemodialysis patients from Salvador predominantly consists of mixed race (black and white admixture), which reflects the distribution of racial categories in the general population. It is important to take into account this peculiarity of the studied hemodialysis population considering the fact that race has been associated with several outcomes among patients with CKD.[29]

However, our results suggest that the observed correlation between HGS and MIS follows a similar pattern across racial categories.

Conclusion

Lower HGS was significantly and independently associated with higher MIS in MHD patients of both genders. Among men and women, inverse correlations were observed in subsets of incident and prevalent patients, for patients with and without diabetes, and for different age and racial groups. The results suggest that HGS is a valid screening instrument for malnutrition and inflammation in patients on MHD.

Acknowledgments

The PROHEMO has been supported by research grants from "The Brazilian National Council for Scientific and Technological Development (CNPq)," grants #484743/2006-6 and #308068/2006-8. The results were presented as an abstract at the Renal Week 2009 (Annual Meeting of the American Society of Nephrology) held in San Diego, CA, United States. The authors report no conflict of interest. The authors thank Professor Friedrich K. Port, MD, MS, FACP for helpful comments and suggestions for this article. The study is administered by the Clinical Epidemiology Unit of the Federal University of Bahia. The study has been supported by research grants from "The Brazilian National Council for Scientific and Technological Development (CNPq)," grants #484743/2006-6 and #308068/2006-8.

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