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RESEARCH PAPER

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Geriatric Nutritional Risk Index is a Significant Parameter for Anemia and Predicts Hospitalization Outcomes in Chronic Dialysis Patients

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ABSTRACT

Malnutrition is associated with adverse consequences in hemodialysis (HD) patients. A new tool Geriatric Nutrition Risk Index (GNRI) was recently proposed to screen malnutrition in this population. We aimed to examine the association between GNRI and hospitalization outcomes in chronic HD patients.

We studied 186 adult HD patients from a single dialysis unit. We compared their GNRI scores with their comprehensive Malnutrition-Inflammation Scores (MIS) scores. Biomarkers reflecting nutritional status and inflammation were measured. Anthropometric measures and hospitalization datas during the study period were also tabulated. The mean GNRI was 98.8±32.6 in study patients. GNRI scores were categorized as: severe risk (<92) and lower risk (≥92). In a multivariable linear regression model, GNRI was independently associated with hemoglobin (r^2=0.118, p=0.00) and the number of hospitalization (r^2=0.864, p=0.04). Patients in the low-GNRI group had significantly higher mortality compared to those in the high- GNRI group (hazard ratio [HR], 2.667; 95% confidence interval [CI]: 1.527–4.651, p<0.001).

The GNRI is calculated by a very simple equation in which only 3 nutritional variables-serum albumin, height and body weight-are involved. GNRI is a significant predictor for morbidity in HD patients. The simple method of GNRI is considered to be a clinically useful marker for detecting of patients who need special care.

Key Words: Geriatric Nutritional Risk Index, Hemodialysis, Anemia, Hospitalization and Mortality.

INTRODUCTION

Malnutrition is prevalent complex conditions that frequently remain undiagnosed and untreated in maintenance hemodialysis (HD) patients and is associated with an increased morbidity and mortality (Lowrie and Lew, 1990). Several studies have evidenced that 23%-76% of patients on HD suffered from malnutrition (Ikizler and Hakim1996). It is recognized that there are several methods for assessing the nutritional statuses of HD patients, including the subjective global assessment (SGA) a malnutrition–inflammation score (MIS) (Kalantar-Zadeh et. al., 2001 and Chan et al., 2007). These methods require well-trained staff member multi disciplinary procedures, anthropometric measurements, body composition measurements, functional and subjective assessments. Recently, a new prognostic index combining albumin with information about body weight entitled the Geriatric Nutritional Risk Index (GNRI). It was proposed as a method to predict nutrition-related complications and validated by Bouillanne et al. for screening malnutrition in elderly medical patients (Bouillanne et al., 2005). Yamada et al. examined the validities of five of the simpler nutritional screening tools and reported that the GNRI was the simplest and most accurate risk index for identifying malnutrition in maintenance HD patients at nutritional risk according to the MIS (Yamada et al., 2008). The GNRI showed the highest sensitivity, specificity and accuracy for predicting hypo-albuminemia among these nutritional screening tools (Cereda et al., 2007 and Fouque et al., 2008). To date, there have been few longitudinal studies that have used GNRI to predict hospitalization outcomes in HD patients. The aim of this study was to evaluate GNRI in these patients by comparing it with conventional measures of nutritional state, including MIS, blood tests and measures of clinical outcome including hospitalization datas and mortality.

MATERIALS AND METHODS

Patients

In this study, 186 adult HD patients (age; 63±13 years, range 50-76 years, 94 males) were enrolled and followed for 36 months in our center. Study inclusion criteria were ongoing HD therapy for ≥6 months and a stable condition with no severe co-morbidities, such as cardiovascular disease, respiratory disease, gastrointestinal disease, neurologic disease, acute illness, malignancy, severe infection, mental disorders or bed-bound patients. HD was performed 3 times/wk for 4 h with the use of hollow-fiber dialyzers and bicarbonate buffered endotoxin-free dialysate. The patients had been educated by dietitians to restrict their intakes of sodium, potassium, and fluids and to ingest 35 kcal energy/kg per day and 1.2 g protein/kg per day. Immediately at the start of the first HD session of the week, total blood was collected, centrifuged for future analysis. The samples were stored at –80°C until performing the assay. Biomarkers reflecting nutritional status and inflammation (serum albumin, C-reactive protein) were measured by standard methods. The study was approved by the local ethical committee and written informed consent was obtained from all patients prior to study entry. The study was conducted according to the declaration of Helsinki.

Anthropometric evaluation

The anthropometric indices assessed were as follows: post-dialysis weight, considered the patient's dry weight (kg); height (cm). Weight was measured in light clothing without on a digital scale (Seca®,

Hamburg), height was measured in standard position with a portable stadiometer and recorded to the nearest mm. Waist circumference (WC) was measured midway between the lowest rib and the iliac crest, hip circumference was measured in undergarments at the place of largest circumference around the buttocks. For all calculations and computations, we used the average of the repeated measurements. Body mass index (BMI) was calculated as kg/m² and waist-to-hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference.

Assessment of Nutritional Status and Hospitalization Datas

Nutritional status was assessed by MIS and GNRI at the beginning of the HD session. The MIS consists of four main parts: a patient's related medical history, physical examination, BMI and laboratory parameters. A patient's medical history includes weight changes, dietary intake, gastrointestinal symptoms, functional capacity, comorbidity, including number of years on dialysis. The physical examination detects any loss of subcutaneous fat and signs of muscle wasting. The sum of all 10 compenents results in an overall score ranging from 0 (normal) to 30 (severely malnourished). We calculated GNRI using serum albumin values, dry weight and ideal body weight. The GNRI was calculated by modifying the Nutritional Risk Index (NRI) for all subjects, as reported by Yamada et al.

GNRI = [1.489 + albumin (g/dL)] + [41.7× (body wt/ideal body wt)]

Body weight or ideal body weight was set to 1 when the patient's body weight exceeded the ideal body weight. The ideal body weight in the present study was defined as the value calculated from the height and a BMI of 22, because of its validity. Clinical characteristics were compared between two groups; low GNRI (<92) with moderate or severe nutritional risk; and high GNRI (≥92) with low or no nutritional risk according to the previous report (Bouillanne et al., 2005).

We evaluated both all cause mortality and hospitalization during 36 months. Hospitalization data during the follow-up period were obtained for all 186 HD patients. It was defined as any hospital admission that included at least one overnight stay in the hospital. The admission day was counted as one full hospitalization day, but the discharge day was not. The hospitalization frequency was the total number of hospital admissions. The access-related hospitalizations were not included in hospitalization data.

Statistical Analysis

Descriptive statistics for all the identified variables (age, sex, and dialytic age) were performed. The results were given as mean ± SD (normally distributed data). The variables associated with MIS at a significance of p≤0.05 were entered in the multivariate models. Multiple logistic regression analysis was performed to determine the associations between MIS as the dependent variable and independent covariates of sex, age, BMI, WHR, duration of HD, GNRI, albumin, CRP. The odds ratio (OR) and 95% confidence interval (CI) were calculated by logistic regression analysis in a stepwise manner. For the comparisons of the groups, Mann–Whitney U-test was used for non-parametric variables and chi-square test for parametric variables. Survival curve during study period was estimated using the Kaplan-Meier method and compared using the logrank test. P-Values less than 0.05 were considered statistically significant. The Statistical package for Social Sciences (version 11.0) (SPSS, Inc., Chicago, IL, USA) was used to perform all

statistical calculations.

RESULTS

Baseline Patient Characteristics According to GNRI

Baseline demographic and clinical data of the study population are summarized in Table 1. The prevalence of diabetes was 28% in all subjects. No significant differences in GNRI were observed between subjects with and without diabetes. The mean value of MIS was 6.3±3.9 (SD). When MIS was considered as the reference standard, 37 patients (11.0%) had moderate to severe malnutrition (MIS≥11), and 61 (33.3%) had mild malnutrition (MIS 6 to 10) at baseline. The GNRI presented a normal distribution, and the mean GNRI (±SD) was 98.8 (±16.9). The mean GNRI value of the subjects with a GNRI<92 was 84.2±5.7 (n=81), and that of the subjects with a GNRI≥92 was 102.1±8.1 (n=105).

Table 1. Baseline Demographic and Clinical Data (number of patients=186).

Parameters	Values (n=186)
Demographic and clinical characteristics	
Age (yr)	63±13
Gender (male/female)	94(51%)/92(49%)
Dialysis duration (years)	8.8±4.1
Kt/V	1.3±0.26
Etiology of ESRD	
Diabetic nephropathy	52(28%)
Hypertension	37(20%)
Chronic glomerulonephritis	31(17%)
Polycystic kidney disease	26(14%)
Unknown etiologies	40(21%)
Dietary intake	
Energy intake (kcal/kg per day)	32.5±4.7
Protein intake (g/kg per day)	0.94±0.46
Blood analysis	
Creatinine (mg/dl)	10.6±2.8
Albumin (g/dl)	4.1±0.3
CRP (mg/l)	6.1±3.9
Cholesterol (mg/dl)	136.9±34.3
Ferritin(ng/ml)	490.1±342.0
Transferrin (mg/dl)	154.4±32.5
Hemoglobin (g/dl)	10.9±1.3
Leukocyte(/µl)	8634.0±3500
Platelet count (per ml)	195.5±61.1
Anthropometric measurements	
BMI (kg/m^2)	23.4±4.1 (19.3-27.5)
Waist-Hip ratio	0.8±0,07
Nutritional scores	
MIS	6.3±3.9 (2.4-10.2)
GNRI	98.8±32.6

Values are presented as mean±SD (median) or %

During the longitudinal part of the study, MIS decreased in 113 patients (61.6%), it remained static in 43 patients (23.3%), and it increased in 30 patients (16.1%). During study period, the overall GNRI score increased 93 (50%), remained static in 63 (34.0%), and decreased in 30 (16%). The change in GNRI had a modest but statistically significant correlation with the change in MIS (r=-0.126, p=0.01), the number of hospitalization (r=-0.24, p=0.02) and hospitalization duration time (r=-0.17, p=0.01).

Baseline GNRI was positively correlated with total protein (r=0.43, p=0.00), albumin (r=0.81, p=0.00), hemoglobin (r=0.25, p=0.03), ferritin (r=0.51, p=0.02) and negatively correlated with MIS (r=-0.35, p=0.02), age (r=-0.41, p=0.02), HD duration (r=-0.53, p=0.01), the number of hospitalization (r=-0.38, p=0.03) and hospitalization duration (r=-0.27, p=0.01).

According to baseline GNRI score, patients were further divided into 2 groups: Group 1 (GNRI<92, n= 81), group 2 (GNRI≥105, n=64). Significant differences in the various nutrition-related indexes, MIS values and laboratory parameters between baseline GNRI groups were given in Table 2.

Table 2. Comparison between groups and study parameters in 186 patients.

Parameter	Group 1 GNRI<92 (n=81)	Group 2 GNRI≥92 (n=105)	P value
MIS	9.0±1.4	7.1±0.9	p<0,05
CRP(mg/l)	6,1±3.0	5,4±2,4	ns
Hemoglobin(g/l)	9,5±1,3	11,5±1,0	p<0,05
Frequency of hospitalization	3.8±2.1	2.9±1.9	p<0,05
Duration of hospitalization	34±19	28±15	p<0,05

Table 3. Nutritional risk factors as predictors for hospitalization (frequency and duration).

Nutritional risk factor	Frequency of hospitalization*	p	Duration of hospitalization**	p
Mean (all patients)	4.1±2.4		53±23	
Clinical Examination score				
BMI <25 kg/m^2				
MIS—index ≥ 11	2.2±0.8	ns	33±12	ns
MIS—index 6 to 10	5.8±0.7	p<0,05	59±15	p<0,05
GNR<92	4.2±0.6	p<0,05	52±17	p<0,05
	4.8±2.1	p<0,05	56±19	p<0,05
Laboratory Parameters				
Cholestrol≤ 3.5 mg/dl	2.6±1.2	p<0,05	54±18	p<0,05
LDL≤2.5 mg/dl	2.6±1	n.s.	42±16	n.s.
CRP≥10 mg/l	3.5±1.2	p<0,05	57±19	n.s
Leucocyte≥(/µl)	4.8±1.4	p<0,05	49±22	p<0,05

*** Admissions per patient year, ** days per patient ye**

Relationship with Hospitalization and Mortality

Hospitalization of patients occurred due to infections (18 admissions, 231 hospitalization days), coronary heart disease (14 admissions, 112 hospitalization days) and peripheral arterial occlusive disease (12 admissions, 150 hospitalization days). The hospital admissions and length of stays stratified by nutritional markers are reported in Table 3. MIS index (≥11; 6 to 10) and GNRI (<92, ≥92) increased significantly frequency and duration of hospitalization. In a multivariable linear regression model, baseline GNRI was independently associated with hemoglobin (r^2=0.118, p=0.00) and the number of hospitalization (r^2=0.864, p=0.04). We found that mean GNRI scores were significantly lower in hospitalized (95.3±6.5) than in hospitalization-free (104.2.2±17.1) patients (p<0.05). A similar GNRI score difference was observed between patients who survived (102.6±9.6) patients who died (89.5±7.114.2) during the study period (p<0.05).

During the 36-month follow-up period 44 patients (24%) died. Of these, 30 patients (68%) had cardiovascular cause death, 14 patients (32%) had non-cardiovascular cause death: infectious disease (n=7), respiratory disease (n=3), gastrointestinal disease (n=1), and others (n=3). Compared with the survivors, patients who died during the observation period had higher MIS (8.5±1.9 vs. 6.2±1.7, p=0.00) than the patients alive. Finally, patients in the low-GNRI group had significantly higher mortality compared to those in the high-GNRI group (hazard ratio [HR], 2.667; 95% confidence interval [CI]: 1.527–4.651, p<0.001). The increased mortality risk was found in both cardiovascular (HR, 2.469; 95% CI: 248–4.902, p<0.001) and non-cardiovascular disease (HR, 3.086; 95% CI: 1.172–8.130, P=0.023).

DISCUSSION

Although the numbers of dialysis patients worldwide have been increasing annually, there is not enough emphasis on nutrition. Malnutrition and nutritional management is important for patients in HD and regular nutritional assessment is recommended for all dialysis patients (Fouque et al., 2008 and K/DOQI, 2000). The nutritional status of patients on dialysis is difficult to assess, due to the lack of a single criterion, sometimes delaying the diagnosis. This complexity is associated with an increased risk of, morbidity, hospitalization and mortality (Fouque, et al., 2008 and Ikizler et al., 1999). Anthropometry is a common method of nutritional assessment, but assessment errors in HD population may occur, due to the alteration in the hydration status of tissues. The GNRI was developed by Bouillanne et al, to identify elderly hospitalized patients at nutritional risk as a simple method to assess nutritional condition (Bouillanne et al., 2005). The GNRI formula consists of serum albumin and weight, both of which are strong independent risk factors for mortality in maintenance HD patients. Recently, Yamada et al. compared the validity of several nutritional tools and reported that GNRI was a useful tool for the assessment of nutritional status, not only for elderly patients but also for all chronic HD patients (Yamada et al., 2008). This prospective study was performed to evaluate the clinical importance of different nutritional markers with regard to the prediction of mortality and hospitalization.

The prevalence of malnutrition is about 44.3% in this study which was mild to moderate in the HD patients. This proportion is the same that found by other studies (23% to76%) performed in patients with ESRD (Kalantar-Zadeh et al., 2001). A possible explanation for

differences between literature results may relate to differences in the baseline demographic and some clinical characteristics of HD patients. It is well known that older age, long dialysis duration and comorbit status may influence the nutritional prevalence of HD patients either by causing a reduced nutritional intake or by promoting catabolism (Pupim et al., 2005).

Because of MISs' detailed scoring system, it is compared with other nutritional status measurements. GNRI is a score which uses only objective information and the equation can be handled by a computer so the patients at high risk of malnutrition can be referred to by numbers. In the present study we found that, the GNRI was considered to be the most accurate screening tool for predicting malnutrition when the MIS was used as the reference standard.

The results of our study suggested that high HD duration, older age, low albumin levels and low hemoglobin levels were significantly correlated with GNRI scores while undergoing dialysis. The presence of low albumin and low hemoglobin appeared to be a significant risk marker for malnutrition while having a chronic condition(s). In case-control studies, serum albumin has been reported to be decreased in patients with chronic diseases compared to controls, but it is possible that it might be lowered because of poor feeding associated with the underlying cognitive impairment which was associated with advanced age (Mutsert**,** et al., 2009 and Rubenstein et al., 2001). Chronic systemic low-grade inflammation may be the common factor mediating the relationships observed in our study. In HD patients, inflammatory activity is increased by cardiovascular risks, infections, declining sex hormone activities and exacerbated by the underlying disease. Although low serum albumin and hemoglobin are conventionally regarded as biochemical and hematological markers of protein-calorie malnutrition, they are also involved in chronic inflammation; on the other hand, albumin is a negative acute-phase protein whose plasma concentration in patients with chronic diseases typically decreases in response to chronic inflammation (Gabay and Kushner, 1999). Anemia is the result of suppressed erythropoiesis by chronic inflammation. In the presence of chronic diseases, low BMI results when there is preferential loss of skeletal muscle mass (sarcopenia), as well as fat tissues and bone mass, and is a manifestation of inflammatory activities that characterize cachexia. The combination of malnutrition and inflammation has been termed 'malnutrition–inflammation complex syndrome' (MICS) and is well described in cachexic patients with renal failure (Kalantar-Zadeh et al., 2003).

As for the cutoff values of GNRI for elderly hospitalized patients, Bouillanne et al. determined four GNRI cutoff values according to weight loss and albumin concentrations, which are components of the GNRI; GNRI <82, major nutrition-related risk; GNRI 82 to <92, moderate nutrition-related risk; GNRI 92 to ≤98, low nutrition related risk; GNRI >98, no risk (Bouillanne et al., 2005). In the study by Yamada et al. on chronic haemodialysis patients, the most accurate GNRI cutoff value to identify malnourished patients was determined to be <91.2, based on the malnutrition–inflammation score (Yamada et al., 2008). In the present study, the cutoff value of GNRI for mortality was set at 92, according to the highest positive likelihood and risk ratios.

The GNRI is calculated by a very simple equation in which only 3 nutritional variables-serum albumin, height and body weight-are involved and the patients at

high risk of malnutrition can be referred by numbers. GNRI is a significant predictor for morbidity in hemodialysis patients.

Our results show that, for the hospitalization outcomes considered, nutritional condition is a predictive factor in HD patients. Comorbid medical conditions, functional status should therefore be considered together with nutritional assessment when trying to predict hospitalization outcome in HD patients. We found that mean GNRI scores were significantly lower in hospitalized than in hospitalization-free patients ($p<0.05$). A similar GNRI score difference was observed between patients who survived patients who died during the study period ($p<0.05$). Kobayashi et, al. demonstrated that malnutrition has been shown to be a significant predictor of morbidity and mortality in HD patients (Yamada et al., 2008). The results of these statistical analyses suggested that the reliability of the GNRI would be high enough for screening HD patients at nutritional risk.

Some limitations of this study should be considered. First, this study is based on a relatively small sample size of prevalent hemodialysis patients from a single center. Second, this study used only an observational approach, without manipulation of exposure factors

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