

## Editorial

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# Distinguishing Between Cachexia, Sarcopenia and Protein Energy Wasting in End-Stage Renal Disease Patients on Dialysis

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Patients with end-stage renal disease (ESRD) receiving dialysis can have altered nutritional status and body composition due to dietary restrictions, level of physical activity, co-morbidities, metabolic alterations and inflammation.<sup>1</sup> As such, weight loss or wasting is common among this population with up to 75% of adults with ESRD undergoing maintenance dialysis displaying some evidence of wasting.<sup>2</sup> There are several forms of loss of lean muscle mass or wasting in ESRD, including 'protein energy wasting', 'cachexia', and 'age-related sarcopenia' and these terms are often used interchangeably alongside 'malnutrition' in current care. Limited understanding of the differences between such terms is arguably a barrier to accurate recognition and management of these disorders in patients with ESRD. For instance, a recent European study of over 700 dietetic participants concluded that only 13% of health care professionals who could differentiate between malnutrition, starvation, cachexia and sarcopenia.<sup>3</sup> Such knowledge is pertinent as for example, loss of muscle mass is a key feature in both sarcopenia and cachexia, but most patients with sarcopenia are not cachectic,<sup>4</sup> as muscle wasting occurs with aging.

Research has informed a disease specific definition (and associated diagnostic criteria) for protein energy wasting (PEW) in renal disease, and while cachexia in ESRD is seen as the severe form of PEW,<sup>5</sup> there remains no consensus definition or diagnostic criteria to differentiate between PEW and cachexia. What distinguishes PEW from cachexia is that the latter relates to only severe forms of metabolic depletion. However, PEW can refer to mild reduction of lean muscle and depletion of energy stores.<sup>6</sup> Alongside, the lack of disease specific definition or diagnostic criteria for cachexia, there is also no such disease specific criterion for sarcopenia in renal disease. The evidence-based development of these terms is essential to enable health care professionals to clearly identify and differentiate between such conditions. This greater understanding of the difference and interplay between cachexia, PEW and sarcopenia in ESRD

has the potential to inform the development and testing of targeted novel therapeutic treatments aimed at reducing morbidity and mortality.<sup>7</sup> Significant progress has been made defining cachexia and its associated clinical characteristics in patients with cancer. An agreed definition and classification of cancer cachexia<sup>8</sup> has contributed to enhanced standardization of screening, staging assessment and management. This is a model that could be applied to cachexia in other chronic conditions, such as ESRD.

Reflecting the current evidence base, Table 1 outlines the characteristics of age-related sarcopenia, cachexia in chronic illness, and PEW in renal disease. These characteristics and associated pathologies are reviewed elsewhere in the literature,<sup>5,9-11</sup> and while the diagnostic criteria share similarities they are not identical. For example, weight loss is part of the definition of both cachexia in chronic illness and PEW in renal disease, but the duration of the weight loss differs (weight loss of 5% over 6 months in cachexia as opposed to 5% over 3 months in PEW). Additionally, the diagnostic criteria for cachexia in chronic illness emphasizes lean mass functionality (decreased muscle strength and fatigue), which is also common in sarcopenia of old age, although the defining characteristics of sarcopenia emphasize the importance of gait speed which cachexia does not. Furthermore, anaemia is considered a feature of cachexia in chronic illness, but not of PEW in renal disease or sarcopenia of old age.

	Sarcopenia of old age <sup>9</sup>	Cachexia in chronic illness <sup>10</sup>	Protein energy wasting in renal disease <sup>5,11</sup>
<b>(i) Weight</b>	Not stated, but weight gain is expected in obese sarcopenia whereas weight loss can occur otherwise	Oedema-free "unintentional" weight loss of at least 5% in 12 months or less in the presence of underlying illness.  In cases where weight loss cannot be documented, a BMI<18.5 kg/m <sup>2</sup> or a drop from higher BMI to a BMI<20 kg/m <sup>2</sup> is sufficient.	Unintentional weight loss over time: 5% over 3 months or 10% over 6 months.  Oedema-free BMI<23 kg/m <sup>2</sup> for example, post-dialysis dry weight.
<b>(ii) Biochemistry</b>	Not stated, but it is expected that serum creatinine relative to kidney function declines.	Increased inflammatory markers CRP (>3.0 mg/L), IL-6>3.0 pg/mL). Anaemia (<10 g/dL). Low serum albumin (<3.5 g/dl BGG or <3.2 BCP)	Serum albumin<3.8 g/dl (bromocresol green). Serum prealbumin (transthyretin)<30 mg/dL (for maintenance dialysis patients only; levels may vary according to GFR level for patients with CKD stages 2-5). Serum cholesterol<100 mg/dL
<b>(iii) Muscle and/or fat mass</b>	Low muscle mass<7.23-7.26 kg/m <sup>2</sup> for men and<5.5-5.67 kg/m <sup>2</sup> for women using appendicular lean tissue/height <sup>2</sup> by DEXA <sup>12</sup>	Low fat-free mass index. Lean tissue depletion i.e. mid upper arm muscle circumference<10 <sup>th</sup> percentile for age and gender); appendicular skeletal muscle index by DEXA <5.45 kg/m <sup>2</sup> in females and<7.25 kg/m <sup>2</sup> in males.	Total body fat percentage<10%. Reduced mid-arm muscle circumference area - reduction >10% in relation to 50th percentile of reference population. Muscle wasting: reduced muscle mass 5% over 3 months or 10% over 6 months. Indirect measure of muscle mass, such as serum creatinine.
<b>(iv) Muscle strength</b>	Low muscle strength, handgrip strength<20 kg women and<30 kg men.	Decreased muscle strength (lowest tertile).	Not stated
<b>(v) Functionality</b>	Gait speed<0.8 metres per second.	Presence of fatigue - defined as physical and/or mental weariness, resulting from exertion; an inability to continue exercise at the same intensity with a resultant deterioration in performance.	Not stated
<b>(vi) Dietary intake</b>	Not stated, but often some decline in appetite and/or protein and energy is observed.	Anorexia. Limited food intake (i.e. total energy intake<20 kcal/kg/day; <70% of usual food intake) or poor appetite.	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 with CKD stages 2-5. Unintentional low dietary energy intake<25 Kcal/kg/day for at least 2 months.
<b>Diagnosis</b>	Person must have column iii plus column iv or v.	Person must have column i plus three of the remaining five columns ii,iii,iv,v,or vi.	Person must have at least three out of the four columns i,ii,iii and vi and at least one test from each of the selected columns.

**Table 1:** Defining characteristics of sarcopenia of old age, cachexia in chronic illness and protein-energy wasting in renal disease.

As seen in Table 1, there are both variations and commonalities in the known clinical characteristics of sarcopenia, cachexia and PEW in a renal population. This may be reflective of the poly-symptomatic nature of ESRD. However, it makes the diagnosis of any of the three conditions more complex. Effectively distinguishing between these three conditions in ESRD is important, acknowledging that elements of sarcopenia and PEW may be present in cachexia, as interventional strategies may be very different for each. Work on delineating key clinical characteristics of PEW in renal disease has progressed extensively<sup>13</sup> and cachexia is viewed as a severe form of PEW.<sup>5</sup> However, the diagnostic criteria for cachexia in ESRD, as opposed to PEW, have not been agreed. This is significant as cachexia may involve additional metabolic abnormalities that are potentially amenable to therapeutic intervention.

What should the next steps be? Adoption of a disease-specific definition of cachexia in ESRD would contribute to standardization of screening, assessment and management strategies that are aimed at improving morbidity and mortality in these patients. Such a definition needs to be derived in such a way to distinguish cachexia from both sarcopenia and PEW, should define a population group with a different prognosis from PEW, and needs to reflect our understanding of the pathophysiology (particularly the role of inflammation) of cachexia in other conditions such as cancer, heart failure and COPD. Such a definition would greatly facilitate screening, diagnosis and development of treatments for this life-limiting complication of end stage renal disease.<sup>14,15</sup>

## REFERENCES

1. Ikizler TA, Cano NJ, Franch H, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: A consensus statement by the International Society of Renal Nutrition and Metabolism. *Kidney Int.* 2013; 84(6): 1096-107. doi: [10.1038/ki.2013.147](https://doi.org/10.1038/ki.2013.147)
2. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: Causes and consequence. *Am J Kidney Dis.* 2003; 42(5): 864-881. doi: [10.1016/j.ajkd.2003.07.016](https://doi.org/10.1016/j.ajkd.2003.07.016)
3. Beek TL, Vanhauwaert E, Slinde F, et al. Unsatisfactory knowledge and use of terminology regarding malnutrition, starvation, cachexia and sarcopenia among dietitians. *Clinical Nutrition.* 2016; 35(6): 1450-1456. doi: [10.1016/j.clnu.2016.03.023](https://doi.org/10.1016/j.clnu.2016.03.023)
4. Cuppari L, Meireles MS, Ramos CI, Kamimura MA. Subjective global assessment for the diagnosis of protein-energy wasting in nondialysis-dependent chronic kidney disease patients. *J Ren Nutr.* 2014; 24(6): 385-389. doi: [10.1053/j.jrn.2014.05.004](https://doi.org/10.1053/j.jrn.2014.05.004)
5. Fouque D, Kalantar-Zadeh K, Kopple J, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int.* 2008; 73: 391-398. doi: [10.1038/sj.ki.5002585](https://doi.org/10.1038/sj.ki.5002585)
6. Jadeja YP, Kher V. Protein energy wasting in chronic kidney disease: An update with focus on nutritional interventions to improve outcomes. *Indian J Endocrinol Metab.* 2012; 16(2): 246-51. doi: [10.4103/2230-8210.93743](https://doi.org/10.4103/2230-8210.93743)
7. Mak RH, Ikizler AT, Kovesdy CP, Raj DS, Stenvinkel P, Kalantar-Zadeh K. Wasting in chronic kidney disease. *J Cachexia Sarcopenia Muscle.* 2011; 2(1): 9-25 doi: [10.1007/s13539-011-0019-5](https://doi.org/10.1007/s13539-011-0019-5)
8. Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: An international consensus. *Lancet Oncol.* 2011; 12(5): 489-495. doi: [10.1016/S1470-2045\(10\)70218-7](https://doi.org/10.1016/S1470-2045(10)70218-7)
9. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the european working group on sarcopenia in older people. *Age Ageing.* 2010; 39(4): 412-423. doi: [10.1093/ageing/afq034](https://doi.org/10.1093/ageing/afq034)
10. Evans WJ, Morley JE, Argiles J, et al. Cachexia: A new definition. *Clin Nutr.* 2008; 27: 793-799. doi: [10.1016/j.clnu.2008.06.013](https://doi.org/10.1016/j.clnu.2008.06.013)
11. Kim JC, Kalantar-Zadeh K, Kopple JD. Frailty and protein-energy wasting in elderly patients with end stage kidney disease. *J Am Soc Nephrol.* 2013; 24(3): 337-351. doi: [10.1681/ASN.2012010047](https://doi.org/10.1681/ASN.2012010047)
12. Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981-2002. *J Nat Prod.* 2003; 66: 1022-1037. doi: [10.1021/np030096l](https://doi.org/10.1021/np030096l)
13. Obi Y, Qader H, Kovesdy CP, Kalantar-Zadeh K. Latest consensus and update on protein-energy wasting in chronic kidney disease. *Curr Opin Clin Nutr Metab Care.* 2015; 18(3): 254-262. doi: [10.1097/MCO.0000000000000171](https://doi.org/10.1097/MCO.0000000000000171)
14. Reid J, Noble H, Davenport A, et al. Defining cachexia in a renal population. *J Ren Care.* 2015; 41(2): 79-80. doi: [10.1111/jorc.12129](https://doi.org/10.1111/jorc.12129)
15. Reid J, Noble HR, Porter S, Shields JS, & Maxwell AP. A literature review of end-stage renal disease and cachexia: Understanding experience to inform evidence-based healthcare. *J Ren Care.* 2013; 39(1): 47-51. doi: [10.1111/j.1755-6686.2013.00341.x](https://doi.org/10.1111/j.1755-6686.2013.00341.x)