

# Subjective global assessment of nutritional status is strongly associated with mortality in chronic dialysis patients<sup>1-4</sup>

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## ABSTRACT

**Background:** The subjective global assessment of nutritional status (SGA) is used to assess the nutritional status of chronic dialysis patients, but longitudinal data in relation to mortality risk are lacking.

**Objective:** Our objective was to study the long-term and time-dependent associations of the SGA with mortality risk in chronic dialysis patients.

**Design:** In a prospective, longitudinal, observational, multicenter study of incident dialysis patients, the 7-point SGA [7 = normal nutritional status; 1 = severe protein-energy wasting (PEW)] was assessed 3 and 6 mo after the start of dialysis and subsequently every 6 mo during 7 y of follow-up. With Cox regression analysis, we calculated hazard ratios (HRs) of the baseline and time-dependent SGA measurements, adjusted for age, sex, treatment modality, primary kidney diseases, and comorbidity.

**Results:** In total, 1601 patients were included [mean ( $\pm$ SD) age: 59  $\pm$  15 y; 61% men; 23% with moderate PEW (SGA<sub>4-5</sub>), and 5% with severe PEW (SGA<sub>1-3</sub>)]. There was a dose-dependent trend of the 7-point SGA with mortality. Compared with a normal nutritional status at baseline, SGA<sub>4-5</sub> (HR: 1.6; 95% CI: 1.3, 1.9) and SGA<sub>1-3</sub> (HR: 2.1; 95% CI: 1.5, 2.8) were associated with an increase in 7-y mortality. Time-dependently, these associations were stronger: SGA<sub>4-5</sub> (HR: 2.1; 95% CI: 1.7, 2.5) and SGA<sub>1-3</sub> (HR: 5.0; 95% CI: 3.8, 6.5).

**Conclusions:** In dialysis patients, PEW at baseline assessed with SGA was associated with a 2-fold increased mortality risk in 7 y of follow-up. Time-dependently, this association was even stronger, which indicated that PEW was associated with a remarkably high risk of short-term mortality. These data imply that the 7-point SGA may validly distinguish different degrees of PEW associated with increasing risks of mortality. *Am J Clin Nutr* 2009;89:787-93.

## INTRODUCTION

Protein-energy wasting (PEW) is highly prevalent in patients with end-stage renal disease maintained on chronic dialysis and is associated with increased mortality (1, 2). The subjective global assessment of nutritional status (SGA) is a relatively inexpensive, easy, and rapidly conducted tool used by nurses, dietitians, or physicians to assess PEW in chronic dialysis patients (3). The SGA is based on the clinical judgment of 4 subscales

representing the patients' recent weight change, dietary intake, and gastrointestinal symptoms, loss of subcutaneous fat, and signs of muscle wasting (4-6). As a result, the SGA may represent the overall concept of nutritional status.

The SGA has been found to be reliable and valid for assessing PEW (6-9). A single SGA assessment has been shown to be associated with morbidity, hospitalization, and mortality in several clinical studies (9-12). Therefore, since 2000 the National Kidney Foundation Kidney Disease/Dialysis Outcomes and Quality Initiative (K/DOQI) has recommended the use of the SGA for assessing the nutritional status of dialysis patients (13).

However, according to the current European Best Practice Guidelines (EBPG) on diagnosis and monitoring of malnutrition, the SGA can only be used to detect severe malnutrition in hemodialysis patients (14). The guidelines refer to a study that showed that the SGA was able to differentiate dialysis patients with severe malnutrition from those with normal nutritional status, but appeared not to be a reliable predictor of the degree of malnutrition (15). Furthermore, longitudinal studies with repeated measurements of the SGA in relation to mortality have not been published.

Therefore, the objective of the present study was to investigate the long-term and time-dependent associations of the 7-point SGA and its subscales with all-cause mortality in a prospective longitudinal observational multicenter study in chronic dialysis patients.

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## SUBJECTS AND METHODS

### Patients

End-stage renal disease patients aged  $\geq 18$  y and starting with their first renal replacement therapy were eligible for inclusion in the Netherlands Cooperative Study on the Adequacy of Dialysis-2 (NECOSAD-II) Study. The Medical Ethical Committees of all participating dialysis centers approved the study, and all participants gave their written informed consent before inclusion. For the present analysis, all patients with an SGA assessment 3 mo after the start of dialysis were included.

### Study design

NECOSAD-II is a prospective, longitudinal, observational, multicenter cohort study that started in 1997 in 38 dialysis centers in the Netherlands. Incident dialysis patients fulfilling inclusion criteria were enrolled in this study. Demographic data and clinical data were collected between 4 wk before and 2 wk after the start of chronic dialysis treatment. Data on dialysis characteristics and measures of health were collected during study visits 3 and 6 mo after the start of dialysis and subsequently at intervals of 6 mo until the end of follow-up. Baseline was defined as 3 mo after the start of dialysis. Dates and causes of mortality were immediately reported during follow-up. Survival time was defined as the number of days between 3 mo after the start of the dialysis treatment (baseline) and the date of death, the date of censoring due to loss to follow-up (kidney transplantation or transfer to a nonparticipating dialysis center), the end of the follow-up on 1 January 2007, or at a set maximum of 7 y after the start of dialysis.

### Data collection

In each dialysis center,  $\geq 2$  research nurses were appointed to collect the data for NECOSAD-II. At 3 common trainings in the Netherlands, all research nurses were trained to collect the data according to standardized procedures. Baseline demographic data and clinical data such as age, sex, body mass index, ethnicity, primary kidney disease, and comorbidity were recorded in the patients' files. Primary kidney diseases and causes of death were classified according to the coding system of the European Renal Association-European Dialysis and Transplantation Association (16). Routine blood laboratory investigations in the dialysis centers included measurements of serum cholesterol and albumin concentrations and plasma urea and creatinine concentrations. In a corresponding 24-h urine sample, urea, creatinine, and protein concentrations were measured. Renal function was calculated from the mean of creatinine and urea clearance, adjusted for body surface area ( $\text{mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ ) and expressed as the residual glomerular filtration rate. The daily protein intake was estimated in the peritoneal dialysis patients from urea excretion in the urine and dialysate according to Bergström et al (17) and expressed as normalized protein equivalent of nitrogen appearance. In the hemodialysis patients, normalized protein nitrogen appearance (nPNA) was calculated from the increase in plasma urea between 2 subsequent dialysis sessions by using a single pool model and was also normalized to standard body weight. Comorbidity conditions were reported by the patients' nephrologists. The comorbidity index of Khan et al

(18) was calculated to classify the patients as having a low, medium, or high mortality risk.

### SGA

The nutritional status of the patients was measured at each study visit with the 7-point SGA. The 7-point SGA is a modification (5) of the 3-point scale SGA originally described by Detsky et al (4) and Baker et al (19). As an additional modification, the question concerning nutritionally related functional impairment was removed, because it is difficult to distinguish nutritionally related functional impairment from other forms of functional impairment in dialysis patients. Furthermore, edema and ascites were no longer included in the physical examination (6). This 7-point SGA has been validated in dialysis patients in NECOSAD-I (6). As part of the training for NECOSAD, the research nurses were trained in a workshop to assess the nutritional status of the patients with the 7-point SGA scoring form according to a standardized protocol. Using a structured evaluation form, the nurses scored the patients' history of weight change in the previous 6 mo (subscale 1), dietary intake, and presence of gastro-intestinal symptoms (loss of appetite, nausea, vomiting, and diarrhea) (subscale 2), and conducted a physical examination of loss of subcutaneous fat mass (subscale 3) and muscle wasting (subscale 4). The criteria for scoring these subscales were similar to those described in detail by Detsky et al (4). To obtain a 7-point classification for each of the 4 subscales, each patient is first classified into 1 of the 3 categories of normal nutritional status, moderate PEW, and severe PEW. Second, the final scoring is fine-tuned on the basis of clinical judgment of the following questions: "Can the status of the patient improve or worsen within the category?," "What has been the development/pattern within the past 2 wk?," and "What has been the change compared with the previous SGA assessment?" For example, when a patient is classified with severe PEW, but his or her nutritional status could get worse or it improved since the previous assessment, a score of 2 is assigned. When a patient is classified with mild-to-moderate PEW, fine-tuning takes place on the basis of the question if the status tends toward severe PEW or to a normal nutritional status or is somewhere in between. When a patient is classified with a normal nutritional status, a score of 6 is assigned when it is possible to improve or when the nutritional status worsened since the previous assessment. In a subjective weighing of the scores of the 4 subscales, assigning slightly more weight to the history part (60%, physical examination 40%), an overall SGA classification of 1–7 is assigned; a score of 7 indicates a normal nutritional status and a score of 1 indicates severe PEW (5, 6).

### Statistical analysis

Mean ( $\pm$ SD) values were calculated for continuous variables at baseline; categorical variables were expressed in proportions. Differences in baseline characteristics between SGA categories were tested with one-factor ANOVA with Bonferroni correction for post hoc comparisons for continuous variables and with chi-square tests for categorical variables. Furthermore, we estimated the relation of the 7-point SGA with the nutritional variables BMI, nPNA, and serum cholesterol and albumin concentrations at baseline with univariate linear regression analysis. Observed



survival per SGA classification was computed with the Kaplan-Meier method. Cox regression analysis was used to calculate hazard ratios (HRs; equivalent to relative risks of mortality) with 95% CIs for 7-y all-cause mortality, by using an SGA classification of 7 at baseline as the reference category. Because only few patients obtained an SGA classification of 1 or 2, we performed all analyses with the patients grouped into 3 SGA categories: a score of 1–3 indicates severe PEW, 4–5 moderate PEW, and 6–7 a normal nutritional status.

Because nutritional status can vary over time on dialysis, we also calculated mortality rates for the 3 SGA categories using the serial SGA measurements of each study visit during follow-up. Per study visit, follow-up time was assigned to 1 of the 3 SGA categories until the next study visit or death or loss to follow-up of the patient. For each SGA category we calculated the sum of person-years and attributed cases to their last SGA assessment. The mortality rates were expressed per 100 person-years. We furthermore performed time-dependent Cox regression analysis to calculate HRs for the association of the serial measurements of SGA with subsequent mortality. These relative risks can be considered as short-term mortality risks. Analyses were adjusted for age, sex, treatment modality, primary kidney disease, and comorbidity and performed separately for the SGA subscales. We used SPSS 14.0 for Windows (SPSS, Chicago, IL) for all analyses.

## RESULTS

### Patient characteristics

Of the 1940 patients with end-stage renal disease who were included in NECOSAD-II, 1819 patients were still receiving dialysis and participating in the study after the first 3 mo of dialysis, which is considered the baseline of the study. Of these, 1601 patients (978 men and 623 women) patients had a fully completed SGA available from 3 mo after the start of dialysis and were included in the present analysis. The mean ( $\pm$ SD) age and BMI of these patients was  $59 \pm 15$  y and  $24.7 \pm 4.1$ , respectively, and 63% started hemodialysis treatment. The main causes of chronic kidney diseases were diabetes mellitus (16%), glomerulonephritis (14%), and renal vascular diseases (18%). At 3 mo after the start of dialysis, 28% of the patients had moderate or severe PEW on the basis of an SGA score of 1–5. With regard to the 4 subscales, 28% of the patients scored 1–5 for weight change, 20% for dietary intake and gastrointestinal symptoms, 31% for loss of subcutaneous fat mass, and 33% for muscle wasting. At baseline, the 7-point SGA classification was positively related to the other nutritional variables: BMI ( $r = 0.298$ ,  $P < 0.001$ ), nPNA ( $r = 0.083$ ,  $P < 0.01$ ), serum cholesterol concentration ( $r = 0.125$ ,  $P < 0.001$ ), and serum albumin concentration ( $r = 0.183$ ,  $P < 0.001$ ). Patient characteristics at baseline per SGA category are shown in **Table 1**. Patients with moderate or severe PEW at baseline were older, had a lower residual renal function, and were at higher risk because of comorbidity compared with patients with a normal nutritional status. Furthermore, BMI, nPNA, and serum cholesterol and albumin concentrations differed between the 3 SGA categories (all  $P < 0.001$ ). The differences in BMI and serum albumin concentrations were statistically significant between all 3 SGA categories (all  $P < 0.001$ ). The difference in nPNA was only statistically significant between patients with a normal nutri-

tional status and those with severe PEW ( $P < 0.01$ ). Serum cholesterol concentrations in patients with a normal nutritional status differed from those with moderate PEW ( $P = 0.012$ ) and those with severe PEW ( $P < 0.01$ ), but not between moderate and severe PEW ( $P = 0.269$ ; **Table 1**).

### Absolute mortality

The median follow-up of the patients from 3 mo until a maximum of 7 y on dialysis was 2.7 y (25th, 75th-percentiles: 1.1, 4.0). During follow-up, 660 patients died, 311 (47%) as a result of cardiovascular disease. Furthermore, 487 patients left the study because of a kidney transplantation. Other reasons for censoring during follow-up included recovery of renal function ( $n = 19$ ), transfer to a nonparticipating dialysis center ( $n = 66$ ), refusal of further participation ( $n = 165$ ), or other ( $n = 19$ ). The cumulative survival during 7 y of follow-up of the dialysis patients in each of the 7 points of the SGA classification at baseline is shown in **Figure 1** and in the 3 SGA categories in **Figure 2**.

On the basis of the serial measurements of SGA, a total of 4202 person-years of follow-up were categorized into the 3 SGA categories, and cases were attributed to the SGA category of their last assessment. Time-dependently, the mortality rate in 7 y of follow-up was 11/100 person-years in those with a normal nutritional status, 30/100 person-years for those with a moderate PEW, and 69/100 person-years for those with severe PEW.

### Relative mortality risks associated with SGA

The long-term and time-dependent associations between the 7 points of the SGA classification and mortality are shown in **Table 2**. Compared with an SGA score of 7, each 1-point lower score was associated with a higher mortality risk. The patients were grouped into the 3 SGA categories for further analyses. Compared with a normal nutritional status at baseline (SGA score: 6–7), the crude HR associated with a moderate PEW (SGA score: 4–5) was 1.9 (95% CI: 1.6, 2.2) and with a severe PEW (SGA score: 1–3) was 2.6 (95% CI: 2.0, 3.5). The mortality risks of the time-dependent measurements of the overall SGA classification and its 4 subscales are shown in **Table 3**, both crude and adjusted for age, sex, treatment modality, primary kidney disease, and comorbidity. Time-dependently, severe PEW was associated with a 5-fold increased mortality risk (HR: 5.2; 95% CI: 4.0, 6.8). Similar to the overall SGA classification, all subscales were dose-dependently associated with mortality. The adjusted mortality risks associated with baseline and time-dependent SGA categories are shown in **Figure 3**.

## DISCUSSION

This prospective observational study in chronic dialysis patients was the first to detect a dose-response trend of the 7-point SGA classification in relation to all-cause mortality. Severe PEW at baseline, as assessed with the 7-point SGA, was independently associated with a 2-fold increased mortality risk in 7 y of follow-up. In time-dependent analyses, this association was even stronger, 5-fold, indicating that PEW was associated with a remarkably high risk of short-term mortality.

Our study showed that, compared with an SGA score of 7, each 1-point lower score was associated with a higher mortality risk,

**TABLE 1**

Characteristics of 1601 chronic dialysis patients 3 mo after the start of dialysis, per subjective global assessment (SGA) category of protein-energy wasting (PEW)<sup>1</sup>

Variable	SGA category <sup>2</sup>		
	Severe PEW	Moderate PEW	Normal nutrition
Subjects at risk [n (%)]	81 (5)	367 (23)	1153 (72)
Sex (% men)	68	59	61
Age (y)	64 ± 15 <sup>3</sup>	63 ± 15	58 ± 15
Ethnicity (% white)	91	92	93
Primary kidney disease (%)			
Diabetes mellitus	10	16	17
Glomerulonephritis	10	11	15
Renal vascular dis.	30	21	16
rGFR (mL · min <sup>-1</sup> · 1.73 m <sup>-2</sup> )	2.3 ± 2.2	3.2 ± 2.9	4.1 ± 3.0
Treatment with HD (%)	79	73	58
Comorbidity			
CVD (%)	51	39	33
Diabetes mellitus (%)	20	24	22
Malignancy (%)	12	13	8
Khan index (% high)	41	37	24
BMI (kg/m <sup>2</sup> ) <sup>4</sup>	20.9 ± 2.9	23.6 ± 4.3	25.3 ± 3.9
nPNA (g · kg <sup>-1</sup> · d <sup>-1</sup> ) <sup>5</sup>	0.93 ± 0.20	1.00 ± 0.23	1.02 ± 0.22
Serum cholesterol (mmol/L) <sup>6</sup>	4.6 ± 1.5	4.9 ± 1.3	5.1 ± 1.3
Serum albumin (g/L) <sup>4</sup>	33.0 ± 5.9	35.5 ± 5.7	36.6 ± 4.8

<sup>1</sup> rGFR, residual glomerular filtration rate corrected for body surface area; CVD, cardiovascular disease; HD, hemodialysis; nPNA, normalized protein nitrogen appearance. Differences in baseline characteristics between the 3 SGA categories were tested by using chi-square tests for categorical variables (all  $P < 0.001$ ) and one-factor ANOVA (all  $P < 0.001$ ) with Bonferroni correction for post hoc comparisons to test the differences between the nutritional variables BMI, nPNA, serum cholesterol and albumin concentrations, age, and rGFR.

<sup>2</sup> Seven-point scale of nutritional status in 3 categories: severe PEW (score: 1–3), moderate PEW (score: 4–5), and normal nutritional status (score: 6–7).

<sup>3</sup> Mean ± SD (all such values).

<sup>4</sup>  $P < 0.001$  for the differences between all 3 SGA categories.

<sup>5</sup>  $P < 0.01$  for the difference between a normal nutritional status and severe PEW,  $P = 0.293$  for the difference between moderate PEW and a normal nutritional status, and  $P = 0.107$  for the difference between moderate PEW and severe PEW.

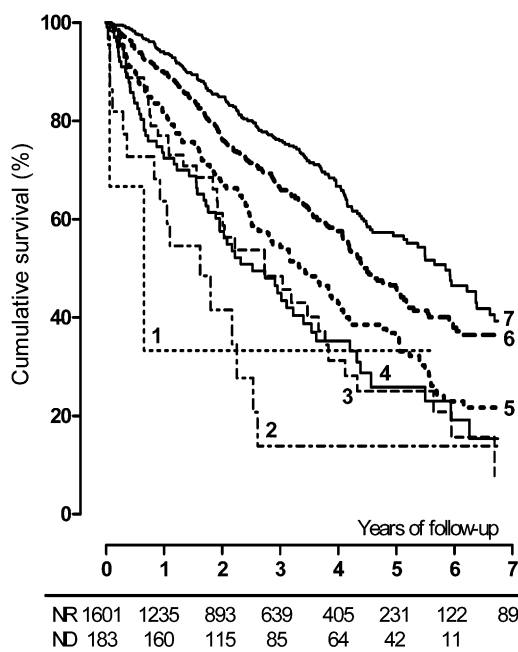
<sup>6</sup>  $P < 0.012$  for the difference between a normal nutritional status and moderate PEW,  $P < 0.01$  for the difference between a normal nutritional status and severe PEW, and  $P = 0.269$  for the difference between moderate and severe PEW.

showing a dose-response trend. A study of the concurrent validity of the 3-point SGA compared with total body nitrogen showed that the SGA was only able to determine the presence of severe malnutrition and not the degree of malnutrition (15). Total body nitrogen can be considered the gold-standard method of nutritional status in dialysis patients. However, only 76 dialysis patients were included in this study, which may not have been sufficient to detect differences between the different SGA categories. In our study of 1601 dialysis patients, the 7-point SGA correlated well with other nutritional variables at baseline. Unfortunately, we could not study concurrent validity by comparing the SGA with a reference method of nutritional status. However, the strength of the association of the SGA with future adverse health outcome may be considered highly clinically relevant. Several studies showed that the SGA is associated with morbidity, hospitalization, and mortality (9–12). In addition to these results, our results imply that the 7-point SGA may validly distinguish different degrees of PEW associated with increasing risks of mortality.

The 7-point SGA provides more possibilities for classifying patients than does the 3-point scale. In addition, our study provides evidence that each point on the 7-point scale may distinguish a different degree of PEW. Furthermore, especially because

the pattern of weight loss is considered important in scoring the SGA classification (4), small improvements or deteriorations within each category may be detected earlier and more easily monitored with the 7-point scale. For routine monitoring of the patient in clinical practice, this implies that every single point change on the 7-point SGA during follow-up can help dietitians detect early any worsening within each category, which would indicate that treatment should be started or altered, or detect the first signs of improvement in response to treatment.

The SGA is a simple method for scoring nutritional status in a standardized way and for capturing different aspects of nutritional status during one clinical examination. The subjective nature of the SGA may appear to be a disadvantage. Despite its subjective nature, both the intraobserver and interobserver reliabilities of the SGA have been found to be adequate in several studies (6, 8, 9). To gain maximum benefit of the reliability of the SGA, it has been suggested that one observer or a select group of observers perform the assessment (6). However, one study even showed substantial reliability of the SGA after web-based training of 54 dietitians with a different background (9). Moreover, the clinical judgment of health care providers may be valuable when obtaining the overall SGA classification. In NECOSAD-II, ≥2 trained research nurses performed the SGA



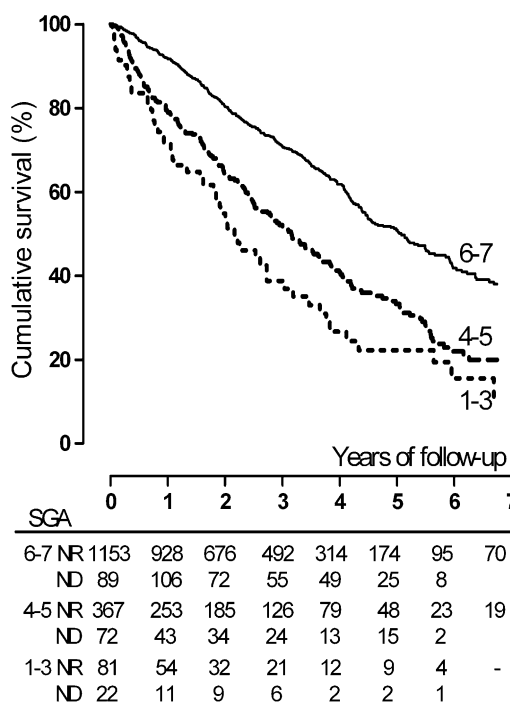
**FIGURE 1.** Kaplan-Meier cumulative survival during 7 y of follow-up of 1601 chronic dialysis patients per subjective global assessment classification at baseline. A score of 7 indicates a normal nutritional status; a score of 1 indicates severe protein-energy wasting. NR, number of patients at risk; ND, number of deaths.

measurements to maximize interobserver and intraobserver reliability. Although we cannot completely rule out misclassification that occurred at baseline or during follow-up, any misclassification would most likely result in bias toward the null, whereas we detected a dose-response relation of the 7-point SGA with mortality.

Because of the low number of patients with an SGA classification score of 1 or 2 at the start of dialysis, we defined an SGA classification score of 1–3 as severe PEW in our study. Only 5% of the patients in our study population were classified as having severe PEW compared with 10% in other dialysis populations (20). A possible explanation may be the duration of predialysis care. On average, our patients had been receiving predialysis care for 1 y before the start of dialysis treatment, which may be shorter in other populations.

In our study, patients with moderate or severe PEW at baseline seemed older and sicker than patients with a normal nutritional status at baseline. Because a poor health status may accompany a poor nutritional status, this may have confounded our results. After adjustment for age, sex, treatment modality, primary kidney disease, and comorbidity, the short-term mortality in patients with PEW was 2- to 5-fold increased. It is unlikely that unknown or imperfectly measured confounders could completely explain these risks. However, because of the observational study design, we cannot rule out residual confounding due to unknown confounders.

Many modifications of the SGA are being used in the dialysis population (4, 21–25). A recent study compared several simplified nutritional screening tools in hemodialysis patients with the Malnutrition-Inflammation Score (MIS), a fully quantitative version of the SGA that includes 3 additional items (BMI, serum albumin, and serum total-iron-binding capacity) and concluded



**FIGURE 2.** Kaplan-Meier cumulative survival during 7 y of follow-up of 1601 chronic dialysis patients per subjective global assessment (SGA) category at baseline. A score of 1–3 indicates severe protein-energy wasting, 4–5 indicates moderate protein-energy wasting, and 6–7 indicates a normal nutritional status. NR, number of patients at risk; ND, number of deaths.

that the Geriatric Nutritional Risk Index, combining weight loss and serum albumin, was the simplest and most accurate risk index for identifying hemodialysis patients at risk of PEW according to the MIS (26). However, by including serum albumin, a marker of inflammation, these tools may in part assess the risk due to inflammation. Indeed, MIS was found to be comparable with

**TABLE 2**

Relative risks of mortality of 7-y (long-term) mortality associated with the 7-point subjective global assessment (SGA) classification at baseline and with the time-dependent SGA measurements in 1601 chronic dialysis patients

SGA <sup>2</sup>	Hazard ratio (95% CI) <sup>1</sup>			
	SGA at baseline		Time-dependent SGA	
	Crude	Adjusted <sup>3</sup>	Crude	Adjusted <sup>3</sup>
7 (n = 564)	1	1	1	1
6 (n = 589)	1.4 (1.1, 1.7)	1.1 (0.9, 1.3)	1.6 (1.3, 2.0)	1.1 (0.9, 1.3)
5 (n = 265)	2.1 (1.6, 2.6)	1.5 (1.2, 1.9)	2.9 (2.3, 3.7)	1.5 (1.2, 1.8)
4 (n = 102)	2.7 (2.0, 3.6)	2.0 (1.5, 2.7)	4.5 (3.4, 5.9)	2.4 (1.8, 3.2)
3 (n = 56)	2.7 (1.8, 3.8)	1.9 (1.3, 2.8)	6.9 (4.8, 9.8)	3.0 (2.1, 4.3)
2 (n = 22)	5.0 (3.0, 8.3)	4.3 (2.5, 7.2)	9.7 (6.3, 14.8)	3.7 (2.4, 5.7)
1 (n = 3)	2.8 (0.7, 11.3)	1.8 (0.4, 7.3)	7.7 (3.4, 17.4)	6.6 (3.7, 11.6)

<sup>1</sup> Cox regression analysis was used to calculate hazard ratios and 95% CIs relative to an SGA score of 7 as the reference.

<sup>2</sup> Seven-point scale of nutritional status: a score of 7 indicates a normal nutritional status, and a score of 1 indicates severe protein-energy wasting.

<sup>3</sup> Analyses were adjusted for age, sex, treatment modality, primary kidney disease, and comorbidity.

**TABLE 3**

Relative risks of mortality associated with serial measurements of the overall subjective global assessment (SGA) classification and its 4 subscales in 1601 chronic dialysis patients

	Hazard ratio (95% CI) <sup>1</sup>				
SGA score <sup>2</sup>	Weight loss	Intake and gastrointestinal symptoms	Loss of fat mass	Muscle wasting	SGA classification
Crude					
6–7	1	1	1	1	1
4–5	2.0 (1.7, 2.4)	2.6 (2.2, 3.1)	2.3 (1.9, 2.7)	2.5 (2.1, 2.9)	2.7 (2.3, 3.2)
1–3	4.1 (3.2, 5.3)	6.2 (4.7, 8.0)	5.0 (3.9, 6.4)	6.0 (4.7, 7.5)	6.4 (4.9, 8.3)
Adjusted <sup>3</sup>					
6–7	1	1	1	1	1
4–5	1.7 (1.4, 2.0)	2.1 (1.8, 2.6)	1.8 (1.5, 2.2)	1.9 (1.6, 2.2)	2.1 (1.8, 2.5)
1–3	3.5 (2.7, 4.5)	5.5 (4.3, 7.2)	3.8 (2.9, 4.9)	4.4 (3.5, 5.5)	5.2 (4.0, 6.8)

<sup>1</sup> Time-dependent Cox regression analysis was used to calculate hazard ratios and 95% CIs relative to an SGA score of 7 as the reference.

<sup>2</sup> Seven-point scale of nutritional status in 3 categories: severe PEW (score: 1–3), moderate PEW (score: 4–5), and normal nutritional status (score: 6–7).

<sup>3</sup> Analyses were adjusted for age, sex, treatment modality, primary kidney disease, and comorbidity.

serum C-reactive protein and serum interleukin-6 concentrations in predicting hospitalization and mortality (24). Our results showed that all 4 subscales of the SGA were strongly associated with mortality, which suggests that the subscales are equally important in the assessment of the nutritional status of dialysis patients.

With the SGA we aimed to associate the presence of PEW in dialysis patients with the risk of mortality due to PEW and not to inflammation or comorbidity. PEW in the dialysis population, however, may be a consequence of both a decreased dietary intake (because of loss of appetite, anorexia, or a protein-restricted diet before the start of dialysis) and increased requirements as a result of disease or increased nutrient losses (because of increased energy expenditure, presence of inflammation, or nutrient losses via the dialysate) (1). Therefore, additional nutrients alone may not be sufficient to restore the nutritional status of the patient. Although results of recent randomized trials with nutritional therapy in combination with resistance exercise and/

or anabolic stimuli are promising (27–29), their effects on survival need to be established.

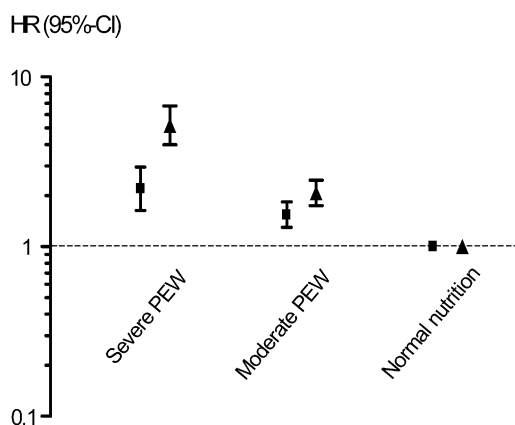
Because severe PEW was associated with a 5-fold increased mortality risk in the subsequent half year, patients progressing to this stage of PEW must be prevented as much as possible. Furthermore, because an SGA classification of as high as 5 was associated with an increased mortality risk, routine monitoring of the nutritional status of dialysis patients is important because PEW is more difficult to treat when it is severe (2). Early detection of the first signs of PEW allows early treatment to anticipate nutritional depletion, and, most importantly, to prevent any further deterioration (2). Therefore, the nutritional status of dialysis patients should be assessed regularly in accordance with the recent EBP guidelines (14). Our results imply that the 7-point SGA can be used in clinical practice to distinguish different degrees of PEW associated with increasing risks of mortality.

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The authors' responsibilities were as follows—RdM, EWB, RTK, and FWD: designed the study; RdM: analyzed the data and wrote the manuscript; DCG, JGvM, EWB, RTK, and FWD: helped interpret the data and write the manuscript; and HB: helped write the manuscript. No conflicts of interest were declared.

## REFERENCES

1. Fouque D, Kalantar-Zadeh K, Kopple J, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int* 2008;73:391–8.
2. Fouque D, Guebre-Egziabher F. An update on nutrition in chronic kidney disease. *Int Urol Nephrol* 2007;39:239–46.



**FIGURE 3.** Relative risks of mortality [hazard ratios (HRs) and 95% CIs] per baseline and time-dependent subjective global assessment (SGA) categories in 1601 chronic dialysis patients, calculated with Cox regression analysis and adjusted for age, sex, treatment modality, primary kidney disease, and comorbidity. PEW, protein-energy wasting. ■, 7-y mortality risk by baseline SGA; ▲, time-dependent mortality risk by SGA.

3. Steiber AL, Kalantar-Zadeh K, Secker D, McCarthy M, Sehgal A, McCann L. Subjective global assessment in chronic kidney disease: a review. *J Ren Nutr* 2004;14:191–200.
4. Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr* 1987;11:8–13.
5. McCusker FX, Teehan BP, Thorpe KE, Keshaviah PR, Churchill DN. How much peritoneal dialysis is required for the maintenance of a good nutritional state? Canada-USA (CANUSA) Peritoneal Dialysis Study Group. *Kidney Int Suppl* 1996;56:S56–61.
6. Visser R, Dekker FW, Boeschoten EW, Stevens P, Krediet RT. Reliability of the 7-point subjective global assessment scale in assessing nutritional status of dialysis patients. *Adv Perit Dial* 1999;15:222–5.
7. Enia G, Sicuso C, Alati G, Zoccali C. Subjective global assessment of nutrition in dialysis patients. *Nephrol Dial Transplant* 1993;8:1094–8.
8. Jones CH, Wolfenden RC, Wells LM. Is subjective global assessment a reliable measure of nutritional status in hemodialysis? *J Ren Nutr* 2004;14:26–30.
9. Steiber A, Leon JB, Secker D, et al. Multicenter study of the validity and reliability of subjective global assessment in the hemodialysis population. *J Ren Nutr* 2007;17:336–42.
10. Pifer TB, McCullough KP, Port FK, et al. Mortality risk in hemodialysis patients and changes in nutritional indicators: DOPPS. *Kidney Int* 2002;62:2238–45.
11. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. Association among SF36 quality of life measures and nutrition, hospitalization, and mortality in hemodialysis. *J Am Soc Nephrol* 2001;12:2797–806.
12. Stenvinkel P, Barany P, Chung SH, Lindholm B, Heimbürger O. A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients. *Nephrol Dial Transplant* 2002;17:1266–74.
13. National Kidney Foundation. Clinical practice guidelines for nutrition in chronic renal failure. *K/DOQI*. *Am J Kidney Dis* 2000;35:S1–140.
14. Fouque D, Vennegoor M, ter Wee P, et al. EBPG guideline on nutrition. *Nephrol Dial Transplant* 2007;22(suppl 2):ii45–87.
15. Cooper BA, Bartlett LH, Aslani A, Allen BJ, Ibels LS, Pollock CA. Validity of subjective global assessment as a nutritional marker in end-stage renal disease. *Am J Kidney Dis* 2002;40:126–32.
16. van Dijk PC, Jager KJ, de Charro F, et al. Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. *Nephrol Dial Transplant* 2001;16:1120–9.
17. Bergstrom J, Heimbürger O, Lindholm B. Calculation of the protein equivalent of total nitrogen appearance from urea appearance: which formulas should be used? *Perit Dial Int* 1998;18:467–73.
18. Khan IH, Catto GR, Edward N, Fleming LW, Henderson IS, MacLeod AM. Influence of coexisting disease on survival on renal-replacement therapy. *Lancet* 1993;341:415–8.
19. Baker JP, Detsky AS, Wesson DE. Nutritional assessment: a comparison of clinical judgement and objective measurements. *N Engl J Med* 1982;306:969–72.
20. Kuhlmann MK, Kribben A, Wittwer M, Horl WH. OPTA—malnutrition in chronic renal failure. *Nephrol Dial Transplant* 2007;22:iii13–9.
21. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. *J Am Soc Nephrol* 1996;7:198–207.
22. Kalantar-Zadeh K, Kleiner M, Dunne E, Lee GH, Luft FC. A modified quantitative subjective global assessment of nutrition for dialysis patients. *Nephrol Dial Transplant* 1999;14:1732–8.
23. Stenvinkel P, Heimbürger O, Paulre F, et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. *Kidney Int* 1999;55:1899–911.
24. Kalantar-Zadeh K, Kopple JD, Humphreys MH, Block G. Comparing outcome predictability of markers of malnutrition-inflammation complex syndrome in haemodialysis patients. *Nephrol Dial Transplant* 2004;19:1507–19.
25. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. *Am J Kidney Dis* 2001;38:1251–63.
26. Yamada K, Furuya R, Takita T, et al. Simplified nutritional screening tools for patients on maintenance hemodialysis. *Am J Clin Nutr* 2008;87:106–13.
27. Feldt-Rasmussen B, Lange M, Sulowicz W, et al. Growth hormone treatment during hemodialysis in a randomized trial improves nutrition, quality of life, and cardiovascular risk. *J Am Soc Nephrol* 2007;18:2161–71.
28. Johansen KL, Painter PL, Sakkas GK, et al. Effects of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: a randomized, controlled trial. *J Am Soc Nephrol* 2006;17:2307–14.
29. Majchrzak KM, Pupim LB, Flakoll PJ, Ikizler TA. Resistance exercise augments the acute anabolic effects of intradialytic oral nutritional supplementation. *Nephrol Dial Transplant* 2008;23:1362–9.

