Nutritional problems, overhydration and the association to quality of life in elderly dialysis patients.

Authors:

Inger Karin Lægreid[1, 2] MD, Asta Bye[3, 5] PhD, Knut Aasarød[1, 2]MD, PhD and Marit Jordhøy[1,3,4] MD, PhD

[1]Department of Cancer Research and Molecular Medicine, The Norwegian University of Science and Technology, NTNU, Trondheim, Norway

[2]Department of Renal Medicine, St.Olavs University Hospital, Trondheim, Norway

[3]Regional Centre for Excellence in Palliative Care, Oslo University Hospital, Oslo, Norway,

[4]Department of Internal Medicine, Innlandet Hospital Trust, Hamar, Norway

[5]Department of Health, Nutrition and Management, Oslo and Akershus University College of Applied Sciences, Norway

Correspondence to:

Inger Karin Lægreid,

Department of Cancer Research and Molecular Medicine, The Norwegian University of Science and Technology, NTNU, Bevegelsessenteret 3rd ET

7006 Trondheim, Norway

Telephone number: 4792498244 email address: inger.k.lagreid@ntnu.no

Abstract

Purpose: The aim of this pilot study was to describe the hydration-, and nutritional status of a cohort of elderly dialysis patients, and to explore the association between these parameters and the quality of life (QoL).

Methods: All patients over 75 years of age being in chronic dialysis by January 2008 at 3 dialysis units (n=34) were asked to participate in this pilot study, 24 patients were entered. Hydration status was assessed by bioimpedance spectroscopy (BIS), and nutritional status by the subjective global assessment (SGA), BIS, anthropometric measures and biochemical parameters. Based on these assessments the patients were classified as being cachectic or not according to newly defined criteria. QoL was measured using the SF-36.

Results: The results showed cachexia in 6 (25%), 37.5% had a body mass index (BMI) below 24, whereas according to SGA 91 % were malnourished. BIS showed low lean tissue index (LTI) in 46 % and overhydration in 35% of the patients. Compared to non-cachectic and normohydrated, cachectic and overhydrated patients reported consistently poorer QoL. For cachectic patients, the differences were clinically significant for all SF-36. BIS was easily applicable when used before dialysis.

Conclusions: The high frequency of nutritional deficits in this study calls for more attention to nutritional status in elderly dialysis patients. There is a need for a general agreement on how nutritional status should be assessed and reported, both in clinics and in research.

Keywords: dialysis, elderly, quality of life, nutritional status, hydration status,

Introduction

The elderly is the fastest growing group in dialysis, and for most of these patients the treatment will be lifelong. Maintaining and improving quality of life (QoL) is therefore a major goal. In general, patients with end stage renal disease (ESRD) are reported to have a poorer QoL compared to matched controls, and this is even more pronounced in older dialysis patients [1,2]. The older patients tend to score particularly low on physical domains, and patients above 75 years of age seem to be most affected [2].

For patients in maintenance dialysis, poor nutritional status may affect QoL and morbidity, and is associated with decreased survival despite adequate dialysis treatment [3,4]. The reported prevalence of nutritional deficits varies substantially between studies, ranging from 20% to 50% of the patients [4-6]. This inconsistency may be explained by a similar wide variation in terminology as well as diagnostic criteria. The International Society of Renal Nutrition and Metabolism ISRNM suggests using the term cachexia for the most severe form of protein and energy mass depletion, whereas the term "protein-energy wasting" (PEW) should be used to describe less prominent loss of body proteins and fuel reserves (muscle and fat tissue). Cachexia is widely recognised as a complex metabolic condition that is always associated with underlying illness and inflammation [7]. There is no general consensus as to how cachexia should be defined and identified. However, according to recently proposed definitions changes in body composition, in particular loss of lean tissue (including muscle mass) is important features [5,6]. Loss of muscle mass is also a phenomenon of aging, these changes may be hidden in the bulk of body weight [8]. Lean tissue mass may be replaced by increased fat mass, and in dialysis patients, muscle loss may also be replaced by water due to overhydration. To maintain an optimal hydration status and determine the patients dry weight is essential, both to avoid overhydration which increases the cardiovascular mortality, as well as hypotensive episodes during dialysis sessions [9]. Dry weight may be estimated by ultrasound of the inferior vena cava, radionuclide dilution techniques and echocardiography. These methods are expensive and time consuming. Most often clinical surrogate parameters are used such as interdialytic weight gain, ultrafiltration rate or blood pressure. Whole body bioimpedance spectroscopy (BIS) can be done bedside and may be used to evaluate nutritional status as well as to determine overhydration. BIS is validated against available gold standard methods with good accordance [10].

The aim of this pilot study was to test the feasibility of using BIS in daily clinical practice, to describe hydration and nutritional status of a cohort of elderly dialysis patients above 75 years of age, and to explore the association between these factors and quality of life.

Patients and Methods

Chronic dialysis (haemodialysis, HD and peritoneal dialysis, PD) patients over 75 years of age, living in Trøndelag County and in dialysis in January 2008 were asked to participate in the study.

A total of 34 patients > 75 years were registered, 10 were excluded (1 due to language problems, 4 were too ill, 1 was transplanted and 4 due to practical problems), thus in total, 24 patients entered the study. The demographic and clinical data that were registered included age, sex, dialysis modality, primary kidney disease, comorbidity, time on dialysis and time of referral to nephrologists'. We also registered serum cholesterol, serum albumin and C reactive protein (CRP).

To assess comorbidity, the Davies comorbidity index was applied. This index is based on seven domains, i.e. malignancy, ischemic heart disease, peripheral vascular disease, left ventricle dysfunction, diabetes mellitus, systemic collagen vascular disease and other significant pathology. Whether the patient has an active or present disease on any of these domains is registered. The co-morbidity score for each patient is calculated as the sum of the number of domains affected, giving a theoretical range from zero to seven. Based on this score, the mortality risk is classified into three grades: low (grade 0, zero score), medium (grade1, score of 1-2 co-morbidities) and high (grade 2, score of ≥ 3 co-morbidities) [11,12].

QoL was measured with a Norwegian validated translation of the Medical Outcomes Study 36 item Short Form health survey (MOS SF-36)[13-15].The SF-36 is a self-administered questionnaire that is well documented and validated in chronic dialysis patients of all ages. The questionnaire consists of 36 items, which are summarised into 8 scales, physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role emotional (RE) and mental health (MH). For each scale, the item scores are summarised and transformed to the eight 0 – 100 scales, (0 = poorest possible health state, 100= best possible health state) according to the SF 36 normed-based scoring algorithms [16]. We also used 3 questions from European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire regarding appetite and gastro-intestinal symptoms.

These questions are answered on a four point categorical scale ranging from “not at all” to “very much” [17].

Assessment of nutritional status

Body weight and height were measured before dialysis. After the dialysis session the patient was weighed again to calculate dry weight body mass index (BMI = weight (kg)/ height (m) ^{2}). The mid-upper arm circumference (MAC) was measured with the millimetre tap at the midpoint of the non-fistula arm, between the olecranon and acromion. The triceps skinfold (TSF) was measured at the same midpoint using a skinfold calliper. All anthropometry measurements were done by the same person.

The subjective global assessment of nutritional status (SGA) covers medical history (weight loss during the last 6 months, changes in food intake and gastrointestinal symptoms) and physical examination (assessment of subcutaneous fat loss, muscle wasting and oedemas) [18]. For this study a Norwegian version was used [19]. The patients' SGA scores was evaluated and classified as described by Detsky et al [18]. Each patient was classified as either; A (normally nourished) meaning stable or increased weight, normal body composition and no symptoms related to poor nutrition; B (moderately malnourished) implying weight loss up to 10% of total body weight without subsequent stabilization or weight increase, reduced energy intake but normal BMI (BMI > 20 kg/m^2) or; C (severely malnourished) meaning that the patient had weight loss more than 10% in 6 months, clear physical signs of impaired nutrition, oedemas and BMI < 20.

Anorexia may clinically be defined as a reduction or loss of appetite. We used one item from the EORTC QLQ-C30 questionnaire; “Have you lacked appetite?” to classify the patients as anorectic or not. Those who answered “not at all” were classified as having no anorexia whereas those who answered “a little”, “quite a bit” or “very much” were defined as having anorexia.

We used whole body bio impedance spectroscopy (BIS) to assess body composition in terms of extracellular (ECW), intracellular (ICW) and total body water (TBW), and to estimate lean tissue mass (LTM) and fat tissue mass (FTM). The measurement was made with the patient in a supine position, with electrodes placed on the hand and the foot, using the Body Composition Monitor (BCM) from Fresenius Medical Care, Germany. The BCM measures the impedance spectroscopy at 50 frequencies. The calculation of ECW, TBW and ICW by this method is validated against corresponding reference methods, i.e. sodium bromide dilution, deuterium dilution, and the total body potassium [20] respectively. The calculated body composition (fat and fat free mass) has been validated against dual-energy X-ray absorptiometry, DEXA and air displacement plethysmography [21,22]. The cut off threshold to define overhydration was set to an excess of ECW of $> 15\%$, which is comparable to overhydration of ~ 2.5 L, and is associated with higher mortality rates [9]. LTM and FTM were normalized to body surface area to obtain lean tissue index, LTI (LTI = LTM/height^2) and fat tissue index (FTI = FTM/height^2). The values for LTI and FTI were compared to an age (18 – 80 years) and gender match reference population [23]. Values below the 10th percentile were regarded as a clinically significant reduction in muscle mass or fat mass.

Hand grip strength (HGS) is a valid method for assessing muscle-strength, a marker of muscle mass, and has shown strong correlation with lean body mass [24-26]. The HGS assessment was done with a single spring handgrip dynamometer, while patient was sitting in an upright and relaxed position. The measurements were repeated three times and the highest score was recorded [24,27,28]. We classified the patients as having "decreased muscle strength" when HGS values were below 85% of the normal age and gender adjusted values [29].

Serum albumin is a marker of protein metabolism and an indicator of visceral protein stores that is widely used in nutritional studies in dialysis patients, and has shown a strong association with survival [30]. C- reactive protein (CRP) is an acute phase protein. A serum concentration of CRP ≥ 10 mg/L indicates the presence of inflammation [31]. Low values of total serum cholesterol (< 100mg/dl) are associated with higher mortality, and this is likely due to inflammation/malnutrition [32,33].

Analysis and statistical strategies.

Based on the data collected for nutritional assessments, we classified our patients as being cachectic or not. According to Evans et al [6] cachexia in adults may be diagnosed by the following criteria:

Weight loss of at least 5% in 12 months or BMI < 20 kg/m², plus at least 3 of the following criteria: 1) decreased muscle strength, 2) fatigue **(**defined as physical and/or mental weariness resulting from exertion), 3) anorexia (limited food intake or poor appetite), 4) low fat free mass index (lean tissue depletion), and 5) abnormal biochemistry; increased inflammatory markers CRP (> 5.0 mg/L), anaemia (Hb < 12 g/L) or low serum albumin (< 3.2 g/dl)[6]. To classify the patients in this study we used weight loss and/or low BMI, plus at least 3 of the following: 1) decreased muscle strength defined as decreased hand grip strength (HGS), 2) anorexia defined as having anorectic symptoms, 3) low fat free mass defined as low LTI (< 10 percentile) and 4) abnormal biochemistry (CRP> 5 or se-albumin < 3.2 g/dl).

All statistical analysis was performed using the statistical package SPSS for Windows version 15. We used descriptive statistics, and comparisons of QoL score between groups were done with non-parametric methods; Mann-Whitney U test, $p < 0.01$ was considered significant. A difference in SF-36 scores > 10 points between groups was considered as clinically significance [34], The Spearman coefficient of correlation was used to test correlation between bioimpedance measures (LTI, FTI) and hand grip strength (HGS), BMI, serum albumin and anthropometric measures.

Results

A total of 24 patients were included, 21 in HD and 3 in PD, 11 were females and 13 male, mean age was 81.4 (3. 2) years (Table 1). Almost all patients (92%) were well known (> 4 months) in the units (Table 1), and only 2 patients had started in dialysis acutely. Nephrosclerosis was the most common cause of ESRD (46%) followed by chronic glomerulonephritis (17%). Only 8 % had diabetic nephropathy.

According to the Davies comorbidity scores, no patient had low mortality risk, 15 (63%) had medium risk and 9 (37%) had high risk. Physical capacity as reported on the SGA questionnaire was reduced in most patients; only 2 had normal capacity, with no limitation, 13 subnormal capacity, with some limitation, 7 reported sitting mostly in a chair. None were mostly in bed and no patient was placed in a nursing home.

There were 7 patients with CRP> 5, 10 patients with serum albumin < 3.8 g/dL and 3 patients < 3.2 g/dL, there were no patients with serum cholesterol < 100 mg/dL (Table 1), 7 patients were using statins.

BIS turned out to be easy to use and the whole procedure lasted for only 15 minutes. All patients who were asked to participate agreed to be measured before the dialysis session started, but refused to wait for a repeated assessment 30 minutes after the dialysis was completed.

Insert Table 1

Nutritional status

We found that 41 % reported weight loss and 32 % reported substantial weight loss. The mean BMI among the participating patients was 24.7 kg/m², and a total of 9 patients had a BMI below 24 kg/m², 50 % reported appetite loss and 46 % had a LTI below the 10th percentile.

According to the SGA only two patients were in the normal category. Five patients could be classified as being severely malnourished (C) whereas the vast majority (68 %) was moderately malnourished (B). Two patients could not be classified due to missing data.

The BIS measures showed a LTI below the 10^{th} percentile of the reference population for a total of 11 patients, among whom only four had a correspondingly low FTI. Decreased muscle strength as measured by HGS and according to predefined criteria was found in 2 men and 8 women. LTI was correlated to HGS ($r = 0.50$, $p < 0.05$), and low LTI (< 10^{th} percentile) was strongly correlated to HGS ($r = 0.84$, $p < 0.01$). FTI showed correlation with TSF ($r = 0.41$, $p = 0.05$) and a strong correlation with BMI ($r = 0.78$, $p < 0.01$). The BCM showed overhydration (OH) > 1.0 L in 17 patients, 8 of these had OH > 2.5L.

Cachexia was identified in 6 patients (25%). Details showing the number of patients meeting the various criteria for the cachexia classifications are shown in Table 2.

Insert Table 2

The mean SF 36 scores for our patients on the various subscales are shown in Table 3.

Insert Table 3

When we compared the SF- 36 scores for cachectic vs non-cachectic patients, we found clinically significant differences for all subscales, but only for PF this difference was statistically significant. We also compared SF- 36 scores for overhydrated vs normohydrated patients, and found consistently better SF 36 scores for the latter group. These differences were clinically significant for five out of 8 scales (BP, GH, SF, RE and MH), but none were statistically significant (Table 3). Comparing patients with high comorbidity risk versus the others, we found better scores in favour of the low risk patients, with clinically significant differences for PF, RP, VT, GH and RE, no difference was statistically significant (data not shown).

Discussion

In this pilot study; BIS, SGA, anthropometry and self-reported appetite were used to assess nutritional status and overhydration in elderly dialysis patients. Independent of method, we found that a large proportion of the patients could be defined as having risk for nutritional deficits. However, the number of patients at risk varied with the measure that was used for identification. According to the SGA,

91 % were moderately or severely malnourished, 32 % reported substantial weight loss, 37.5 % had a BMI below 24, 50 % reported appetite loss and 46 % had a LTI below the tenth percentile. There was no consistent overlap between the assessments; hence, the results underline the need for a general agreement on how poor nutritional status should be identified in this group of patients.

To identify patients with severe protein and energy mass depletion, we used parameters according to a recently proposed cachexia definition by Evans et al [6] Six patients were defined as cachectic, and our results indicate that this approach enables the identification of a group of patients requiring special attention. Comparing the group of patients defined as cachectic with the non-cachectic patients, revealed that the former consistently reported poorer on all QoL scales.

As recommended by the ISRNM, it would also have been relevant to identify protein energy wasting (PEW) which is regarded as a pre-stage of the more serious cachexia. However, the PEW classification requires a criteria based on dietary intake. Detailed registrations of protein/energy intake, are time consuming, require assistance of skilled personnel, and could not be carried out for practical reason. The procedure might be too extensive for most clinical settings, [35], hence, we find that using the proposed cachexia definition may be an alternative to ensure that the most seriously affected patients are identified.

SGA is a recommended and validated method for assessing nutritional status in the adult dialysis population [36]. In our study, the majority of the patients were found to have some degree of malnutrition by this method. This frequency is higher than reported from most studies on nutritional status in dialysis patients [27,37], and may be explained by the older age of our patients [38]. In general, nutritional problems are more frequent in the elderly and a higher incidence of appetite loss has formerly been revealed in the older dialysis population compared younger ones [39]. Malnutrition refers to the presence of inadequate nutrient intake while PEW and cachexia are reckoned to be influenced by other factors such as inflammatory processes and nutrient losses into dialysate [5]. It is possible that malnutrition as identified by SGA predisposes to PEW and cachexia, but this is not proven. Considering the likely importance of treating malnutrition early, SGA should be used for nutritional assessment in the adult dialysis population in addition to methods to identify PEW or cachexia.

In addition to an association between severe nutritional problems and poor QoL, our results indicate that overhydration and comorbidity may negatively affect QoL, particularly the physical domains. These domains were also those mostly affected in the overall patient sample. Compared to younger Norwegian dialysis patients, scores were lower for PF, RP and VT, but quite similar for mental health and social function.

[40]. Even poorer SF-36 scores have been reported from other elderly dialysis populations, but the pattern has been similar [2,1].

Due to the cross-sectional design and the small sample size, our results should be interpreted with caution. Another study limitation is that the BIS assessments were done only before dialysis, based on the patients' preferences. This is adequate for hydration status, but may affect the estimates for measures like LTI and FTI. A smaller study demonstrated that pre- and post-treatment LTI mean may vary 1.12 kg ± 1.7, indicating that our LTI results might be overestimated [41]. Furthermore, the age reference range for the Body Composition Monitor (BCM; Fresenius) is from 18 to 80 years, and there are few studies addressing the elderly dialysis population > 75 years of age and the studies have small sample sizes. Thus reference values for the older population might be connected with some uncertainty.

BIS was found to be an easy and acceptable method for body composition assessment in this cohort, provided that the patients did not have to spend time repeating the analysis after the dialysis session. The method enabled identification of muscle loss, which is regarded an important feature of both cachexia and PEW and is associated with increased morbidity and mortality [42,43]. As exemplified by our results, muscular depletion is difficult to reveal by simpler measures. Six out of 11 patients with low LTI had BMI within normal range, whereas four out of nine patients with BMI < 24 did not have muscle loss. We also found that very few patients had low FTI ($<10^{th}$ percentile) even if they had low muscular mass, and despite a high frequency of nutritional deficits and cachexia, measures of triceps skin fold were higher in this study than reported from younger populations [28,8]. These findings further underline the particular importance of assessing body composition to reveal nutritional risks in the elderly where muscle mass tend to be replaced by fat as a part of the aging process. Furthermore, BIS detected overhydration in 17 patients and serious overhydration in 8 patients (33 %), which is a higher frequency than reported from a European multi centres study [10]. The result may suggest that overhydration is also a greater problem among the oldest dialysis patients. As overhydration is associated with increased mortality and, as shown in this study, probably also reduced quality of life, accurate assessment is crucial, giving further arguments to routine use of BIS.

In this study, only a small minority of the patients were within normal or optimal range on all parameters used to assess nutritional status. A high proportion had pathological body composition, most of whom had severe muscular depletion, and a quarter of the patients were classified as being cachectic. Our findings call for more attention to nutritional status in elderly dialysis patients, including more thorough assessments and the use of nutritional supplements when indicated. Furthermore, our study demonstrates how the reported frequency of poor nutritional status may vary with assessment method, hence, underlining the need for a general agreement on how nutritional status should be assessed, identified and reported.

There are very few studies dealing with nutrition and hydration status in this population. More focus is clearly needed as well as bigger studies to confirm our findings.

Conflict of interest: The authors declare that they have no conflict of interest

References

1. Carmichael P, Popoola J, John I, Stevens PE, Carmichael AR (2000) Assessment of quality of life in a single centre dialysis population using the KDQOL-SF questionnaire. Qual Life Res 9 (2):195-205

2. Loos C, Briancon S, Frimat L, Hanesse B, Kessler M (2003) Effect of end-stage renal disease on the quality of life of older patients. J Am Geriatr Soc 51 (2):229-233

3. Kuhlmann MK, Kribben A, Wittwer M, Hörl WH (2007) OPTA - Malnutrition in chronic renal failure. Nephrol Dial Transplant 22 (suppl 3):iii13-iii19. doi:10.1093/ndt/gfm016

4. Chauveau P, Combe C, Laville M, Fouque D, Azar R, Cano N, Canaud B, Roth H, Leverve X, Aparicio M (2001) Factors influencing survival in hemodialysis patients aged older than 75 years: 2.5-year outcome study. Am J Kidney Dis 37 (5):997-1003

5. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, Franch H, Guarnieri G, Ikizler TA, Kaysen G, Lindholm B, Massy Z, Mitch W, Pineda E, Stenvinkel P, Trevino-Becerra A, Wanner C (2008) A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney Int 73 (4):391-398

6. Evans WJ, Morley JE, Argiles J, Bales C, Baracos V, Guttridge D, Jatoi A, Kalantar-Zadeh K, Lochs H, Mantovani G, Marks D, Mitch WE, Muscaritoli M, Najand A, Ponikowski P, Rossi Fanelli F, Schambelan M, Schols A, Schuster M, Thomas D, Wolfe R, Anker SD (2008) Cachexia: a new definition. Clin Nutr 27 (6):793-799

7. Evans WJ Skeletal muscle loss: cachexia, sarcopenia, and inactivity. The American journal of clinical nutrition 91 (4):1123S-1127S

8. Ohkawa S, Odamaki M, Ikegaya N, Hibi I, Miyaji K, Kumagai H (2005) Association of age with muscle mass, fat mass and fat distribution in non-diabetic haemodialysis patients. Nephrol Dial Transplant 20 (5):945-951

9. Wizemann V, Wabel P, Chamney P, Zaluska W, Moissl U, Rode C, Malecka-Masalska T, Marcelli D (2009) The mortality risk of overhydration in haemodialysis patients. Nephrol Dial Transplant 24 (5):1574-1579

10. Wabel P, Chamney P, Moissl U, Jirka T (2009) Importance of whole-body bioimpedance spectroscopy for the management of fluid balance. Blood Purif 27 (1):75-80

11. Davies SJ, Phillips L, Naish PF, Russell GI (2002) Quantifying comorbidity in peritoneal dialysis patients and its relationship to other predictors of survival. Nephrol Dial Transplant 17 (6):1085-1092

12. Davies SJ, Russell L, Bryan J, Phillips L, Russell GI (1995) Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis patients: their interrelationship and prediction of survival. Am J Kidney Dis 26 (2):353-361

13. Ware JE, Jr., Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30 (6):473-483

14. Loge JH, Kaasa S, Hjermstad MJ, Kvien TK (1998) Translation and performance of the Norwegian SF-36 Health Survey in patients with rheumatoid arthritis. I. Data quality, scaling assumptions, reliability, and construct validity. J Clin Epidemiol 51 (11):1069-1076

15. Loge JH, Kaasa S (1998) Short form 36 (SF-36) health survey: normative data from the general Norwegian population. Scand J Soc Med 26 (4):250-258

16. Medical Outcomes Trust (ed) (1994) How to score the SF-36 health survey. Medical Outcomes Trust, Boston

17. Kaasa S, Bjordal K, Aaronson N, Moum T, Wist E, Hagen S, Kvikstad A (1995) The EORTC core quality of life questionnaire (QLQ-C30): validity and reliability when analysed with patients treated with palliative radiotherapy. Eur J Cancer 31A (13-14):2260-2263

18. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, Jeejeebhoy KN (1987) What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr 11 (1):8-13

19. Thoresen L, Fjeldstad I, Krogstad K, Kaasa S, Falkmer UG (2002) Nutritional status of patients with advanced cancer: the value of using the subjective global assessment of nutritional status as a screening tool. Palliative medicine 16 (1):33-42

20. Moissl UM, Wabel P, Chamney PW, Bosaeus I, Levin NW, Bosy-Westphal A, Korth O, Muller MJ, Ellegard L, Malmros V, Kaitwatcharachai C, Kuhlmann MK, Zhu F, Fuller NJ (2006) Body fluid volume determination via body composition spectroscopy in health and disease. Physiol Meas 27 (9):921-933

21. Moissl U (2007) Validation of a 3C model for determination of body fat mass. J Am Soc Nephrol 18:257A

22. Chamney PW, Wabel P, Moissl UM, Muller MJ, Bosy-Westphal A, Korth O, Fuller NJ (2007) A whole-body model to distinguish excess fluid from the hydration of major body tissues. Am J Clin Nutr 85 (1):80-89

23. Wieskotten S, Heinke S, Wabel P, Moissl U, Becker J, Pirlich M, Keymling M, Isermann R (2008) Bioimpedance-based identification of malnutrition using fuzzy logic. Physiol Meas 29 (5):639-654
24. Heimburger O, Qureshi AR, Blaner WS, Berglund L, Stenvinkel P (2000) Hand-grip muscle strength, lean body mass, and plasma proteins as markers of nutritional status in patients with chronic renal failure close to start of dialysis therapy. Am J Kidney Dis 36 (6):1213-1225
25. Stenvinkel P, Barany P, Chung SH, Lindholm B, Heimburger O (2002) A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients. Nephrol Dial Transplant 17 (7):1266-1274
26. Konings CJ, Kooman JP, Schonck M, van Kreel B, Heidendal GA, Cheriex EC, van der Sande FM, Leunissen KM (2003) Influence of fluid status on techniques used to assess body composition in peritoneal dialysis patients. Perit Dial Int 23 (2):184-190
27. Wang AY, Sea MM, Ho ZS, Lui SF, Li PK, Woo J (2005) Evaluation of handgrip strength as a nutritional marker and prognostic indicator in peritoneal dialysis patients. Am J Clin Nutr 81 (1):79-86
28. Qureshi AR, Alvestrand A, Danielsson A, Divino-Filho JC, Gutierrez A, Lindholm B, Bergstrom J (1998) Factors predicting malnutrition in hemodialysis patients: a cross-sectional study. Kidney Int 53 (3):773-782
29. Klidjian AM, Archer TJ, Foster KJ, Karran SJ (1982) Detection of dangerous malnutrition. JPEN J Parenter Enteral Nutr 6 (2):119-121
30. Tentori F, Hunt WC, Rohrscheib M, Zhu M, Stidley CA, Servilla K, Miskulin D, Meyer KB, Bedrick EJ, Johnson HK, Zager PG (2007) Which targets in clinical practice guidelines are associated with improved survival in a large dialysis organization? J Am Soc Nephrol 18 (8):2377-2384
31. Tsirpanlis G, Bagos P, Ioannou D, Bleta A, Marinou I, Lagouranis A, Chatzipanagiotou S, Nicolaou C (2004) Exploring inflammation in hemodialysis patients: persistent and superimposed inflammation. A longitudinal study. Kidney Blood Press Res 27 (2):63-70
32. Liu Y, Coresh J, Eustace JA, Longenecker JC, Jaar B, Fink NE, Tracy RP, Powe NR, Klag MJ (2004) Association between cholesterol level and mortality in dialysis patients: role of inflammation and malnutrition. Jama 291 (4):451-459
33. Kilpatrick RD, McAllister CJ, Kovesdy CP, Derose SF, Kopple JD, Kalantar-Zadeh K (2007) Association between serum lipids and survival in hemodialysis patients and impact of race. J Am Soc Nephrol 18 (1):293-303

34. Osoba D, Rodrigues G, Myles J, Zee B, Pater J (1998) Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 16 (1):139-144
35. Rockett HR, Berkey CS, Colditz GA (2003) Evaluation of dietary assessment instruments in adolescents. Current opinion in clinical nutrition and metabolic care 6 (5):557-562. doi:10.1097/01.mco.0000087971.83880.08
36. Steiber A, Leon JB, Secker D, McCarthy M, McCann L, Serra M, Sehgal AR, Kalantar-Zadeh K (2007) Multicenter study of the validity and reliability of subjective global assessment in the hemodialysis population. J Ren Nutr 17 (5):336-342
37. de Mutsert R, Grootendorst DC, Boeschoten EW, Brandts H, van Manen JG, Krediet RT, Dekker FW (2009) Subjective global assessment of nutritional status is strongly associated with mortality in chronic dialysis patients. Am J Clin Nutr 89 (3):787-793
38. Bossola M, Giungi S, Luciani G, Tazza L (2009) Appetite in chronic hemodialysis patients: a longitudinal study. J Ren Nutr 19 (5):372-379
39. Bossola M, Luciani G, Rosa F, Tazza L (2011) Appetite and gastrointestinal symptoms in chronic hemodialysis patients. J Ren Nutr 21 (6):448-454
40. Østhus TB, Dammen T, Sandvik L, Bruun CM, Nordhus IH, Os I (2010) Health-related quality of life and depression in dialysis patients: associations with current smoking. Scand J Urol Nephrol 44 (1):46-55
41. Wabel P (2007) Accuracy of bioimpedance spectroscopy (BIS) to detect fluid status changes in hemodialysis patients. Nephrol Dial Transplant 22 (suppl 6):VI 129
42. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel J-P, Rolland Y, Schneider SM, TopinkovÃ¡ E, Vandewoude M, Zamboni M (2010) Sarcopenia: European consensus on definition and diagnosis. Age Ageing 39 (4):412-423. doi:10.1093/ageing/afq034
43. Cawthon PM, Marshall LM, Michael Y, Dam T-T, Ensrud KE, Barrett-Connor E, Orwoll ES, for the Osteoporotic Fractures in Men Research G (2007) Frailty in older men: Prevalence, progression, and relationship with mortality. J Am Geriatr Soc 55 (8):1216-1223