Published in final edited form as:
Semin Dial. 2012 July ; 25(4): 423–427. doi:10.1111/j.1525-139X.2012.01097.x.

Accuracy and Limitations of the Diagnosis of Malnutrition in Dialysis Patients

Csaba P Kovesdy, MD[1,2] and **Kamyar Kalantar-Zadeh, MD, MPH**[3,4]

[1]Division of Nephrology, Salem Veterans Affairs Medical Center, Salem Virginia

[2]Division of Nephrology, University of Virginia, Charlottesville, Virginia

[3]Harold Simmons Center for Chronic Disease Research and Epidemiology, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California

[4]David Geffen School of Medicine at UCLA, Los Angeles, California

Abstract

Uremic malnutrition, also known as protein-energy wasting (PEW), is a common phenomenon in maintenance dialysis patients and a risk factor for poor clinical outcomes including worse quality of life and increased hospitalization and mortality. The paradoxical association between traditional cardiovascular risk factors and better outcomes in dialysis patients also referred to as “reverse epidemiology”, is a good example of the powerful effect-modifying impact of the nutritional status in this population. Measures of food intake, body composition tools, nutritional scoring systems, and laboratory values such as serum albumin are used to diagnose PEW and to assess the degree of severity of PEW without clearly validated diagnostic criteria. Some observational studies suggest that inflammation is a missing link between the PEW and poor clinical outcome in dialysis patients, although PEW per se may also predispose to illness and inflammation. Ongoing debate as to whether such surrogates as serum albumin or prealbumin concentrations are markers of nutritional status, inflammation, comorbidity or other conditions has led to confusion and diagnostic and therapeutic nihilism. Irrespective of the cause of hypoalbuminemia in dialysis patients, evidence suggests that nutritional interventions can increase serum albumin in dialysis patients. Hence, we should continue assessing serum albumin and other surrogates of nutritional status to risk-stratify patients and to allocate nutritional therapy, while well designed, large-scale, randomized, controlled trials of the effects of nutritional intake on clinical outcome are awaited.

Keywords

Dialysis; nutrition; inflammation; protein-energy malnutrition; food intake

Correspondence: Csaba P Kovesdy, MD, Salem VAMC (111D), 1970 Roanoke Blvd., Salem, VA 24153, Tel: 540-982 2463, Fax: 540-224 1963, csaba.kovesdy@va.gov.
Reprint Request: Kamyar Kalantar-Zadeh, MD PhD MPH, Harold Simmons Center for Chronic Disease, Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, 1124 West Carson Street, C1-Annex, Torrance, CA 90509-2910, Phone: 310-222-3891, Fax: 310-782-1837, kamkal@ucla.edu

Potential Conflict of Interest:
KKZ has received honoraria from Abbott Nutrition and BBraun, the manufacturers of oral nutritional supplements for CKD patients.

Introduction

Patients undergoing maintenance dialysis (MD) experience lower quality of life, significantly greater morbidity, higher hospitalization rates and higher mortality as compared to the general population.(1;2) Malnutrition, defined as a decline in protein and calorie intake followed by a decrease in the levels of various nutritional markers, develops once glomerular filtration rate (GFR) decreases to approximately <25–38 ml/min.(1) The prevalence of PEW is common even in patients with non-dialysis dependent CKD, as shown in a recent study of 1220 non-dialysis dependent CKD patients, of whom 45% had a serum albumin <3.6 g/dL and 22% <3.4 g/dL.(2) Numerous reports indicate that there is a similarly high rate of malnutrition ranging from 18% to 75% in MD patients.(3) In contrast to the general population where *over*-nutrition is associated with increased risk of cardiovascular disease, decreased nutritional measures such as a low body mass index or weight-for-height(4) or a reduced serum cholesterol concentration (<150 mg/dL)(5) appear to be strongly correlated with increased morbidity and mortality including higher risk of cardiovascular death in non-dialysis dependent chronic kidney disease (CKD) and in MD patients. This paradoxical observation can be referred to as “reverse epidemiology” in the CKD and MD population, and has been observed with regard to the impact of blood pressure on mortality in MD patients as well as in other conditions associated with chronic illnesses or debility.(6;7)

The strong predictive value of malnutrition in patients with all stages of CKD makes its accurate diagnosis important from a prognostic standpoint. Furthermore, its accurate diagnosis is imperative if therapeutic interventions against malnutrition are contemplated with a goal towards improving clinical outcomes. Diagnostic accuracy requires comparisons to gold standard tests. “Malnutrition” in CKD does not even have a uniformly agreed upon definition, let alone a gold standard test, which makes formal testing of clinically useful diagnostic tests difficult. We will first discuss the nomenclature of “malnutrition” arguing for the need for a more comprehensive terminology, and we will review the various diagnostic tests available to diagnose “malnutrition”, and their clinical utility as prognostic markers and as potential therapeutic targets.

Malnutrition: Nomenclatural clarification

The dictionary definition of malnutrition is “faulty nutrition due to inadequate or unbalanced intake of nutrients or faulty digestion or utilization of foods”.(8) The nomenclatural confusion related to malnutrition in CKD and MD is largely a result of a strict focus on low nutrient intake as the sole determinant of “malnutrition”, whereas in uremic patients one will most often detect a state of “wasting” as a result of more complex processes. MD patients have a high prevalence of comorbid conditions that are often associated with inflammatory processes.(9;10) There appears to be a strong association between malnutrition and inflammation in MD patients with both playing complementary roles in the development of wasting (11) and in these individuals both malnutrition and inflammation are associated with increased morbidity and mortality, including risk of cardiovascular death.(10;12) Since one of the effects of inflammation (and of other conditions such as metabolic acidosis or insulin resistance) can be the “faulty utilization of foods” in the form of hyper-catabolism, one can

indeed argue that the term “malnutrition” can and should be used broadly to encompass all pathologic states leading to an under-nourished state, not just the ones related to low food intake. Nevertheless, to better underscore the complex nature of uremic malnutrition a recent expert panel has recommended the use of the term protein-energy wasting (PEW) to describe states of under nutrition that could result from a complex interplay of decreased nutrient intake and/or increased catabolism.(13)

Protein Energy Wasting: Diagnostic criteria

According to the International Society of Renal Nutrition and Metabolism (ISRNM) expert panel the diagnosis of PEW can be made using four main diagnostic criteria: (1) biochemical measures (serum albumin, prealbumin, transferrin and cholesterol); (2) measures of body mass (body mass index [BMI], unintentional weight loss and total body fat), (3) measures of muscle mass (total muscle mass, mid-arm muscle circumference and creatinine appearance) and (4) measures of dietary intake (dietary protein and energy intake) (Table 1). The expert panel also recognized additional measures such as appetite, food intake, energy expenditure, various measures of body composition, multiple laboratory markers (such as specific markers of inflammation) and also integrative nutritional scoring systems (subjective global assessment of nutrition and malnutrition-inflammation score).(13) The expert panel recommended that at least three out of the four diagnostic categories (and at least one test in each of the selected category) must be abnormal for the diagnosis of PEW. Optimally, each criterion should be documented on at least three occasions, preferably 2–4 weeks apart.(13) As none of the proposed tests are validated for PEW their use has to be applied with an understanding of their limitations.

Controversies surrounding the diagnostic tests of PEW

Biochemical measures

A low serum albumin is one of the strongest predictors of outcomes in CKD and MD patients,(2;14) but it remains unclear to what extent a low serum albumin, or its decline in time are a result of low nutrient intake, increased catabolism, protein losses, or a combination of these. Nevertheless, a broad definition such as PEW which encompasses a spectrum of abnormalities makes it possible to use serum albumin as a somewhat specific diagnostic criterion. Hypoalbuminemia secondary to decreased production due to liver disease may, however, not be representative of PEW. Low serum prealbumin (a.k.a. transthyretin) is also recommended as a biochemical marker of PEW, as they can develop either as a result of malnutrition, or inflammation.(15;16) However, serum prealbumin itself is also not a pure marker of PEW, as its levels can be increased in CKD as a result of retinol-binding protein degradation by the renal tubules and a consequent increase in the amount of transthyretin bound by it.(16) Nevertheless, low serum prealbumin, and especially a decrease in prealbumin over time has been shown to be a predictor of poor outcomes even in patients with normal serum albumin,(17) which suggests that it could be a bona fide diagnostic tool to be used in conjunction with other biomarkers. Low serum cholesterol levels represent one of the more controversial diagnostic criteria of PEW, due to the belief that such low levels are beneficial towards preventing cardiovascular events and cardiovascular mortality in the general population.(18) These beliefs persist in spite of the

consistent associations of low serum cholesterol with adverse clinical outcomes in MD(19–25) and in CKD patients,(26) and the failure of multiple large clinical trials of cholesterol lowering to show a lowering in mortality rates.(27–29) While decreased cholesterol levels that are the result of cholesterol-lowering therapy should obviously not be used to diagnose PEW, such diagnosis could be confounded by hypocholesterolemia induced by intentional dietary restrictions, although uncommon in the stage IV–V CKD population.

Measures of body mass

Body mass index is the most commonly applied measure representing the weight-for-height relationship, and a BMI level <23 kg/m^2 can be used as a means to define PEW.(13) The accuracy of this threshold will, however, be influenced by race-ethnicity, especially in Southeast Asians, whereby similar levels may not indicate a pathologic state.(30) Indeed BMI may have differential associations with survival when African American, Hispanic and non-Hispanic Caucasian dialysis patients are compared,(31) Furthermore, the effect of BMI on outcome in ESRD patients may be to a great extent related to muscle mass than body fat.(32–34) Indeed higher muscle mass has been shown to be associated with greater survival in dialysis patients.(35;36) Furthermore, it is worth mentioning that the normal BMI in the general population according to the World Health Organization is 18.5–25 kg/m^2; hence, a significant proportion of CKD and MD patients with PEW based on a BMI <23 kg/m^2 may be erroneously classified as having an ideal weight by practitioners not aware of the CKD-specific differences in this diagnostic criterion. Observational studies have suggested that a decline in BMI over time may be associated with increased mortality,(37;38) and unintentional weight loss in itself is considered a diagnostic criterion of PEW: it is recommended that a loss of 5% dry weight over 3 months should be considered diagnostic of PEW independent of the baseline weight.(13) Intentional weight loss is considered a beneficial (albeit regrettably infrequent) event in the general population, and hence it should probably not be regarded as a diagnostic criterion for PEW in CKD or MD. Whether or not intentional weight loss is beneficial or harmful, and whether the baseline body weight modifies the effect of intentional weight loss in these populations remains an open question that requires future testing in clinical trials. A third measure of body mass that can be considered to diagnose PEW is a low percentage of body fat, which has also been associated with adverse outcomes.(39–41) A percentage of body fat value of <10% was suggested as diagnostic of PEW,(13) but the specificity of this diagnostic criterion is also questionable in persons who are very muscular and athletic.

Measures of muscle mass

Due to potential confounding by body water or fat mass BMI is not a reliable measure of body composition, and hence of PEW; a more reliable measure is low muscle mass, albeit the sarcopenia that develops as a result of ageing could again be considered a physiologic phenomenon and hence could decrease the specificity of this diagnostic criterion of PEW.(13) This criterion is in addition also not very practically feasible, since there are currently no universally accepted easily applicable and accurate tools to measure muscle mass or its changes over time in clinical practice.(42) Methods such as bioelectrical impedance analysis and near-infrared interactance have been shown to reliably correlate with other measures of nutritional status and to predict outcomes,(43–47) but they require specialized equipment

and are still not available for mainstream clinical use. An alternative method is to indirectly assess muscle mass based on pre-dialysis serum creatinine or on urinary creatinine appearance.(48–50) The accuracy of this is, however, affected by intestinal creatinine degradation and by the dialysis dose (in MD patients).(51)

Measures of dietary intake

Assessment of dietary intake in dialysis patients is somewhat challenging.(52) Moreover, there are racial and ethnic differences in the amount of protein and fat intake in that African American dialysis patient appear to have higher fat intake.(53) Unintentional decrease of dietary protein intake of <0.80 g/kg/day for at least 2 months for dialysis patients or <0.6 g/kg/day for patients with CKD stages 2–5, and unintentional decrease in dietary energy intake of <25 kcal/kg/day for at least 2 months are also recognized as indicative of PEW. (13) The precise measurement of these indicators is, however, problematic.(54;55) Furthermore, the above thresholds are considered rather conservative as the daily protein and energy needs of most dialysis patients are thought to be significantly higher,(56) hence it is likely that their specificity would be high, but their sensitivity would be low.

Conclusions

Determining the accuracy of the diagnosis of PEW would require a formal assessment of a certain diagnostic test against a gold standard. The lack of either a well-defined formal test or a gold standard test for PEW makes formal assessment of diagnostic accuracy impossible. Furthermore, the multitude of potential diagnostic criteria that can be employed to define PEW and the many flaws of these criteria could even make the very diagnosis of PEW difficult. Using a combination of criteria that encompass various different aspects of PEW makes an accurate diagnosis of this condition more likely, but one has to be cognizant of the pitfalls and exceptions that could render the applied diagnostic criteria invalid.

Acknowledgments

None

Funding Source: The study was supported by a research grant from the National Institute of Diabetes, Digestive and Kidney Disease of the National Institutes of Health R01 DK078106. KKZ was also supported by a philanthropist grant from Mr. Harold Simmons and a research grant from DaVita Clinical Research.

Reference List

1. Kopple JD, Greene T, Chumlea WC, Hollinger D, Maroni BJ, Merrill D, Scherch LK, Schulman G, Wang SR, Zimmer GS. Relationship between nutritional status and the glomerular filtration rate: results from the MDRD study. Kidney Int. 2000; 57:1688–1703. [PubMed: 10760105]
2. Kovesdy CP, George SM, Anderson JE, Kalantar-Zadeh K. Outcome predictability of biomarkers of protein-energy wasting and inflammation in moderate and advanced chronic kidney disease. Am J Clin Nutr. 2009; 90:407–414. [PubMed: 19535427]
3. Mehrotra R, Kopple JD. Nutritional management of maintenance dialysis patients: why aren't we doing better? Annu Rev Nutr. 2001; 21:343–379. [PubMed: 11375441]
4. Kopple JD, Zhu X, Lew NL, Lowrie EG. Body weight-for-height relationships predict mortality in maintenance hemodialysis patients. Kidney Int. 1999; 56:1136–1148. [PubMed: 10469384]

5. Lowrie EG, Lew NL. Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis. 1990; 15:458–482. [PubMed: 2333868]
6. Zager PG, Nikolic J, Brown RH, Campbell MA, Hunt WC, Peterson D, Van Stone J, Levey A, Meyer KB, Klag MJ, Johnson HK, Clark E, Sadler JH, Teredesai P. "U" curve association of blood pressure and mortality in hemodialysis patients. Medical Directors of Dialysis Clinic, Inc. Kidney Int. 1998; 54:561–569. [PubMed: 9690224]
7. Coresh J, Longenecker JC, Miller ER III, Young HJ, Klag MJ. Epidemiology of cardiovascular risk factors in chronic renal disease. J Am Soc Nephrol. 1998; 9:S24–S30. [PubMed: 11443765]
8. Merriem Webster's Medical Dictionary. 2007
9. Kaysen GA. Malnutrition and the acute-phase reaction in dialysis patients-how to measure and how to distinguish. Nephrol Dial Transplant. 2000; 15:1521–1524. [PubMed: 11007817]
10. Bergstrom J, Lindholm B, Lacson E Jr, Owen W Jr, Lowrie EG, Glassock RJ, Ikizler TA, Wessels FJ, Moldawer LL, Wanner C, Zimmermann J. What are the causes and consequences of the chronic inflammatory state in chronic dialysis patients? Semin Dial. 2000; 13:163–175. [PubMed: 10833777]
11. Kim Y, Molnar MZ, Rattanasompattikul M, Hatamizadeh P, Benner D, Kopple JD, Kovesdy CP, Kalantar-Zadeh K. Relative contributions of inflammation and inadequate protein intake to hypoalbuminemia in patients on maintenance hemodialysis. Int Urol Nephrol. 2012 In Press.
12. Yeun JY, Levine RA, Mantadilok V, Kaysen GA. C-Reactive protein predicts all-cause and cardiovascular mortality in hemodialysis patients. Am J Kidney Dis. 2000; 35:469–476. [PubMed: 10692273]
13. 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, Trevinho-Becerra A, Wanner C. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney Int. 2008; 73:391–398. [PubMed: 18094682]
14. Kalantar-Zadeh K, Kilpatrick RD, Kuwae N, McAllister CJ, Alcorn H Jr, Kopple JD, Greenland S. Revisiting mortality predictability of serum albumin in the dialysis population: time dependency, longitudinal changes and population-attributable fraction. Nephrol Dial Transplant. 2005; 20:1880–1888. [PubMed: 15956056]
15. Kopple JD, Mehrotra R, Suppasyndh O, Kalantar-Zadeh K. Observations with regard to the National Kidney Foundation K/DOQI clinical practice guidelines concerning serum transthyretin in chronic renal failure. Clin Chem Lab Med. 2002; 40:1308–1312. [PubMed: 12553435]
16. Cano NJ. Metabolism and clinical interest of serum transthyretin (prealbumin) in dialysis patients. Clin Chem Lab Med. 2002; 40:1313–1319. [PubMed: 12553436]
17. Rambod M, Kovesdy CP, Bross R, Kopple JD, Kalantar-Zadeh K. Association of serum prealbumin and its changes over time with clinical outcomes and survival in patients receiving hemodialysis. Am J Clin Nutr. 2008; 88:1485–1494. [PubMed: 19064507]
18. Pekkanen J, Linn S, Heiss G, Suchindran CM, Leon A, Rifkind BM, Tyroler HA. Ten-year mortality from cardiovascular disease in relation to cholesterol level among men with and without preexisting cardiovascular disease. N Engl J Med. 1990; 322:1700–1707. [PubMed: 2342536]
19. Lowrie EG, Lew NL. Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis. 1990; 15:458–482. [PubMed: 2333868]
20. Degoulet P, Legrain M, Reach I, Aime F, Devries C, Rojas P, Jacobs C. Mortality risk factors in patients treated by chronic hemodialysis. Report of the Diaphane collaborative study. Nephron. 1982; 31:103–110. [PubMed: 7121651]
21. Iseki K, Yamazato M, Tozawa M, Takishita S. Hypocholesterolemia is a significant predictor of death in a cohort of chronic hemodialysis patients. Kidney Int. 2002; 61:1887–1893. [PubMed: 11967041]
22. Liu Y, Coresh J, Eustace JA, Longenecker JC, Jaar B, Fink NE, Tracy RP, Powe NR, Klag MJ. Association between cholesterol level and mortality in dialysis patients: role of inflammation and malnutrition. JAMA. 2004; 291:451–459. [PubMed: 14747502]

23. Kalantar-Zadeh K, Horwich TB, Fonarow GC, et al. A low, rather than a high, serum LDL cholesterol is associated with increased mortality in hemodialysis patients even after controlling for inflammation. (abstract). J Am Soc Nephrol. 2004; 15:173A.
24. Kilpatrick RD, McAllister CJ, Kalantar-Zadeh K. Comparing mortality-predictability of serum total cholesterol and low density lipoprotein (LDL) cholesterol in hemodialysis patients. (abstract). J Am Soc Nephrol. 2005; 16:728A.
25. Habib AN, Baird BC, Leypoldt JK, Cheung AK, Goldfarb-Rumyantzev AS. The association of lipid levels with mortality in patients on chronic peritoneal dialysis. Nephrol Dial Transplant. 2006; 21:2881–2892. [PubMed: 16735386]
26. Kovesdy CP, Anderson JE, Kalantar-Zadeh K. Inverse Association between Lipid Levels and Mortality in Men with Chronic Kidney Disease Who Are Not Yet on Dialysis: Effects of Case Mix and the Malnutrition-Inflammation-Cachexia Syndrome. J Am Soc Nephrol. 2007; 18:304–311. [PubMed: 17167114]
27. Fellstrom BC, Jardine AG, Schmieder RE, Holdaas H, Bannister K, Beutler J, Chae DW, Chevaile A, Cobbe SM, Gronhagen-Riska C, De Lima JJ, Lins R, Mayer G, McMahon AW, Parving HH, Remuzzi G, Samuelsson O, Sonkodi S, Sci D, Suleymanlar G, Tsakiris D, Tesar V, Todorov V, Wiecek A, Wuthrich RP, Gottlow M, Johnsson E, Zannad F. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. N Engl J Med. 2009; 360:1395–1407. [PubMed: 19332456]
28. Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, Wanner C, Krane V, Cass A, Craig J, Neal B, Jiang L, Hooi LS, Levin A, Agodoa L, Gaziano M, Kasiske B, Walker R, Massy ZA, Feldt-Rasmussen B, Krairittichai U, Ophascharoensuk V, Fellstrom B, Holdaas H, Tesar V, Wiecek A, Grobbee D, de ZD, Gronhagen-Riska C, Dasgupta T, Lewis D, Herrington W, Mafham M, Majoni W, Wallendszus K, Grimm R, Pedersen T, Tobert J, Armitage J, Baxter A, Bray C, Chen Y, Chen Z, Hill M, Knott C, Parish S, Simpson D, Sleight P, Young A, Collins R. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011; 377:2181–2192. [PubMed: 21663949]
29. Wanner C, Krane V, Marz W, Olschewski M, Mann JF, Ruf G, Ritz E. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med. 2005; 353:238–248. [PubMed: 16034009]
30. Stevens J, Nowicki EM. Body mass index and mortality in asian populations: implications for obesity cut-points. Nutr Rev. 2003; 61:104–107. [PubMed: 12723643]
31. Ricks J, Molnar MZ, Kovesdy CP, Kopple JD, Norris KC, Mehrotra R, Nissenson AR, Arah OA, Greenland S, Kalantar-Zadeh K. Racial and ethnic differences in the association of body mass index and survival in maintenance hemodialysis patients. Am J Kidney Dis. 2011; 58:574–582. [PubMed: 21658829]
32. Kalantar-Zadeh K, Streja E, Kovesdy CP, Oreopoulos A, Noori N, Jing J, Nissenson AR, Krishnan M, Kopple JD, Mehrotra R, Anker SD. The obesity paradox and mortality associated with surrogates of body size and muscle mass in patients receiving hemodialysis. Mayo Clin Proc. 2010; 85:991–1001. [PubMed: 21037042]
33. Kalantar-Zadeh K, Streja E, Molnar MZ, Lukowsky LR, Krishnan M, Kovesdy CP, Greenland S. Mortality prediction by surrogates of body composition: an examination of the obesity paradox in hemodialysis patients using composite ranking score analysis. Am J Epidemiol. 2012; 175:793–803. [PubMed: 22427612]
34. Kovesdy CP, Czira ME, Rudas A, Ujszaszi A, Rosivall L, Novak M, Kalantar-Zadeh K, Molnar MZ, Mucsi I. Body mass index, waist circumference and mortality in kidney transplant recipients. Am J Transplant. 2010; 10:2644–2651. [PubMed: 21087417]
35. Noori N, Kopple JD, Kovesdy CP, Feroze U, Sim JJ, Murali SB, Luna A, Gomez M, Luna C, Bross R, Nissenson AR, Kalantar-Zadeh K. Mid-arm muscle circumference and quality of life and survival in maintenance hemodialysis patients. Clin J Am Soc Nephrol. 2010; 5:2258–2268. [PubMed: 20947789]
36. Noori N, Kovesdy CP, Dukkipati R, Kim Y, Duong U, Bross R, Oreopoulos A, Luna A, Benner D, Kopple JD, Kalantar-Zadeh K. Survival predictability of lean and fat mass in men and women

undergoing maintenance hemodialysis. Am J Clin Nutr. 2010; 92:1060–1070. [PubMed: 20844076]

37. Kalantar-Zadeh K, Kopple JD, Kilpatrick RD, McAllister CJ, Shinaberger CS, Gjertson DW, Greenland S. Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. Am J Kidney Dis. 2005; 46:489–500. [PubMed: 16129211]
38. Molnar MZ, Streja E, Kovesdy CP, Bunnapradist S, Sampaio MS, Jing J, Krishnan M, Nissenson AR, Danovitch GM, Kalantar-Zadeh K. Associations of body mass index and weight loss with mortality in transplant-waitlisted maintenance hemodialysis patients. Am J Transplant. 2011; 11:725–736. [PubMed: 21446975]
39. Kalantar-Zadeh K, Kuwae N, Wu DY, Shantouf RS, Fouque D, Anker SD, Block G, Kopple JD. Associations of body fat and its changes over time with quality of life and prospective mortality in hemodialysis patients. Am J Clin Nutr. 2006; 83:202–210. [PubMed: 16469976]
40. Kakiya R, Shoji T, Tsujimoto Y, Tatsumi N, Hatsuda S, Shinohara K, Kimoto E, Tahara H, Koyama H, Emoto M, Ishimura E, Miki T, Tabata T, Nishizawa Y. Body fat mass and lean mass as predictors of survival in hemodialysis patients. Kidney Int. 2006; 70:549–556. [PubMed: 16788699]
41. Fujino Y, Ishimura E, Okuno S, Tsuboniwa N, Maekawa K, Izumotani T, Yamakawa T, Inaba M, Nishizawa Y. Annual fat mass change is a significant predictor of mortality in female hemodialysis patients. Biomed Pharmacother. 2006; 60:253–257. [PubMed: 16740375]
42. Workeneh BT, Rondon-Berrios H, Zhang L, Hu Z, Ayehu G, Ferrando A, Kopple JD, Wang H, Storer T, Fournier M, Lee SW, Du J, Mitch WE. Development of a diagnostic method for detecting increased muscle protein degradation in patients with catabolic conditions. J Am Soc Nephrol. 2006; 17:3233–3239. [PubMed: 17005936]
43. Kaysen GA, Zhu F, Sarkar S, Heymsfield SB, Wong J, Kaitwatcharachai C, Kuhlmann MK, Levin NW. Estimation of total-body and limb muscle mass in hemodialysis patients by using multifrequency bioimpedance spectroscopy. Am J Clin Nutr. 2005; 82:988–995. [PubMed: 16280429]
44. Johansen KL, Kaysen GA, Young BS, Hung AM, da SM, Chertow GM. Longitudinal study of nutritional status, body composition, and physical function in hemodialysis patients. Am J Clin Nutr. 2003; 77:842–846. [PubMed: 12663281]
45. Conway JM, Norris KH, Bodwell CE. A new approach for the estimation of body composition: infrared interactance. Am J Clin Nutr. 1984; 40:1123–1130. [PubMed: 6507337]
46. Kalantar-Zadeh K, Dunne E, Nixon K, Kahn K, Lee GH, Kleiner M, Luft FC. Near infrared interactance for nutritional assessment of dialysis patients. Nephrol Dial Transplant. 1999; 14:169–175. [PubMed: 10052499]
47. Kalantar-Zadeh K, Block G, Kelly MP, Schroepfer C, Rodriguez RA, Humphreys MH. Near infra-red interactance for longitudinal assessment of nutrition in dialysis patients. J Ren Nutr. 2001; 11:23–31. [PubMed: 11172450]
48. Canaud B, Garred LJ, Argiles A, Flavier JL, Bouloux C, Mion C. Creatinine kinetic modelling: a simple and reliable tool for the assessment of protein nutritional status in haemodialysis patients. Nephrol Dial Transplant. 1995; 10:1405–1410. [PubMed: 8538933]
49. Bhatla B, Moore H, Emerson P, Keshaviah P, Prowant B, Nolph KD, Singh A. Lean body mass estimation by creatinine kinetics, bioimpedance, and dual energy x-ray absorptiometry in patients on continuous ambulatory peritoneal dialysis. ASAIO J. 1995; 41:M442–M446. [PubMed: 8573842]
50. Keshaviah PR, Nolph KD, Moore HL, Prowant B, Emerson PF, Meyer M, Twardowski ZJ, Khanna R, Ponferrada L, Collins A. Lean body mass estimation by creatinine kinetics. J Am Soc Nephrol. 1994; 4:1475–1485. [PubMed: 8161729]
51. Mitch WE, Collier VU, Walser M. Creatinine metabolism in chronic renal failure. Clin Sci (Lond). 1980; 58:327–335. [PubMed: 7379458]
52. Bross R, Noori N, Kovesdy CP, Murali SB, Benner D, Block G, Kopple JD, Kalantar-Zadeh K. Dietary assessment of individuals with chronic kidney disease. Semin Dial. 2010; 23:359–364. [PubMed: 20673254]

53. Noori N, Kovesdy CP, Dukkipati R, Feroze U, Molnar MZ, Bross R, Nissenson AR, Kopple JD, Norris KC, Kalantar-Zadeh K. Racial and ethnic differences in mortality of hemodialysis patients: role of dietary and nutritional status and inflammation. Am J Nephrol. 2011; 33:157–167. [PubMed: 21293117]

54. Avesani CM, Kamimura MA, Draibe SA, Cuppari L. Is energy intake underestimated in nondialyzed chronic kidney disease patients? J Ren Nutr. 2005; 15:159–165. [PubMed: 15648027]

55. Kloppenburg WD, de Jong PE, Huisman RM. The contradiction of stable body mass despite low reported dietary energy intake in chronic haemodialysis patients. Nephrol Dial Transplant. 2002; 17:1628–1633. [PubMed: 12198214]

56. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure. Am J Kidney Dis. 2000; 35:s1–s140. [PubMed: 10895784]

Table 1

Diagnostic criteria of protein-energy wasting in chronic kidney disease, and their potential drawbacks

	Diagnostic criteria	Advantages	Drawbacks
Biochemical Markers	Serum albumin <3.8 g/dL	Widely available. Robust association with adverse outcomes.	Decreased production may not represent PEW.
	Serum prealbumin (transthyretin) <30 mg/dL	Robust association with adverse outcomes.	Level affected by kidney function.
	Serum cholesterol <100 mg/dl	Widely available. Robust association with adverse outcomes.	Low level as a result of diet and exercise may not reflect PEW.
Body Mass and Composition	BMI <22 kg/m^2 (under 65 years) <23 kg/m^2 (>65 years)	Widely available. Robust association with adverse outcomes.	Low level as a result of diet and exercise may not reflect PEW.
	Unintentional weight loss over time: 5% over 3 months or 10% over 6 months	Specificity may be high.*	May be masked by fluid gain in MD patients.
	Total body fat percentage <10%	Sensitivity may be high.*	Low level as a result of diet and exercise may not reflect PEW.
Muscle Mass	Muscle wasting: Reduced muscle mass of 5% over 3 months or 10% over 6 months	Sensitivity may be high.*	Decrease in muscle mass could be a result of normal ageing. Measurement tools not widely available.
	Urinary creatinine appearance	Practically feasible method.	Can be affected by intestinal creatinine degradation and by the dialysis dose.
Dietary Intake	Unintentional low dietary protein intake: <0.80 g/kg/day for at least 2 months for dialysis patients or <0.6 g/kg/day for patients on CKD stages 2 to 5	Specificity may be high.*	Conservative cutoffs may result in low sensitivity.*

* No formal assessment of sensitivity and specificity available.