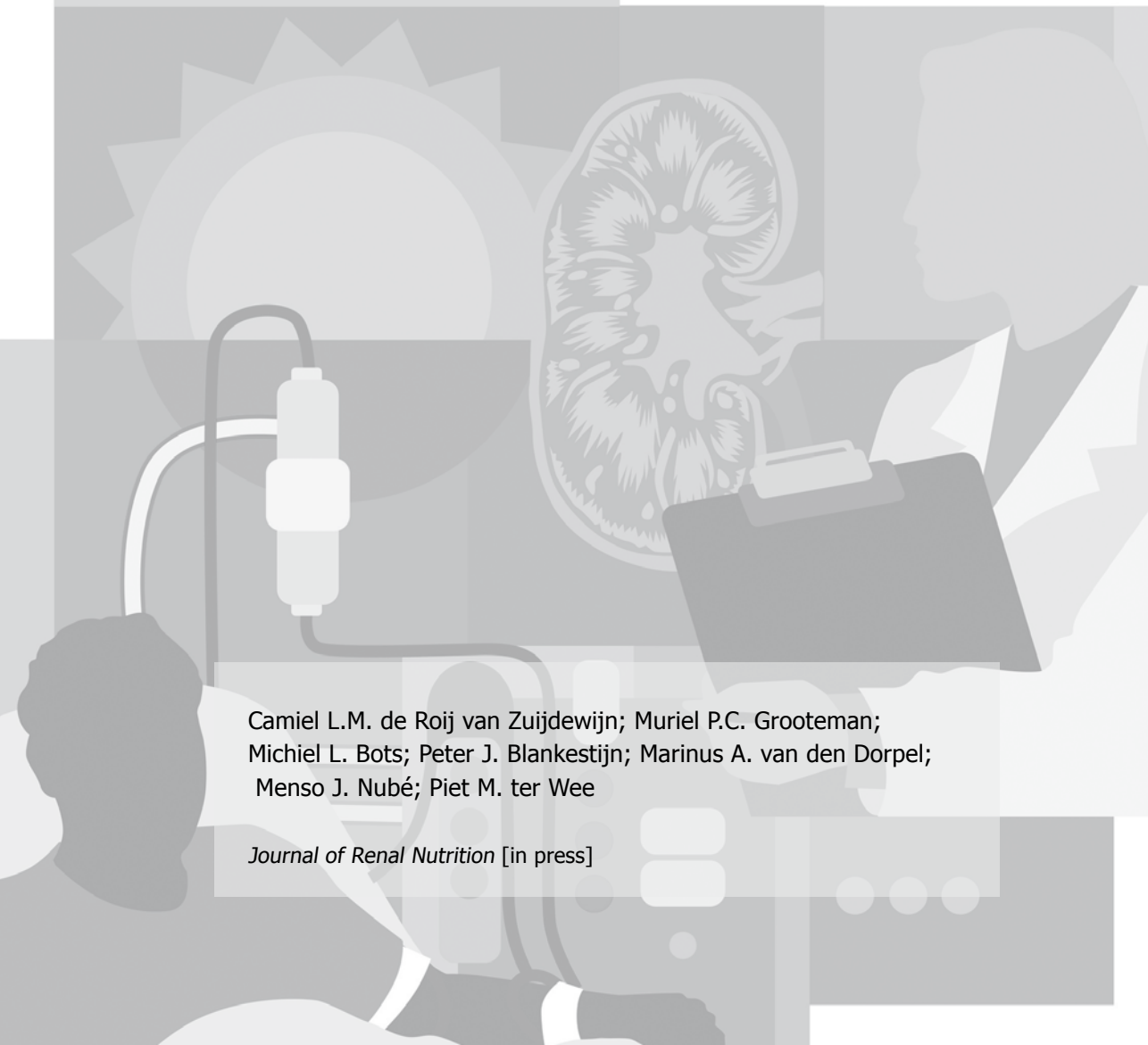
Chapter 2.2

Comparing scores assessing protein-energy wasting: relation with quality of life



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Journal of Renal Nutrition [in press]

ABSTRACT

Introduction

Protein-energy wasting (PEW), a state of decreased bodily protein and energy fuels, is highly prevalent among hemodialysis patients. The best method to determine PEW, however, remains debated. As an independent, negative association between PEW and quality of life (QOL) has been demonstrated, establishing which nutrition-related test correlates best with QOL may help to identify how PEW should preferably be assessed.

Methods

Data were used from CONTRAST, a cohort of end-stage kidney disease patients. At baseline, Subjective Global Assessment (SGA), Malnutrition Inflammation Score (MIS), Geriatric Nutritional Risk Index, composite score on Protein-Energy Nutritional Status, normalized Protein Nitrogen Appearance, BMI, serum albumin and serum creatinine were determined. QOL was assessed by the Kidney Disease Quality of Life Short Form 1.3. The present study reports on 2 general and 11 kidney-disease specific QOL scores. Spearman's rho (ρ) was calculated to determine correlations between nutrition-related tests and QOL domains. Twelve months after randomization a sensitivity analysis was performed to test the robustness of the results.

Results

Out of 714 patients, 489 representative subjects were available for analysis. All tests correlated with the Physical Component Score, except BMI. Only SGA and MIS correlated significantly with the Mental Component Score. SGA correlated significantly with 10 out of 11 kidney-disease specific QOL domains. The MIS not only correlated significantly with all (11) kidney-disease specific QOL domains, but also with higher correlation coefficients.

Conclusion

Of the eight investigated nutrition-related test, only MIS correlates with all QOL domains (13/13) with the strongest associations.

INTRODUCTION

Many end-stage kidney disease (ESKD) patients need lifelong dialysis treatment. Despite continuous developments in dialysis techniques and improving knowledge concerning the uremic syndrome over the last decades,[1] not only remains the life expectancy of these patients severely impaired but also is their quality of life (QOL) usually severely negatively affected in comparison to the general population.[2,3] Among others, QOL is influenced by appetite,[4] quality of sleep[5] and nutritional status i.e. protein-energy wasting (PEW).[6,7]

The International Society of Renal Nutrition and Metabolism (ISRNM) introduced the term PEW in 2008 to determine the state of decreased bodily protein and energy fuels in chronic kidney disease patients. PEW appears to be highly prevalent among hemodialysis (HD) patients.[8,9] The following diagnostic criteria were proposed for this syndrome: (1) low blood chemistry (albumin, prealbumin or cholesterol), (2) low or decreasing body mass, (3) low or decreasing muscle mass and (4) low dietary intake.[10] In the absence of a gold standard, however, the debate on how this syndrome should be assessed is ongoing.[11,12] Although randomized interventional trials are awaited, observational studies and experts suggest that patients suffering from PEW may benefit from supplementation of proteins and energy.[13-15] In addition, a recent randomized trial showed that in patients with a low serum albumin concentration, help with patient-specific barriers such as cooking or improvement of nutritional knowledge resulted in increased serum albumin levels.[16] Hence, it appears important to find a reliable way to identify PEW in these patients accurately and easily.

The quest for a gold standard has resulted in many clinical scoring lists, tools and parameters to diagnose malnutrition or PEW. The most widely investigated clinical nutrition-related scoring lists are the three-point scaled Subjective Global Assessment[17,18] as well as its modified successors, such as the 7-point scaled SGA (SGA-7)[19] and the Malnutrition Inflammation Score (MIS).[20] Other clinical nutrition-related scoring lists that have been proposed to assess PEW include the Geriatric Nutritional Risk Index (GNRI)[21] and the composite score on Protein-Energy Nutritional Status (cPENS).[22] Furthermore, a number of more or less individual parameters have been associated with PEW, such as serum albumin,[23] BMI[24] and the normalized Protein Nitrogen Appearance (nPNA) rate.[25,26]

In short, presently, it is unknown how PEW can be determined best. With respect to mortality, we recently showed that serum albumin and MIS as markers for PEW

predict mortality equally well.[27] Besides an impaired life expectancy, a consequence of PEW is a decrease in QOL, as has been stated by the ISRNM in 2008.[10] As such, it appears justified to assume that a preferred nutrition-related test should correlate with QOL. To contribute a piece of the puzzle in finding the preferred test to assess PEW, various nutrition-related tests are compared in their relation with various domains of QOL in the present study.

Methods

Various cross-sectional analyses were performed using data from the CONvective TRAnsport STudy (CONTRAST, NCT00205556). Details concerning the design and methods of this study are described elsewhere.[28,29] In brief, CONTRAST was a randomized controlled trial primarily evaluating the effect of post-dilution online hemodiafiltration (HDF) compared to low-flux HD on all-cause mortality and cardiovascular events. 714 patients were enrolled between 2004 and 2010 in 29 dialysis centers in 3 countries (the Netherlands [n=26], Canada [n=2] and Norway [n=1]). Patients aged 18 years or older were eligible if treated with HD 2 or 3 times per week for over two months. Patients were considered ineligible in case of severe incompliance to dialysis prescription, treatment with HDF or high-flux HD in the six months preceding randomization or a life expectancy under three months due to non-renal disease. Written informed consent was given by all patients prior to randomization. The study was performed in accordance with the Good Clinical Practice Guidelines and the Declaration of Helsinki. The study protocol was approved by a central medical ethics review board.

Participants were included in the present study if all investigated nutrition-related tests could be assessed at baseline. For this, the following information was necessary: SGA-7, gender, BMI, dry body weight, medical history, dialysis vintage, serum albumin, serum creatinine, nPNA and total iron binding capacity.

Nutrition-related tests

SGA-7

Four items are scored on a scale from 1 (severely malnourished) to 7 (well nourished): (1) change in dry weight, (2) dietary intake change and gastro-intestinal (GI) symptoms, (3) decrease of subcutaneous fat and (4) muscle atrophy. An overall subjective score between 1 and 7 is then assigned by the professional conducting the test.[19]

MIS

The MIS is a modified and extended version of the SGA, in which 10 items are scored between 0 (normal) and 3 (severely abnormal), resulting in an overall score between 0 (well nourished) and 30 (severely malnourished): (1) change in post-dialysis weight, (2) dietary intake, (3) GI symptoms, (4) functional capacity, (5) co-morbidity including dialysis vintage, (6) decreased fat stores or loss of subcutaneous fat, (7) signs of muscle wasting, (8) BMI, (9) serum albumin and (10) serum TIBC. In the present analysis, the different MIS items were converted from various parts of the case-record form, as described previously.[27] Of note, this is the only score in which a higher score indicates worse nutritional status.

GNRI

This continuous score was derived from the Nutritional Risk Index (NRI)[30] and originally designed for the elderly.[31] It is calculated by the formula:

GNRI = (1.489 * albumin [g/L]) + (41.7* [body weight/ideal body weight])

The ideal body weight was calculated using the Lorenz formula.[31] The part [body weight/ideal body weight] was set to 1 when the dry weight exceeded the ideal body weight.[30]

cPENS

The weighted nutrition-related score cPENS contains 4 items, based on the 4 diagnostic criteria for PEW as proposed by the ISRNM:[10] (1) creatinine, (2) albumin, (3) BMI and (4) nPNA. If a patients' BMI was above 23 kg/m^2, 1.0 point was assigned, 1.5 points were assigned if nPNA was above 0.80 g/kg/d, 2.0 points if serum creatinine was above 10 mg/dL and 2.5 points if albumin was above 3.80 g/dL. In total, this resulted in a score between 0 (severely malnourished) and 7 (well nourished).[22]

Creatinine

Creatinine was determined in serum at each centers laboratory using standard techniques. Blood samples were drawn prior to dialysis.

Albumin

Serum albumin was measured at local laboratories. Values assessed with the bromcresol purple method were converted to bromcresol green values using the equation: bromcresol green = bromcresol purple + 5.5 (g/dL).[32]

BMI

BMI was calculated at baseline as the ratio of post-dialysis body weight (kg) to height (m) squared.

nPNA

Blood urea nitrogen (BUN) was determined using samples drawn before and after dialysis. nPNA (g/kg/d) was calculated from two BUN measurements and adjusted for residual kidney urea clearance.[33]

Quality of Life assessment

QOL was assessed with the Kidney Disease Quality of Life Short Form version 1.3 (KDQOL-SF 1.3) (http://www.rand.org/content/dam/rand/pubs/papers/2006/P7994.pdf).[34] This validated self-assessment results in values for 20 domains of QOL: 8 general scores and 12 kidney-disease specific scores. In every domain, 0 is the minimum and 100 the maximum score. Higher scores imply a better QOL. The 8 general domains can be summarized in two scores, the Mental Component Score (MCS) and the Physical Component Score (PCS). These two values are standardized with a value of 50 being the mean of the general United States (US) population.[35] Furthermore, 12 kidney-disease specific domains of QOL can be determined: (1) symptoms/problems, (2) effects of kidney disease on daily life, (3) burden of kidney disease, (4) work status, (5) cognitive function, (6) quality of social interaction, (7) sexual function, (8) sleep, (9) social support, (10) dialysis staff encouragement, (11) overall health rate and (12) patient satisfaction. The substantive meaning of these domains is described elsewhere.[36] These values are not standardized. Values can therefore be interpreted relative within a certain domain or relative to each other.

Statistical analysis

Baseline characteristics of the entire cohort and the investigated cohort were compared using independent sample t-tests for normally distributed continuous variables, Mann-Whitney U-tests for not-normally distributed continuous data and chi-square tests for categorical variables. Linearity between nutrition-related tests and QOL domains was checked with scatterplots. Given the not-normally distributed data of most QOL domains and the discrete ordinal character of most nutrition-related tests, Spearman's rank correlation coefficient rho (ρ) was calculated to determine correlations between the various nutrition-related tests and the different domains of QOL. All statistical analyses were performed using IBM SPSS Statistics 22.0 (SPSS Inc, Chicago, IL, USA).

Sensitivity analyses

A sensitivity analysis was performed using cross-sectional data from CONTRAST twelve months after randomization. All nutrition-related tests and the KDQOL-SF 1.3 were again assessed. The statistical approach was identical. By comparing the correlation coefficients between the nutrition related tests and the QOL domains at baseline and 12 months thereafter, the robustness of the findings at baseline was checked.

To further substantiate the comparison between the various nutrition-related tests and QOL, multivariable logistic regression analyses were used to calculate odds ratios (ORs) for being in the upper half of a certain QOL domain when a person is in the better half of a certain nutrition-related test. The following covariates were included in the model as these variables may associate with both PEW and QOL, are not part of any nutrition-related test and cannot be considered to be intermediate variables: age, gender, race, diabetes, previous renal transplantation, $spKt/V_{urea}$ and hematocrit.

RESULTS

Demographical, clinical and laboratory characteristics

Baseline patient characteristics of the entire cohort (n=714) and the investigated cohort (n=489) are shown in table 1. No marked differences between these groups were observed, suggesting that this cohort is a representative sample of the CONTRAST cohort. Patients excluded from the present analysis mostly had a missing nPNA value (n=120) or lacked information on a MIS item (n=125). In the investigated cohort, mean age was 63.3±13.8 years. The majority was male (60.5%) and more than half of the patients had residual kidney function (52.1%). Median dialysis vintage was 2.0 years and mean $spKt/V_{urea}$ 1.39±0.21.

QOL domains

Values of 13 QOL domains are listed in table 2. Mean MCS and PCS were 50 and 37, respectively. In view of the standardized aspect of these two values, this indicates an equal MCS and a lower PCS when compared to the general US population. For the kidney disease specific domains of QOL, it appears that the quality of social interaction was least affected (mean 81) and the work status most (mean 17). Interestingly, questions concerning the domain sexual function were answered by only 46/489 patients (9.4%). Because of this small proportion and the high chance for a response bias, the correlation coefficients between the nutrition-related tests

and this QOL domain are considered unreliable estimates and hence not reported. In brief, we report on 13 QOL domains.

Scatterplots

The visual test of a linear relation between a nutrition-related test and a QOL domain resulted in 104 scatterplots. The assumption of linearity held in all cases.

Correlations at baseline

The correlation coefficients between the various nutrition-related tests and QOL domains are shown in table 3. These results show a significant correlation between PCS and 7 out of 8 nutrition-related tests with correlation coefficients between +0.10 and -0.47. MCS correlated only with SGA and MIS (ρ 0.13 and 0.20, respec-

Table 1. Baseline patient characteristics.

Characteristic	All patients (n=714)	Investigated patients (n=489)	*p* for difference
Demographic			
Age (years)	64.1 (13.7)	63.3 (13.8)	0.32
Sex (male)	445 (62.3%)	296 (60.5%)	0.53
BMI (kg/m^2)	25.4 (4.8)	25.4 (4.9)	0.93
Ethnicity (Caucasian)	600 (84.0%)	404 (82.6%)	0.90
Medical history			
Residual kidney function* (yes)	376 (52.7%)	255 (52.1%)	0.86
History of cardiovascular disease (yes)	313 (43.8%)	213 (43.6%)	0.92
Diabetes (yes)	170 (23.8%)	118 (24.1%)	0.83
Previous renal transplantation (yes)	78 (10.9%)	63 (12.9%)	0.30
Laboratory values			
Hematocrit (%)	36 (4)	36 (4)	0.50
Phosphate (mg/dL)	5.08 (1.53)	5.08 (1.49)	0.90
Albumin# (g/dL)	4.04 (0.38)	4.04 (0.38)	0.97
Creatinine (mg/dL)	9.74 (2.89)	9.76 (2.86)	0.88
Cholesterol (mg/dL)	142.0 (37.0)	142.9 (36.8)	0.66
Medication			
RAS inhibitor (yes)	351 (49.2%)	244 (49.9%)	0.88
Beta-blocker (yes)	381 (53.4%)	264 (54.0%)	0.91
Calcium antagonists (yes)	230 (32.2%)	160 (32.7%)	0.91
Statin (yes)	369 (51.7%)	254 (51.9%)	0.99
Platelet aggregation inhibitor (yes)	240 (33.6%)	166 (33.9%)	0.96
Dialysis properties			
Dialysis vintage (years)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	0.92
spKt/V	1.40 (0.22)	1.39 (0.21)	0.84

Data are shown as mean (standard deviation), median (interquartile range) or number (percentage), when appropriate

* defined as diuresis ≥ 100 mL/24h

Bromcresol green values

Abbreviations: BMI = Body Mass Index; RAS = Renin Angiontensin System

tively). Furthermore, apart from some incidental correlations, it is quite remarkable that the SGA-7 correlated with 12 out of 13 QOL domains with correlation coefficients between +0.10 and +0.22. The correlation between MIS and every domain of QOL is striking, as MIS correlated with all domains of QOL (ρ's between -0.12 and -0.49) and the correlation coefficients were the highest in every domain when compared to the other nutrition-related tests.

Sensitivity analyses

Results of the analysis at M12 are shown in supplementary table 1. As can be seen from these results, MIS correlated again best with QOL in terms of quantity and strength of the correlation coefficients. The drift of the results at baseline and at M12 is thus similar. The results of the multivariable logistic regression analyses are shown in supplementary table 2. These results underscore the finding that MIS associated best with QOL out of the eight investigated nutrition-related tests.

Table 2. Scores of QOL domains.

	Score (0-100)		
Domain	n	Mean (sd)	Median (IQR)
General domains			
Physical Component Score	447	37 (11)	37 (28-46)
Mental Component Score	447	50 (12)	53 (42-58)
Kidney disease specific domains			
Burden of kidney disease	482	46 (25)	44 (25-63)
Quality of social interaction	481	81 (17)	87 (70-93)
Cognitive function	481	77 (20)	80 (67-93)
Symptoms/problems	489	79 (14)	81 (71-89)
Effects of kidney disease	489	72 (19)	75 (63-86)
Work status	479	17 (27)	0 (0-50)
Sleep	480	62 (20)	63 (48-78)
Social support	474	78 (24)	83 (67-100)
Dialysis staff encouragement	479	77 (21)	75 (63-100)
Patient satisfaction	475	69 (23)	67 (50-83)
Overall health rate	478	58 (17)	60 (50-70)

The general QOL domains (PCS and MCS) are standardized with a value of 50 being the mean of the general population of the United States. The kidney-disease specific domains are not standardized. In all domains, a value of 0 is the minimum and a value of 100 the maximum; a higher score implies a better QOL.

Abbreviations: QOL = quality of life; n = number; sd = standard deviation; IQR = interquartile range

Table 3. Spearman correlation coefficients (ρ) between nutrition-related tests and QOL domains at baseline (n=489).

	PCS	MCS	Symp-toms	Effects disease	Burden disease	Work status	Cog-nitive function	Social interaction	Sleep	Social support	Dialysis Staff	Patient satisfaction	Overall health rate
MIS	-0.47[&&]	-0.20[&&]	-0.43[&&]	-0.49[&&]	-0.31[&&]	-0.24[&&]	-0.23[&&]	-0.17[&&]	-0.24[&&]	-0.12[&]	-0.19[&&]	-0.14[&]	-0.36[&&]
SGA	0.22[&&]	0.13[&]	0.21[&&]	0.21[&&]	0.20[&&]	0.13[&]	0.11[&]	0.10[&]	0.13[&]	0.06	0.10[&]	0.10[&]	0.21[&&]
GNRI	0.20[&&]	-0.02	0.03	0.01	0.05	0.02	-0.02	-0.05	0.09[&]	-0.06	0.08	0.06	0.10[&]
cPENS	0.22[&&]	-0.05	0.00	-0.03	0.05	0.04	-0.06	-0.11[&]	0.04	-0.02	0.03	-0.02	0.06
Albumine	0.20[&&]	-0.04	0.01	-0.01	-0.01	0.02	-0.01	-0.08	0.08	-0.09	0.05	0.04	0.09
Creatinine	0.19[&&]	-0.04	0.02	-0.03	-0.01	0.03	-0.10[&]	-0.14[&]	-0.01	-0.04	-0.05	-0.12[&]	0.00
BMI	-0.05	-0.02	0.02	-0.08	-0.05	-0.02	-0.07	-0.01	-0.01	0.02	0.09	0.05	-0.01
nPNA	0.10[&]	-0.07	-0.04	-0.03	0.06	0.08	0.03	-0.05	0.04	-0.04	-0.01	0.04	0.11[&]

Abbreviations: PCS = Physical Component Score; MCS = Mental Component Score; MIS = Malnutrition Inflammation Score; SGA = Subjective Global Assessment; GNRI = Geriatric Nutritional Risk Index; cPENS = composite score on Protein-Energy Nutritional Status; BMI = Body Mass Index; nPNA = normalized Protein Nitrogen Appearance

[&] Correlation is significant at the 0.05 level (two-tailed)

[&&] Correlation is significant at the 0.001 level (two-tailed)

DISCUSSION

The present study investigated relations between eight well-established nutrition-related tests and QOL. We clearly demonstrated that of these nutrition-related tests, MIS correlates best with QOL. The other seven tests had either no or an inferior relation with QOL. We know of no previous study comparing various nutrition-related tests using the correlations of these tests with QOL. From this study, two important conclusions can be drawn. First, MIS correlates best with QOL. This adds evidence towards its identification of being the best test to assess PEW. Second, this analysis underscores the idea that MIS measures more than just inflammation, as albumin (a negative acute phase protein) did not correlate with QOL whereas MIS (in which albumin is 1 out of the 10 items) did.

The association between malnutrition/PEW and QOL has been thoroughly investigated, but many questions remain. An independent association between QOL and different measurements of PEW has repeatedly been described for MIS,[5,7] SGA-7[37,38] and serum albumin.[39-44] There are conflicting results regarding the relation between QOL and the nutritional measurements BMI,[39,41] PCR/PNA[39-42] and serum creatinine.[39-41] None of these studies provided correlations between the kidney-disease specific QOL domains and the various nutrition-related tests. We did not find any literature describing the relation between GNRI and QOL or weighted cPENS and QOL. Of note, a previous study on the CONTRAST cohort did show the correlations at baseline between QOL, including the kidney-disease specific parts, and SGA-7, albumin, creatinine, BMI, nPNA and cPENS.[6] However, this concerned a none-weighted cPENS including 6 items, which is thus a different score. That study did not include MIS or GNRI. All these studies have an etiologic goal: to determine the independent association between QOL and nutrition. No study aims to compare the appropriateness of the nutrition-related tests by correlating these with QOL. This is the first study that primarily compares these tests. As we tested only subjects in whom all nutrition-related tests were available, patient characteristics between tests are identical and no statistical adjustment is necessary.

Interestingly, questions concerning sexual performance were answered by less than 10% of the investigated participants. Subjects seem unwilling to share information regarding sexual performance, even when anonymity is guaranteed. Perhaps, more focus should be drawn to such issues by treating physicians, as sexual inactivity and sexual dysfunction supposedly are highly prevalent among this patient group.[45-47]

Previously, we showed in the same cohort comparing the currently investigated nutrition-related tests that albumin and MIS are the best tools to predict all-cause mortality.[27] PEW is independently associated with both mortality[48] and QOL.[7] Therefore, the previous and the present study are complementary. Taken together and in the absence of a gold standard, the results of both studies indicate that MIS might be the preferred nutrition-related test to asses PEW.

Our study has multiple strengths. First, the magnitude of the cohort (n=489) ensures sufficient power to generate reliable estimates. Second, the investigated cohort encompasses a representative sample from the CONTRAST cohort and thus, as this cohort is representative for the dialysis population in the Netherlands,[29] of all Dutch dialysis patients. Third, the self-assessment tool used quantifies not only general aspects of QOL, but also disease-specific QOL. As HD patients experience more and other problems compared to the general population, it seems appropriate to take this into account. Furthermore, we compared eight different well-established nutrition-related tests in parallel. As we ensured the availability of all tests in every investigated patient, this enhances reliability of our results. Fifth, appropriate statistics were used, in which linearity was checked and non-parametric correlation coefficients were calculated. Finally, the sensitivity analysis at 12 months after randomization and by multivariable logistic regression analyses strengthen our findings tremendously.

There are also some limitations to our analysis. First, MIS was not actively assessed, but calculated from various parts of the baseline case-report form. We met with this objection by performing all subjective conversions twice by independent investigators (CdRvZ and IC). Second, the general scores MCS and PCS have not been standardized for the Dutch population, but for the American. To avoid any confusion, the American standardization method was used. However, given the fact that our results mostly correspond to (American) literature, this appears appropriate. Third, we tested 104 potential correlations. Thus, by chance, 5.2 correlations are significant at the level of $p \leq 0.05$. However, as the results are very pronounced and point in one direction, we see no reason to question the conclusion that MIS correlates best with QOL. Finally, from these observational analyses, it is impossible to prove causality. Whether PEW causes an impaired QOL, or an impaired QOL induces a reduced appetite and thus PEW, or whether co-morbidity induces both an impaired QOL and PEW, cannot be concluded from these data.

In conclusion, the present study showed in a large cohort using concise methods that the MIS is the nutrition-related score that correlated best with QOL. In the

absence of a gold standard and taking previous findings into account, MIS seems to be the preferred test to assess PEW. Confirmation of our results in an external cohort could increase the reliability of our findings. Furthermore, the quest to the preferred test to assess PEW should be further investigated in longitudinal and/or interventional studies, preferably in a randomized setting.

SUPPLEMENTARY TABLES

Supplementary table 1. Spearman correlation coefficients (ρ) between nutrition-related tests and QOL domains 12 months after randomization (n=278).

	PCS	MCS	Symp-toms	Effects disease	Burden disease	Work status	Cog-nitive function	Social interaction	Sleep	Social support	Dialysis Staff	Patient satisfaction	Overall health rate
MIS	-0.62[&&]	-0.35[&&]	-0.53[&&]	-0.52[&&]	-0.29[&&]	-0.21[&&]	-0.26[&&]	-0.24[&&]	-0.31[&&]	-0.21[&&]	-0.05	-0.03	-0.42[&&]
SGA	0.36[&&]	0.22[&&]	0.29[&&]	0.27[&&]	0.14[&]	0.09	0.10	0.13[&]	0.18[&]	0.14[&]	0.07	0.1	0.29[&&]
GNRI	0.26[&&]	0.13[&]	0.19[&]	0.14[&]	0.18[&]	0.18[&]	0.04	-0.01	0.11	0.06	0.10	0.13[&]	0.16[&]
cPENS	0.22[&&]	0.17[&]	0.15[&]	0.06	0.05	0.12	0.07	0.02	0.06	0.03	-0.00	0.04	0.08
Albumine	0.28[&&]	0.08	0.17	0.14[&]	0.16[&]	0.17[&]	0.01	-0.06	0.12	0.04	0.08	0.08	0.14[&]
Creatinine	0.21[&&]	0.08	0.11	0.06	-0.04	0.04	-0.01	0.01	0.02	-0.03	-0.05	-0.08	0.00
BMI	-0.02	0.11	-0.08	-0.06	-0.03	-0.07	-0.03	0.02	-0.06	0.02	0.10	0.18[&]	-0.01
nPNA	0.06	0.01	0.08	-0.11	-0.02	0.06	-0.00	-0.05	-0.10	-0.04	-0.04	0.03	-0.03

Abbreviations: PCS = Physical Component Score; MCS = Mental Component Score; MIS = Malnutrition Inflammation Score; SGA = Subjective Global Assessment; GNRI = Geriatric Nutritional Risk Index; cPENS = composite score on Protein-Energy Nutritional Status; BMI = Body Mass Index; nPNA = normalized Protein Nitrogen Appearance

[&] Correlation is significant at the 0.05 level (two-tailed)

[&&] Correlation is significant at the 0.001 level (two-tailed

Supplementary table 2. Results of multivariable logistic regression analysis at baseline (n=489)*.

	PCS	MCS	Symp-toms	Effects disease	Bur-den disease	Work status	Cog-nitive function	Social inter-action	Sleep	Social support	Dialysis staff	Patient satis-faction	Overall health rate
MIS	4.47[&&] (2.94-6.80)	1.91[&] (1.28-2.86)	3.88[&&] (2.60-5.81)	5.25[&&] (3.45-7.99)	3.30[&&] (2.20-4.93)	2.05[&] (1.34-3.14)	2.20[&&] (1.48-3.25)	1.74[&] (1.16-2.61)	2.76[&&] (1.87-4.07)	1.47 (0.99-2.17)	2.02[&&] (1.37-2.98)	1.58[&] (1.08-2.32)	4.94[&&] (3.10-7.88)
SGA	2.18[&&] (1.47-3.22)	1.34 (0.91-1.98)	2.53[&&] (1.72-3.71)	2.38[&&] (1.63-3.50)	2.45[&&] (1.66-3.60)	1.96[&] (1.29-2.97)	1.38 (0.94-2.01)	1.61[&] (1.08-2.38)	1.97[&&] (1.35-2.86)	1.58[&] (1.08-2.34)	1.35 (0.92-1.96)	1.42 (0.97-2.07)	2.50[&&] (1.65-3.80)
GNRI	1.56[&] (1.06-2.29)	0.98 (0.66-1.43)	0.96 (0.67-1.38)	1.24 (0.86-1.79)	1.52[&] (1.05-2.21)	1.08 (0.73-1.61)	0.96 (0.66-1.39)	0.91 (0.62-1.34)	1.30 (0.90-1.87)	0.91 (0.62-1.33)	1.27 (0.87-1.84)	1.38 (0.95-2.00)	1.72[&] (1.16-2.55)
cPENS	1.28 (0.71-2.32)	1.03 (0.57-1.86)	0.94 (0.53-1.67)	0.93 (0.52-1.64)	1.45 (0.80-2.63)	1.73 (0.96-3.12)	0.82 (0.45-1.50)	1.05 (0.55-1.99)	1.29 (0.73-2.28)	0.98 (0.54-1.78)	1.21 (0.68-2.16)	0.91 (0.50-1.64)	2.55[&] (1.40-4.64)
Albumine	1.60[&] (1.09-2.35)	0.96 (0.65-1.41)	1.02 (0.70-1.47)	1.29 (0.89-1.87)	1.21 (0.83-1.76)	1.25 (0.84-1.87)	1.11 (0.76-1.62)	0.78 (0.53-1.15)	1.27 (0.88-1.83)	0.74 (0.51-1.09)	1.20 (0.83-1.75)	1.15 (0.79-1.67)	1.73[&] (1.16-2.58)
Creatinine	1.25 (0.82-1.90)	1.33 (0.87-2.04)	1.08 (0.72-1.62)	0.87 (0.58-1.31)	1.25 (0.83-1.89)	0.80 (0.52-1.25)	0.89 (0.59-1.35)	0.95 (0.62-1.45)	0.95 (0.63-1.42)	0.99 (0.65-1.52)	0.94 (0.62-1.42)	0.67 (0.44-1.01)	1.06 (0.69-1.63)
BMI	0.91 (0.61-1.35)	0.68 (0.46-1.02)	0.73 (0.50-1.06)	0.71 (0.48-1.03)	0.96 (0.65-1.41)	0.88 (0.58-1.34)	0.70 (0.47-1.02)	1.11 (0.74-1.66)	1.28 (0.87-1.86)	1.19 (0.80-1.78)	1.03 (0.70-1.51)	1.04 (0.71-1.53)	0.95 (0.63-1.42)
nPNA	1.21 (0.82-1.77)	0.64[&] (0.43-0.94)	1.14 (0.79-1.64)	1.03 (0.71-1.49)	1.03 (0.71-1.49)	1.26 (0.85-1.88)	1.19 (0.82-1.73)	0.90 (0.61-1.32)	0.99 (0.69-1.43)	1.00 (0.68-1.47)	0.89 (0.61-1.28)	1.11 (0.76-1.61)	1.93[&] (1.30-2.88)

*Results presented as Odds Ratios (ORs) with 95% confidence intervals (CIs) for being above the median in a certain QOL domain for those in the best half as divided by the median in a certain nutritional test; results are corrected for age, sex, diabetes, Kt/V, Ht, previous renal transplantation and race.

[&] Adjusted association is significant at the 0.05 level (two-tailed)

[&&] Adjusted association is significant at the 0.001 level (two-tailed)

Abbreviations: PCS = Physical Component Score; MCS = Mental Component Score; MIS = Malnutrition Inflammation Score; SGA = Subjective Global Assessment; GNRI = Geriatric Nutritional Risk Index; cPENS = composite score on Protein-Energy Nutritional Status; BMI = Body Mass Index; nPNA = normalized Protein Nitrogen Appearance

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