

## Malnutrition in chronic kidney failure: what is the best diagnostic method to assess?

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### ABSTRACT

**Introduction:** Protein-energy malnutrition, systemic inflammation, and metabolic disorders are frequent among patients with chronic kidney failure undergoing dialysis, contributing to their morbidity and mortality. **Material and Methods:** In the present study, the prevalence of malnutrition in chronic renal patients undergoing hemodialysis in one single center in the Northeastern region of Brazil was assessed according to the following: three different methods of subjective global assessment (SGA); body mass index (BMI); percent of standard body weight; adequacy to the 50th percentile of triceps skinfold (TSF) and arm muscle circumference (AMC) thicknesses; pre-dialysis albumin; phase angle; and percentage of body cell mass (%BCM). Agreement of the nutritional status diagnosis performed through SGA with anthropometric, biochemical, and bioelectrical impedance measures was assessed. **Results:** The study assessed 58 patients [females, 30 (51.7%); mean age = 49 years]. The prevalence of malnutrition according to the different methods ranged from 12.1% to 94.8%. Conventional SGA showed a moderate agreement with patient-generated SGA (PG-SGA), BMI (cutoff point, 22.0 kg/m<sup>2</sup>), and AMC; a fair agreement with BMI (cutoff point, 18.5 kg/m<sup>2</sup>), percent of standard body weight, AC, and phase angle; and a poor agreement with SGA adapted to the renal patient, TSF, and %BCM. **Conclusions:** The nutritional assessment methods commonly used in clinical practice are subject to restrictions when applied to the dialysis population, considering the different percentages obtained with the different methods. Longitudinal, prospective studies on the association of nutritional markers with adverse events, such as hospitalization and mortality, should be carried out to clarify remaining issues.

**Keywords:** malnutrition, chronic kidney disease, renal dialysis.

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### INTRODUCTION

Protein-energy malnutrition is one of the major factors adversely affecting the prognosis of patients with chronic kidney disease, being associated with an increase in morbidity and mortality in those patients.<sup>1,2</sup> Several studies have evidenced malnutrition in 23%-76% of patients on hemodialysis (HD) and in 18%-50% of patients on peritoneal dialysis.<sup>3,4,5</sup> The wide variation in malnutrition prevalence in patients on HD may be attributed to the different assessment methods, and to the multiple factors contributing to its development.

The physiopathology of protein-energy malnutrition in patients with renal disease is complex and involves a great number of factors that contribute to anorexia and catabolism. It may be secondary to deficient nutritional ingestion, severe dietary restrictions, hormonal and gastrointestinal disorders, metabolic acidosis, interference of medications with food absorption, intercurrent diseases, nutrient losses during dialysis, and inadequate dialysis.<sup>6,7</sup>

The National Kidney Foundation - *Kidney/Dialysis Outcome Quality Initiative* guidelines 2000 (NKF K/DOQI, 2000)<sup>8</sup> have recommended for HD patients a dietary protein intake of 1.2 g/kg of body weight/day, of which at least 50% should be of high biologic value, and a dietary energy intake of 35 kcal/kg/day. In the HEMO study<sup>9</sup>, the mean dietary protein intake was 0.93 ± 0.36 g/kg/day and the mean dietary energy intake was 22.9 ± 8.4 kcal/kg/day, and 81%

and 92% of the patients, respectively, had protein and energy intakes below the K/DOQI (2000) recommended values.

Nutrient loss during the HD procedure may be an important factor for malnutrition in those patients. Amino acids, peptides, and water soluble vitamins are primarily lost. The mean amino acid loss for the dialysate is 4-8 g/day.<sup>10</sup>

A low chronic inflammatory state (the micro-inflammatory state of uremia) with elevated circulating levels of protein C reactive (PCR) and proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-alpha) and interleukin 6 (IL-6), has been increasingly recognized as one of the more important factors for protein-energy malnutrition in patients with chronic kidney failure (CRF).<sup>11</sup> The proinflammatory cytokines can increase protein catabolism and baseline energy expenditure, in addition to interfering with appetite. Assessment of inflammatory markers is useful for distinguishing between both types of malnutrition in CRF: type 1 or pure malnutrition and type 2 or inflammatory malnutrition.<sup>12</sup> The prognosis of patients with type 1 malnutrition and no inflammation is usually more favorable.

Periodical monitoring of the nutritional status should be part of the follow-up of dialysis patients, and is fundamental for preventing, diagnosing, and treating protein-energy malnutrition. Early identification and treatment of nutritional deficit can reduce the risk of infections, other complications, and mortality for those patients. An ideal nutritional marker should be associated with morbidity and mortality, such as hospitalization and death, and identify patients who should undergo nutritional intervention.<sup>1</sup>

The methods for nutritional status assessment can be subjective (clinical history and nutritional physical examination) or objective (anthropometry, biochemical exams, and bioelectrical impedance).

Subjective global assessment (SGA) is a useful and reproducible instrument for assessing the nutritional status of dialysis patients. The NKF K/DOQI guidelines 2008 have recommended that SGA be performed every six months in the dialysis population with that purpose. According to the National Kidney Foundation, the SGA technique needs greater validation regarding sensitivity, specificity, accuracy, intra- and interobserver variability, and correlation with other nutritional measures. In the Canada-USA Peritoneal Dialysis Study

Group 13, both albumin and SGA were predictors of death or treatment failure.

There are several modified SGA versions for using in HD patients.<sup>14,15,16</sup> The components of conventional SGA were adapted for use in patients with CRF 14 and a malnutrition-inflammation scoring system was created.<sup>15</sup> Those scoring systems have been directly associated with morbidity and mortality.

Subjective global assessment adapted to the patient with chronic kidney disease is based on subjective and objective aspects of clinical history and physical examination. Clinical history comprises five criteria, including weight loss in the last six months, gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea), dietary intake, functional capacity, and comorbidities. The physical examination comprises three items, with emphasis on subcutaneous fat and muscle mass losses. Each component was assigned a score from 0 (normal) to 5 (very severe), and this malnutrition score lies between 7 and 35.

The patient-generated subjective global assessment (PG-SGA) classifies patients as follows: well nourished (SGA-A); moderately or suspected of being malnourished (SGA-B); and severely malnourished (SGA-C). In addition, that evaluation results in a numerical score (ranging from 0 to 35), which depends on the impact of each component of the nutritional status, and adds to the conventional SGA data referring to clinical history, such as recent weight loss, and a component of metabolic stress. The PG-SGA has high sensitivity and specificity as compared to the conventional SGA classification in patients with cancer.<sup>17</sup> The PG-SGA score relates to quality of life and has been used as a prognostic measure in clinical studies in oncology.

The PG-SGA has the advantage of being more sensitive to small alterations in the nutritional status, as compared to the conventional SGA. That assessment was initially developed for patients with cancer; however, it is not specific for oncology. Its use for patients on HD was first reported in April 2005, and allowed fast identification of malnutrition in HD patients.<sup>18</sup>

Anthropometry is used in HD centers because it is a simple, safe, practical, and cost-effective method, in addition to being a valid and clinically useful way of assessing the protein-energy nutritional status of patients with chronic kidney disease.<sup>19</sup> Anthropometry is useful for assessing the

disease.<sup>19</sup> Anthropometry is useful for assessing the patient's amount of adiposity and lean mass, and comprises height, body weight, percent of standard body weight (the patient's current weight expressed as a percentage of ideal weight), body mass index (BMI), skinfold thickness, arm circumference (AC), and arm muscle area (AMA).

The lack of reference patterns considering sex, age and ethnicity jeopardizes the accuracy of the anthropometric data of dialysis patients. In addition, the interpretation of anthropometric data may be impaired by the intra-observer variability, which was 4.7% for arm muscle circumference and 22.6% for triceps skinfold thickness when comparing measurements taken by three observers.<sup>20</sup>

Anthropometry identifies neither nutritional alterations in short time periods, nor the specific deficiency of a nutrient. In addition, the hydration status may significantly influence anthropometric assessment.<sup>21</sup>

Of the biochemical indices available, serum albumin has been the most used for assessing the nutritional status of HD patients.<sup>22</sup> Biochemical indices may be difficult to interpret in the presence of concomitant liver disease, iron-deficiency anemia, and chronic inflammation.

Albumin has high specificity but low sensitivity for diagnosing malnutrition, because, in addition to nutritional deficit, other causes, such as reduced synthesis due to liver disease and increased losses through gastrointestinal tract, kidneys, burns, and peritonitis, alter its levels. Serum albumin concentration results from albumin synthesis, degradation, volume of distribution, exchanges between intra- and extravascular spaces, and losses.<sup>23</sup> In addition, albumin is a late marker of malnutrition, due to its long half life (approximately 14-20 days) and large distribution in the body.<sup>23</sup>

Serum albumin levels decrease in situations of hypervolemia, which is very frequent among patients on dialysis.<sup>24</sup> Serum albumin levels significantly increase after dialysis and inversely correlate with fluid withdrawal; thus, predialysis albumin levels may not be a valid indicator of the nutritional status due to the effects of interdialytic weight gain.<sup>25</sup>

The chronic inflammatory state may cause a reduction in the albumin synthesis and an increase in its catabolism, with consequent hypoalbuminemia. Caution should be taken when serum albumin is used for diagnosing malnutrition in the presence of inflammation and hypervolemia.

Some authors have identified albumin as a marker of the nutritional status associated with mortality, regardless of the presence of inflammation.<sup>16</sup> Jones, Wolfenden and Wells<sup>26</sup> have found no correlation of albumin with other nutritional parameters assessed [percentage of standard body weight, BMI, triceps skinfold (TSF), arm muscle circumference (AMC), SGA]; according to those authors, albumin related to inflammation, but not to the nutritional status per se.

Despite the limitations of the method, mainly the influence of the presence of inflammation and other comorbidities, albumin level is a strong indicator of nutritional status and mortality risk.<sup>27</sup>

Bioelectrical impedance (BEI) is a fast, noninvasive, painless, relatively inexpensive, and reproducible method for assessing body compartments. In addition, it requires minimum training of the examiner. Bioelectrical impedance is based on the principle that body components offer a differentiated resistance to the flow of electric current. Lean tissues are good electric current conductors, because of the great amount of water and electrolytes. Fat, bone, and skin have low conductivity and high resistance.

During bioimpedance, an electric current of 500-800  $\mu$ A and 50 kHz is introduced through distal electrodes (hand and foot) and captured by proximal electrodes (ankle and fist), generating vectors of resistance and reactance. Resistance is the measure of opposition to the flow of electric current through the body and reactance is opposition to the flow of electric current caused by the capacitance produced by cell membranes. From the identification of resistance and reactance levels of the organism, total body water, lean mass, fat mass, and extracellular water are obtained.<sup>28</sup> Phase angle and body cell mass (BCM), which have been used as nutritional markers, can also be calculated.

The phase angle is derived from the tangent arch between reactance and resistance, indicating alterations in the integrity of cell membranes and intercellular space. The phase angle for a healthy individual may range from 3 to 10 degrees, depending on gender. Lower phase angles seem to be consistent with low reactance, cell death, or loss of the selective permeability of cell membrane.<sup>29</sup>

Body cell mass is a marker of combined visceral and somatic protein deposits. Body mass can be divided into two compartments: fat mass and lean mass. Lean body mass can be divided into

a multicompartamental model as follows: skeleton, tegument, skeletal muscle, visceral organs, and total body water, which can be divided into intra- and extracellular water.

Body cell mass is defined as lean body mass without bone mineral mass or extracellular water, and is the most metabolically active body compartment.

By using bioimpedance measures, Guida *et al.*<sup>30</sup> have detected a reduction in BCM and phase angle in overweight and obese HD patients, suggesting that even patients with BMI values above normal may be at risk for malnutrition.

Chertow *et al.*<sup>31</sup> have validated BEI measures for assessing body composition of HD patients, comparing total body water and BCM obtained by use of BEI with the methods of deuterium oxide and sodium bromide dilution and dual-energy X-ray absorptiometry (DEXA). Later, Chertow *et al.*<sup>32</sup> standardized the BEI parameters (resistance, reactance, phase angle) for HD. In another assessment, Chertow *et al.*<sup>33</sup> have reported an increase in the relative risk of death for patients with a phase angle lower than 4 degrees. However, it is still not clear if the relation between phase angle and survival relates to the nutritional status.

An alteration in the hydration status is the main limitation of the method, because if the patient is hyper-hydrated, lean mass will be overestimated.<sup>34</sup> Other BEI-derived measures, such as reactance and phase angle, can be less affected by alterations in blood volume.<sup>35</sup>

The assessment of 913 dialysis patients undergoing BEI compared with 10,263 individuals assessed on NHANES III (Third National Health and Nutrition Examination Survey)<sup>36</sup> revealed that the former had lower resistance (3%), reactance (6%), phase angle (28%), intracellular water (9%), BCM (9%), lean mass (3%), and fat mass (12%).<sup>37</sup> On the other hand, extracellular water was 17% higher in individuals on dialysis.<sup>38</sup> Currently, BEI is not recommended by the K/DOQI guidelines (2000) for routine assessment of the nutritional status of HD patients.

The nutritional status of every HD patient should be assessed at the beginning of treatment and periodically. Knowing the nutritional status of a HD population is fundamental for both preventing malnutrition and properly approaching already malnourished patients, thus contributing to enhance the quality of the care provided. Further

studies in this research line are required to identify the most reliable methods for the early identification of HD patients at nutritional risk. This stresses the importance of the present study, which emphasizes the nutritional status of HD patients with chronic kidney failure at a dialysis center in the city of Fortaleza. This study assessed the prevalence of malnutrition in that population and correlated the nutritional status diagnosed through different techniques of nutritional assessment.

## MATERIAL AND METHODS

The study assessed 58 HD patients with CRF from a single dialysis center in the Northeastern region of Brazil. The study protocol was approved by the Committee on Ethics and Research of the institution. The study comprised patients over the age of 18 years, on dialysis for more than 3 months, who could complete the SGA questionnaire and undergo the following measurements: body weight, height, skinfold thickness, and arm circumference. All patients provided written informed consent. The following were excluded from the study: pregnant women, patients with lower limb amputation or paraplegia.

The population studied underwent nutritional assessment, by use of clinical, anthropometric, and biochemical indicators, and bioelectrical impedance.

The clinical indicator of nutritional status used was Subjective Global Assessment (SGA), performed according to three techniques: conventional SGA, SGA adapted to the patient with chronic kidney disease<sup>14</sup>, and SGA generated by the patient him/herself.<sup>17</sup>

The anthropometric indices assessed were as follows: postdialysis weight, considered the patient's dry weight (kg); height (cm); the patient's current weight expressed as a percentage of ideal weight (%); BMI calculated from postdialysis weight and height; measurement of the triceps (TSF), biceps (BSF), subscapular (SSSF), and supra-iliac (SISF) skinfold thicknesses, based on which, fat and lean masses were calculated; arm circumference (AC); and arm muscle circumference (AMC). Skinfold thicknesses and circumferences were measured after HD, and the mean of three measurements taken on the limb without the vascular access to dialysis was considered for study.

The results of the adequacy of TSF, AC, or AMC to the 50th percentile were used to classify



the nutritional status<sup>39</sup>, and patients with an adequacy percentage lower than 90% were considered malnourished.

The anthropometric measures were entered into the Nutwin software<sup>40</sup> (a nutrition support program), version 1.5, which calculated the adequacy percentage to the 50th percentile of TSF, AC, and AMC, and also fat and lean masses.

The biochemical index assessed was predialysis serum albumin measured by use of the bromocresol purple method. The interpretation of the reference values of albumin was in accordance with the protocol of Blackburn *et al.*<sup>41</sup>, and patients with albumin lower than 3.5 g/dL were considered malnourished.

Bioelectrical impedance was performed 30 minutes after the end of dialysis. Resistance and reactance were measured directly and the results were entered into the Fluids and Nutrition software (Comp Corp for Windows 95/98) for body assessment by use of BEI. The other parameters of BEI (phase angle, lean mass, fat mass, BCM) were indirectly obtained.

The patients with a phase angle lower than 5 degrees were considered malnourished in accordance with Barbosa-Silva *et al.*<sup>42</sup>

Body cell mass in kilograms was then converted into a percentage of BCM according to the following formula: BCM percentage =  $100 \times \text{BCM} / \text{current weight}$ . Male patients with BCM percentage lower than 35% and female patients with BCM percentage lower than 30% were considered malnourished.<sup>42</sup>

The results were expressed as mean  $\pm$  standard deviation. The variables with normal distribution were compared by use of the Student *t* test; for those of non normal distribution, Mann-Whitney test was used. The association between categorical variables was assessed by using the *Chi*-square test or Fisher exact test. Pearson's test was used to assess the linear correlation between the variables studied. The concordance between methods was evaluated based on the *kappa* coefficient, using the interpretation suggested by Altman (1991) 43 as follows: *kappa* < 0.20, poor concordance;  $0.21 \leq \text{kappa} \leq 0.40$ , regular concordance;  $0.4 \leq \text{kappa} \leq 0.60$ , moderate concordance;  $0.61 \leq \text{kappa} \leq 0.80$ , good concordance; *kappa* > 0.80, very good concordance. Statistical analysis was performed with the SPSS software, version 10.0, and a *p* value lower than 5% was considered statistically significant.

## RESULTS

The population studied comprised 58 patients [female sex, 30 (51.7%); mean age,  $49.22 \pm 14.85$  years (18 to 77 years)].

The etiology of renal failure was as follows: undetermined, 48.3% of the patients; hypertension, 22.4%; diabetes, 8.6%; polycystic kidney disease, 5.2%; familial nephritis, 5.2%; other causes, 10.3%. The mean dialysis time was  $4.27 \pm 2.50$  years (0.42 to 9.5 years).

The demographic/anthropometric/laboratory characteristics of the population studied are shown in Table 1. Figure 1 shows the variation of the prevalence of malnutrition in the population studied according to the nutritional marker used.

According to conventional SGA, 39.7% of the patients were mildly/moderately malnourished, and 60.3% were well nourished. According to the SGA adapted to the patient with chronic kidney disease, 94.8% of the patients were at nutritional risk or mildly malnourished. The mean nutritional score obtained with SGA was  $11.66 \pm 2.76$ , being 8.0 for eutrophic patients and  $11.85 \pm 2.69$  for those at nutritional risk or mildly malnourished.

When PG-SGA was used, 79.3% of the patients were classified as well nourished, 19.0% as moderately malnourished or suspected of being malnourished, and one patient (1.7%) was not assessed with that method. The mean nutritional score obtained with PG-SGA was  $2.54 \pm 3.62$ , being 1.65  $\pm$  2.19 for well nourished patients and  $6.27 \pm 5.73$  for those moderately malnourished.

The linear correlation between the scores of the SGA adapted to the patient with chronic kidney disease and PG-SGA and the variables studied was investigated. The score of the SGA adapted to the renal patient had a significantly negative linear correlation with BMI, percentage of ideal weight, AC, AMC, lean mass (4 skinfolds), fat mass (BEI), reactance and phase angle. On the other hand, the PG-SGA score was negatively correlated with BMI, percentage of ideal weight, AC, AMC, lean mass (4 skinfolds and BEI), fat mass (BEI), and phase angle, and positively correlated with resistance (Table 2).

A significant linear correlation between the scores of the two SGA methods was also observed (Pearson correlation coefficient = 0.851; *p* < 0.001) (Figure 2).

The estimate of *kappa* is an index that measures concordance between both methods. Concordance

means that a patient diagnosed as malnourished (or well nourished) by use of a method was also diagnosed as malnourished (or well nourished) by use of another method. Concordance in the nutritional diagnosis of conventional SGA was as follows: moderate with PG-SGA ( $kappa = 0.551$ ), BMI (cutoff point of  $22.0 \text{ kg/m}^2$ ) ( $kappa = 0.503$ ), and AMC ( $kappa = 0.432$ ); regular with BMI (cutoff point of  $18.5 \text{ kg/m}^2$ ) ( $kappa = 0.264$ ), the patient's current weight expressed as a percentage of ideal weight ( $kappa = 0.306$ ), AC ( $kappa = 0.376$ ), and phase angle ( $kappa = 0.316$ ); and poor with the SGA adapted to the renal patient ( $kappa = 0.149$ ), TSF ( $kappa = 0.095$ ), and percentage of BCM ( $kappa = 0.066$ ).

## DISCUSSION

The nutritional status of patients on dialysis is difficult to assess, due to the lack of a single criterion that can be used for its identification, sometimes delaying the diagnosis. Assessment of malnutrition of dialysis patients has been suggested to be based on multiple indicators of the nutritional status, comprising the assessment of visceral protein deposits (by use of biochemical parameters) and somatic deposits by use of the analysis of body composition (weight, anthropometry, BEI, total body nitrogen, and DEXA).<sup>4</sup>

The present study assesses the problem of diagnosing malnutrition in HD patients. Of the methods commonly used in clinical practice, which should be preferred for monitoring nutritional status? This

**Table 1**

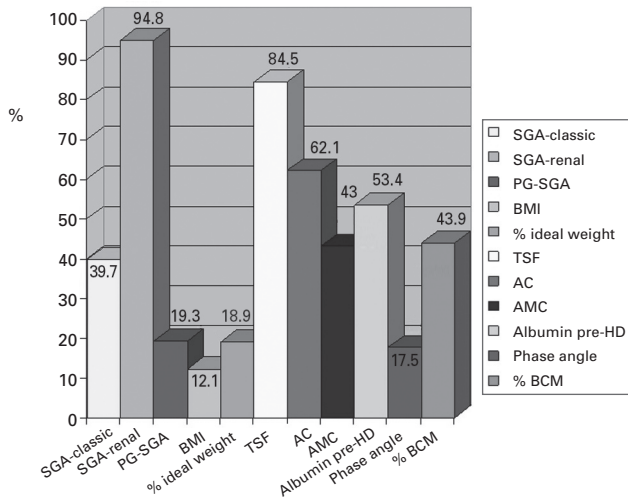
DEMOGRAPHIC, ANTHROPOMETRIC, AND LABORATORY CHARACTERISTICS OF THE POPULATION STUDIED, ACCORDING TO THE PATIENT'S SEX.

Characteristic	Mean $\pm$ SD	Female	Male	p
Mean age (years)	49.22 $\pm$ 14.85	49.33 $\pm$ 14.32	49.11 $\pm$ 15.65	0.954
Weight (kg)	56.51 $\pm$ 12.35	49.28 $\pm$ 8.45	64.27 $\pm$ 11.16	0.000
Height (cm)	156 $\pm$ 10	149 $\pm$ 7	164 $\pm$ 6	0.000
Dialysis time (years)	4.27 $\pm$ 2.50	4.33 $\pm$ 2.66	4.20 $\pm$ 2.35	0.847
% of diabetes	8.6	6.7	10.7	0.665
Interdialytic weight gain (kg)	1.93 $\pm$ 1.04	1.66 $\pm$ 1.01	2.23 $\pm$ 1.02	0.039
BMI (kg/m <sup>2</sup> )	22.89 $\pm$ 3.61	21.94 $\pm$ 3.30	23.90 $\pm$ 3.71	0.038
Mean TSF (mm)	10.89 $\pm$ 4.92	12.7 $\pm$ 4.91	8.95 $\pm$ 4.19	0.003
Adequacy to P50 of TSF	66.69 $\pm$ 32.20	55.57 $\pm$ 21.01	78.60 $\pm$ 37.81	0.005
Mean AC (cm)	26.28 $\pm$ 3.78	25.09 $\pm$ 3.66	27.54 $\pm$ 3.52	0.012
Mean AMC (cm)	22.86 $\pm$ 3.52	21.12 $\pm$ 2.81	24.73 $\pm$ 3.28	0.000
Adequacy to P50 of AMC	92.62 $\pm$ 12.32	95.23 $\pm$ 12.63	89.83 $\pm$ 11.57	0.096
Lean mass (sum of 4 skinfolds - kg)	43.61 $\pm$ 10.33	35.39 $\pm$ 4.68	52.13 $\pm$ 7.12	0.000
Fat mass (sum of 4 skinfolds - kg)	13.26 $\pm$ 5.74	14.49 $\pm$ 4.93	11.98 $\pm$ 6.31	0.099
Lean mass - BEI (kg)	40.97 $\pm$ 8.80	34.73 $\pm$ 4.61	47.91 $\pm$ 6.94	0.000
Fat mass - BEI (kg)	15.05 $\pm$ 6.16	14.31 $\pm$ 5.96	15.86 $\pm$ 6.38	0.349
Pre-dialysis albumin (g/dL)	3.45 $\pm$ 0.55	3.25 $\pm$ 0.59	3.65 $\pm$ 0.41	0.004
Reactance (ohms)	643.28 $\pm$ 110.81	70.70 $\pm$ 16.82	66.93 $\pm$ 12.97	0.351
Resistance (ohms)	68.91 $\pm$ 15.11	706.8 $\pm$ 102.34	572.70 $\pm$ 70.27	0.000
Phase angle (degrees)	6.19 $\pm$ 1.33	5.73 $\pm$ 1.27	6.70 $\pm$ 1.23	0.005
BCM percentage	33.75 $\pm$ 5.91 %	30.27 $\pm$ 4.79	37.61 $\pm$ 5.91	0.000

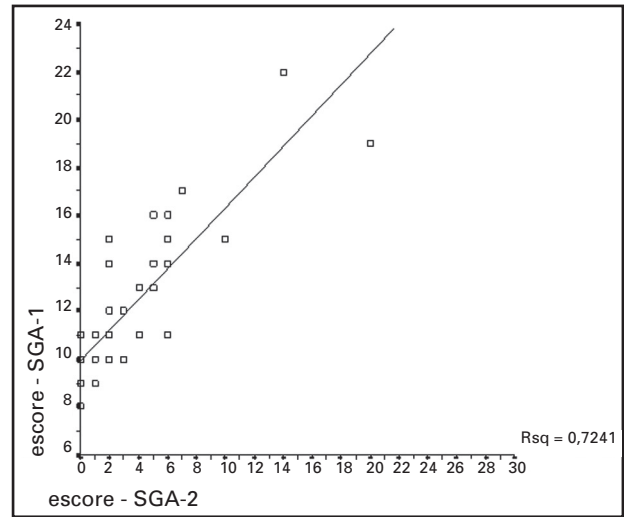
BMI = body mass index; TSF = triceps skinfold; AC = arm circumference;

AMC = arm muscle circumference; BEI = bioelectrical impedance; BCM = body cell mass

**Figure 1.** Prevalence of malnourished patients, according to the nutritional marker, in the population studied. – PG-SGA: patient-generated subjective global assessment; BMI: body mass index; TSF: triceps skinfold; AC: arm circumference; AMC: arm muscle circumference; BCM: body cell mass



**Figure 2.** Positive linear correlation between the SGA adapted to the renal patient score (SGA-1) and the PG-SGA score (SGA-2) in the population studied.



**Table 2**

LINEAR CORRELATION BETWEEN THE SGA ADAPTED TO THE PATIENT WITH CHRONIC KIDNEY DISEASE AND PG-SGA SCORES AND THE VARIABLES OF NUTRITIONAL STATUS.

	SGA adapted to the renal patient score			PG-SGA score		
	n	Pearson correlation	p	n	Pearson correlation	p
BMI	58	-0.360	0.006	57	-0.326	0.013
% of standard body weight	57	-0.341	0.010	57	-0.340	0.010
TSF	58	-0.171	0.200	57	-0.075	0.577
Adequacy of TSF	58	-0.250	0.058	57	-0.150	0.266
AC	58	-0.488	<0.001	57	-0.460	<0.001
Adequacy of AC	58	-0.522	<0.001	57	-0.460	<0.001
AMC	58	-0.448	<0.001	57	-0.451	0.000
Adequacy of AMC	58	-0.415	0.001	57	-0.341	0.009
Lean mass 4 SF	57	-0.270	0.042	57	-0.345	0.009
Fat mass 4 SF	57	-0.182	0.175	57	-0.157	0.243
Albumin	58	-0.253	0.056	57	-0.219	0.102
Lean mass BEI	57	-0.236	0.077	56	-0.314	0.018
Fat mass BEI	57	-0.359	0.006	56	-0.280	0.037
Resistance	57	0.168	0.213	56	0.280	0.037
Reactance	57	-0.400	0.002	56	-0.223	0.098
Phase angle	57	-0.533	0.000	56	-0.453	0.000
% of BCM	57	-0.162	0.229	56	-0.204	0.131

PG-SGA = patient-generated subjective global assessment; BMI = body mass index; TSF = triceps skinfold; AC = arm circumference; AMC = arm muscle circumference; 4SF = sum of 4 skinfolds; BEI = bioelectrical impedance; BCM = body cell mass.

question requires a more definitive answer, so that the results of the several studies conducted on that topic can be compared, when using the same criteria of nutritional assessment.

The prevalence of malnutrition in the population studied varied a lot (from 12.1% to 94.8%), depending on the method used for diagnosis. In the literature, the prevalence of malnutrition is 25%-80% in different studies<sup>1,4</sup> and that variability is due to the different criteria used for diagnosing the nutritional status.

The population studied was younger than that of the North-American literature, with a mean age of  $49.22 \pm 14.85$  years as compared with that of several international publications, whose mean age ranged from 55 to 70 years.<sup>1,9</sup> Batista, Vieira and Azevedo<sup>44</sup> assessed the nutritional status of 55 HD patients with a mean age of 48.5 years. In a study of 165 patients on dialysis in the Brazilian State of Amazonas, the mean age was  $44.9 \pm 15$  years.<sup>45</sup> In another Brazilian study about nutritional evaluation of HD patients, the mean age was  $50.4 \pm 16.3$  years.<sup>46</sup>

The K/DOQI guidelines (2000) have recommended that GSA be performed every six months in the dialysis population, as a screening test, for the early detection of patients at nutritional risk. However, it is not clear whether SGA is a nutritional marker. According to Cooper *et al.*<sup>47</sup>, SGA was not good for detecting the degree of malnutrition, when compared to total body nitrogen content. Nevertheless, that same study has shown that the SGA score can effectively differentiate malnourished patients from those with a normal nutritional status. It is worth emphasizing that total body nitrogen is gold standard to assess protein malnutrition, but it does not consider calorie malnutrition, which is an important component of nutritional assessment.

As previously mentioned, an ideal nutritional marker should be associated with morbidity and mortality, and identify patients who should undergo nutritional intervention.

Pifer *et al.*<sup>16</sup> have used modified SGA as an indicator of nutritional status, in addition to BMI, albumin, and others, in a population of 7,719 adults on hemodialysis. The prevalence of moderate/severe malnutrition was 18.6%, and the score of modified SGA associated independently with a greater risk of mortality. In the CANUSA Study<sup>13</sup> and the study by Van Manen *et al.*<sup>48</sup>, SGA was also a predictor of mortality.

Although SGA has several advantages, such as low cost, easy performance, and predictive value

for mortality, it is worth noting that visceral proteins are not assessed by use of that method, and its sensitivity, accuracy, and reproducibility over time has not been studied.

Conventional SGA diagnosed 39.7% of the patients in this study as mildly to moderately malnourished. Qureshi *et al.*<sup>49</sup>, studying 128 HD patients with a mean age of 61 years, have reported a 65% prevalence of malnutrition by use of SGA. The conventional SGA technique seems to have been very efficient in the present study, because the diagnosis of malnutrition by use of that method had a moderate concordance with the classification based on BMI (cutoff point, 22.0) and AMC, and a regular concordance with the classification based on percentage of ideal weight, AC, and phase angle. In addition, conventional SGA identified malnourished patients with significantly lower BMI, TSF, AC, AMC, predialysis albumin, lean mass, fat mass, phase angle, and BCM as compared with the group of eutrophic patients with a significantly greater resistance (data not shown in a table).

Subjective global assessment adapted to the patient with chronic kidney disease revealed 94.8% of malnutrition in the group studied and identified no significant difference in BMI, TSF, AC, AMC, pre-dialysis albumin, lean mass, and fat mass in eutrophic and malnourished patients (data not shown in a table). The present study identified a disadvantage of the technique adapted to the renal patient, because all patients undergoing dialysis for more than 2 years, even in the presence of normal parameters of clinical history and physical examination, obtain score 9, which classifies them as at nutritional risk or mildly malnourished. This explains the high prevalence of malnutrition, assessed by use of that technique, observed in the population studied, since the mean dialysis time was  $4.2 \pm 2.5$  years, and 82.7% of the patients had a dialysis time longer than 2 years.

Nevertheless, the SGA score adapted to the renal patient showed a significant linear correlation with the following parameters: BMI; percentage of ideal weight; AC; AMC; lean mass (sum of the 4 skinfolds); fat mass (BEI); reactance; and phase angle. The SGA score adapted to the renal patient per se may be a better indicator of nutritional risk than the classification into different categories (A, B, or C).

The PG-SGA has only been used in the dialyzed population recently 18, and, thus, the experience



reported in the literature is scarce. In that study, the prevalence of malnutrition was 20%, and the authors have reported that, as the PG-SGA score is a continuous variable, it may be more sensitive to small alterations in the nutritional status, representing, thus, an advantage over conventional SGA, which classifies the nutritional status into categories.

A 19.3% prevalence of malnutrition was observed in the present study by use of the PG-SGA. A significant correlation of PG-SGA nutritional score was observed with other nutritional parameters, such as BMI, percentage of ideal weight, AC, AMC, lean mass (sum of 4 skinfolds and BEI), fat mass (BEI), resistance, and phase angle. Those findings suggest that such modality of SGA may be well used in the dialysis population. The use of a nutritional score may allow the earlier identification of patients at nutritional risk.

Anthropometry is a common method of nutritional assessment, but assessment errors in the population with chronic kidney disease may occur, due to the alteration in the hydration status of tissues. In addition, anthropometry is relatively inefficient for identifying malnutrition in HD, especially in an early phase, due to lack of reliable patterns for comparison.<sup>50</sup> Another disadvantage is that the method depends on the examiner. Some authors have suggested that anthropometry markedly underestimates the degree of protein loss in chronic kidney failure.<sup>51</sup> However, Nelson *et al.*<sup>50</sup> have shown that anthropometry may be reproducible and its sensitivity is 90%.

There are few and non definitive studies showing the association of malnutrition assessed by use of anthropometry with greater mortality.<sup>52,53</sup> Marcén *et al.*<sup>54</sup> have assessed 574 patients of 20 dialysis centers, by using four anthropometric indices (BMI, AC, TSF, AMC), in addition to biochemical and clinical indices. The prevalence of moderate/severe malnutrition was 51.6% among men and 46.3% among women, and the only nutritional markers predictive of morbidity and mortality were serum albumin and total lymphocyte count, respectively. Segall *et al.* (2009)<sup>55</sup> have found no anthropometric marker associated with 12-month survival of HD patients (BMI, AC, AMC, TSF); however, SGA was associated.

Nevertheless, the anthropometric indices, especially BMI, are easily applied in clinical practice at dialysis units. An important question concerning BMI is: which should be the limit to diagnose malnutrition in the dialysis population? According to the World Health Organization<sup>56</sup>, that diagnosis

would apply to patients of the general population with a BMI lower than 18.5 kg/m<sup>2</sup>. Beddhu *et al.*<sup>57</sup>, studying 50,732 dialysis patients, have reported that 7.98% of them had a BMI < 18.5 kg/m<sup>2</sup>, and, in 46% of them, BMI was equal to or higher than 25 kg/m<sup>2</sup>. Mancini *et al.*<sup>58</sup> and Valenzuela *et al.*<sup>45</sup> have also considered as malnourished patients with BMI lower than 18.5 kg/m<sup>2</sup>, and, according to that criterion, they have reported incidences of malnutrition of 12.8% and 4.0%, respectively. Stenvinkel *et al.*<sup>59</sup> and Aparicio *et al.*<sup>60</sup> have considered to be low a BMI under 20 kg/m<sup>2</sup>.

The choice of a BMI cutoff point of 18.5 kg/m<sup>2</sup> for the dialysis population can be questioned, because patients with a BMI lower than 22 kg/m<sup>2</sup> already seem to be at a greater risk of mortality. Some authors have shown that, in dialysis, a high BMI associates with a better prognosis.<sup>61</sup> Leavey *et al.*<sup>62</sup> have reported that a BMI lower than 23.9 kg/m<sup>2</sup> associated with an increase in the mortality rate. Tokunaga *et al.*<sup>63</sup> have reported that the BMI associated with lower morbidity was 22.2 kg/m<sup>2</sup> for men and 21.9 kg/m<sup>2</sup> for women, and have suggested that the ideal body weight would be the one associated with a BMI of 22.0 kg/m<sup>2</sup>.

In the present study, the mean BMI was 22.89 ± 3.61 kg/m<sup>2</sup> and a significant difference was observed between the sexes ( $p = 0.038$ ). When adopting the limit of 22.0 kg/m<sup>2</sup>, the prevalence of malnutrition was 43.1% (vs 12.1% for the limit of 18.5 kg/m<sup>2</sup>). The concordance in the nutritional diagnosis between conventional SGA and BMI (cutoff point of 18.5 kg/m<sup>2</sup>) was only regular ( $kappa = 0.264$ ). On the other hand, when the cutoff point of BMI was 22.0 kg/m<sup>2</sup>, the concordance between the methods was moderate ( $kappa = 0.503$ ), suggesting that such cutoff point may be more adequate for nutritional assessment.

Malnutrition was diagnosed by adequacy of the triceps skinfold (TSF) to the 50th percentile in 84.5% of the patients in this study (75% of men and 93.3% of women;  $p = 0.075$ ), the mean TSF being significantly lower in male patients (8.95 ± 4.19 mm vs 12.7 ± 4.91 mm;  $p = 0.003$ ). In the present study, the percentage of adequacy of the TSF was a bad method for nutritional assessment, evidencing a very high prevalence of malnutrition even in patients assessed as normal by use of all other parameters. Presence of examiner-dependent error is less probable, since the measures were checked three times by the same examiner. That skinfold reflects the deposits of body fat.

Marcén *et al.*<sup>54</sup> have reported a moderate/severe reduction in TSF in 41% of the patients and in AMC in 19.8% of men and 8.1% of women. Fat depletion, estimated from TSF, was the predominant type of malnutrition in both sexes. Billbrey & Cohen<sup>53</sup> have found better preservation of TSF in men, by using the same criterion of malnutrition (adequacy to the 50th percentile lower than 80%-90%). Valenzuela *et al.*<sup>45</sup> have assessed several nutritional markers, but the classification of the nutritional status was based on TSF and AMC measurements, considering malnourished or at risk for malnutrition patients with TSF and/or AMC values equal to or lower than the 5th percentile of the referral pattern. Those authors have diagnosed 44.8% of the patients as malnourished.

Arm circumference (AC) reflects protein deposits. That method is easily applied and not subject to examiner-dependent errors. Adequacy of AC to the 50th percentile has identified 62.1% of malnutrition. Arm circumference correlated negatively with the SGA score adapted to renal patient ( $p < 0.001$ ) and with the PG-SGA score ( $p < 0.001$ ). Concordance between SGA methods and AC was only regular ( $kappa = 0.376$ ).

In a study of 72 patients on dialysis, an abnormal SGA identified a group of patients with AC and AMC significantly reduced; on the other hand, the percentage of ideal weight and BMI were lower than those in the group with normal SGA, but did not reach statistic significance.<sup>26</sup> In the present study, the conventional SGA compatible with malnutrition detected patients with AC and AMC significantly lower (AC:  $25.09 \pm 3.66$  vs  $27.54 \pm 3.52$ ;  $p = 0.012$ ; AMC:  $20.59 \pm 2.60$  vs  $24.35 \pm 32.6$ ;  $p < 0.001$ ).

Arm muscle circumference also reflects protein deposits. It is subject to the same errors of TSF, because it derives from a formula that includes TSF and AC values. Adequacy of AMC to the 50th percentile detected 43.1% of malnutrition. Arm muscle circumference correlated negatively with the SGA score adapted to the renal patient ( $p < 0.001$ ) and with the PG-SGA score ( $p = 0.000$ ). Concordance between the methods was moderate ( $kappa = 0.432$ ;  $p = 0.001$ ).

Schoenfeld *et al.*<sup>64</sup> have reported that the mean AMC in the male sex is frequently reduced as compared with the patterns established by the Third National Health and Nutrition Examination Survey (NHANES III) 36 for the North-American population. In the present study, AMC was significantly

higher in male patients as compared with female patients ( $24.73 \pm 3.28$  cm *versus*  $21.13 \pm 2.81$  cm;  $p = 0.000$ ). Protein depletion estimated based on AMC was present in 50% of men and in 36.7% of women ( $p = 0.427$ ).

In the study by Valenzuela *et al.*<sup>45</sup>, AMC was below the eutrophy range only in male patients, indicating greater muscle mass loss in men, while adequacy of TSF was low in both sexes, with no difference between them. Cuppari & Draibe<sup>65</sup> have reported a greater reduction in muscle mass in the male sex, and a greater reduction in fat in the female sex. In the present study, the mean adequacy of AMC to the 50th percentile was below normality only in male patients, but the difference was not significant as compared with that of the female sex ( $89.83 \pm 11.57\%$  *versus*  $95.23 \pm 12.63\%$ ;  $p = 0.096$ ). On the other hand, mean adequacy of TSF to the 50th percentile was below normality for both sexes, and the reduction was greater in the female sex ( $55.57 \pm 21.01\%$  *versus*  $78.60 \pm 37.81\%$ ;  $p = 0.005$ ).

Therefore, in the population studied, considering that TSF assessed fat storages and AMC assessed protein reserves, fat depletion predominated. Patients on dialysis have the same energy expenditure and the same requirements of healthy individuals. However, their energy intake is usually lower, although their protein intake is close to the levels prescribed<sup>64,66</sup>, which may contribute to fat depletion.

Albumin is a marker of visceral protein storage, but its use as an indicator of the nutritional status is complicated by several factors, as previously described. The dispute regarding the cutoff point of albumin for the diagnosis of malnutrition has not yet been settled. The NHANES III 36 has suggested that the cutoff point of albumin be 3.6 g/dL, which is the 10th percentile of NHANES III, in which albumin was measured by use of bromocresol green (BCG). On the other hand, Jones *et al.*<sup>67</sup> have suggested that the cutoff point be 3.7 g/dL by use of the bromocresol purple (BCP). Blackburn *et al.*<sup>41</sup> have classified as malnourished patients with albumin levels lower than 3.5 g/dL. The ESRD Clinical Performance Measures Project<sup>68</sup> has defined that serum albumin lower than 3.5 g/dL by use of BCG and 3.2 g/dL by use of BCP indicate an inadequate serum albumin level, and values greater than 4.0g/dL by use of BCG and 3.7g/dL by use of BCP characterize an optimal serum albumin level.

Mancini *et al.*<sup>58</sup> have considered malnourished patients with albumin lower than 4.0 g/dL by use of the BCG method, and they reported 79.2% of malnourished patients. Lowrie & Lew 1, assessing 19,746 patients, reported 66% of patients with albumin levels lower than 4 g/dL, with a mortality risk at least twice greater than that of patients with albumin levels greater than 4.0 g/dL. In a national study in France involving 7,123 patients 60, the cutoff point of albumin was 3.5 g/dL, and 20% of the patients had an albumin level below the cutoff point.

Valenzuela *et al.*<sup>45</sup>, studying 165 patients on dialysis, have reported albumin levels lower than 3.5 g/dL (BCG method) in only 8% of the patients, no difference being found in albumin levels between eutrophic and malnourished ones. On the other hand, in another Brazilian study, 54.1% and 94.6% of the patients had albumin lower than 3.5 g/dL and 4.0 g/dL, respectively, by the BCG method.<sup>46</sup>

In the present study, the nutritional assessment through predialysis albumin detected 53.4% of malnourished patients, and the concordance between the methods of conventional GSA and predialysis albumin was poor ( $kappa = 0.184$ ;  $p = 0.145$ ).

In regard to BEI, the values of reactance and phase angle have been recently shown to have a good correlation with nutritional markers, and clinical studies have associated the phase angle with morbidity and mortality of patients on hemodialysis.<sup>69</sup>

The phase angle have been correlated with some nutritional indices, such as SGA, anthropometric measures, nPNA, albumin, prealbumin, and creatinine.<sup>69</sup> Chertow *et al.*<sup>32</sup>, assessing 3,009 HD patients, have reported a modest, but significant, direct correlation ( $r = 0.20-0.45$ ) between phase angle and body cell mass and other nutritional parameters, such as creatinine, albumin, and prealbumin.

The advantage of assessing nutritional status based on BCM and not on lean mass is that lean mass includes extracellular water, which is a typically increased compartment in patients with chronic kidney failure, which can overestimate the nutritional status. A reduction in visceral or somatic protein mass can be concealed by the concomitant increase in extracellular water.

Estimation of BCM can be the most important aspect of BEI. Nephrologists are currently basing

their assessments mainly on physical examination and serum proteins, and malnutrition may be underestimated or detected late.

In the present study, the prevalence of malnutrition was 17.5% for phase angle and 43.9% according to the percentage of BCM. Phase angle and BCM percentage correlated negatively with the SGA adapted to the renal patient and PG-SGA scores. The concordance in the diagnosis of the nutritional status between conventional SGA and phase angle was fair ( $kappa = 0.316$ ), and the concordance between conventional SGA and BCM percentage was poor ( $kappa = 0.066$ ). In a previous study, BCM percentage showed no significant correlation with SGA, albumin, and creatinine.<sup>31</sup>

The K/DOQI (2000) guidelines and the European Consensus on nutritional status of patients on dialysis 70 have considered that body composition estimation based on BEI parameters (reactance and resistance) is not valid or reliable enough to recommend its routine use. Further studies are required to assess the sensitivity to changes and association with survival, hospitalization, and functional status, and for better defining the role played by BEI.

## CONCLUSION

The ideal method for the nutritional assessment of dialysis patients is yet to be defined. With the results obtained in the present study, of the SGA techniques available, conventional SGA seems to be the one that should be used for screening and following up dialysis patients aiming at nutritional diagnosis, followed by PG-SGA. In addition, BMI should be used in that population with a cutoff point different from the one recommended by the World Health Organization for the general population. 55 Assessment by use of skinfold thickness seems to be a method subject to examiner-dependent errors, and should not be adopted in the near future. Bioelectrical impedance will have a more significant role in assessing dialysis patients.

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