Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 79 (2016) 299–300

www.jcma-online.com

Editorial

Interaction between protein–energy wasting and geriatric nutritional risk index in elderly patients on dialysis

Protein–energy malnutrition has been proposed to be a cause of refractory anemia that accompanies the malnutrition–inflammation complex (or cachexia) syndrome in dialysis patients.[1] Malnutrition–inflammation complex syndrome and the obesity paradox are also the main etiology for "reverse epidemiology" of cardiovascular risk factors and outcomes in dialysis patients.[1,2] However, in some dialysis patients, protein-energy wasting (PEW) is not related to inadequate nutrient intake.[3] The 2013 International Society of Renal Nutrition and Metabolism meeting report notes that PEW is responsible for loss of protein mass and fuel reserve, and that PEW is a nonspecific inflammatory process. The term kidney disease wasting emphasizes the strong association between kidney diseases and PEW.[3] However, kidney disease wasting does not provide any insight into the different causes of PEW in kidney disease. Moreover, the lack of association between kidney disease (acute kidney injury and chronic kidney disease) and PEW may be found between young (pancreatitis) and elderly individuals (chronic obstructive pulmonary disease) with different etiologies. Therefore, the expert panel reached the conclusion that the term kidney disease wasting is not a suitable substitute for PEW.

There is a wide variety of causes of PEW and frailty in elderly patients with end-stage renal disease, including genotype, phenotype, comorbid conditions, duration and severity of renal failure, psychosocial problems, and lifestyle, in addition to low anabolic (insulin, growth hormone, and insulin growth factor-1) but high catabolic hormones (parathyroid hormone and glucagon), and age-related mitochondrial dysfunction and oxidative stress.[3–6] Numerous different terminologies have been used to describe the phenomena of malnutrition and inflammatory wasting coexisting in patients with kidney diseases, such as uremic malnutrition, protein–energy malnutrition, malnutrition–inflammation atherosclerosis syndrome, and malnutrition–inflammation complex syndrome. Several inflammatory markers, such as C-reactive protein, interleukin-6, tumor necrosis factor-α, interleukin-1, and serum amyloid A, have recently been shown to be associated with concomitant malnutrition and inflammatory wasting.[6]

Geriatric Nutritional Risk Index (GNRI) was first used to evaluate malnutrition and related morbidity and mortality in elderly patients.[7] It was validated to be a simple and objective screening tool requiring serum albumin, adjusted for ideal body weight and knee height. Recent studies applied GNRI to predict outcomes of heart failure and PEW in maintenance hemodialysis patients.[8,9] A wide variety of other instruments have been used for nutritional evaluation, such as the Subjective Global Assessment, Mini Nutritional Assessment-Screening Form, Malnutrition Universal Screening Tool, and Nutritional Risk Screening 2002.[8] Physical performance is also an important predictor of outcomes in the elderly and frail people. Chronic kidney disease and end-stage renal disease facilitate the process of wasting before the onset of frank cachexia. The Comprehensive Dialysis Study of the United States Renal Data System investigated the frailty, dialysis initiation, and mortality in maintenance dialysis.[10] However, the questionnaires, including the Research ANd Development (RAND) 12-item Short Form, 36-item Kidney Disease Quality of Life symptom scale, and Human Activity Profile via telephone interviews were subjective.[10]

Tsai et al[11] applied GNRI and demonstrated its long-term predictive value in a prospective cohort of elderly patients who underwent chronic hemodialysis. The authors concluded that patients with a GNRI of < 92 at baseline had significantly increased all-cause mortality during long-term follow-up. In addition, a low body mass index but high erythropoietin resistance index and high-sensitivity C-reactive protein were correlated with a low GNRI. Those patients with a low GNRI also had a low body weight, low body mass index, low serum albumin, low hemoglobin, and high erythropoietin resistance index initially. These variables are compatible with the symptoms of PEW.

This study had some limitations. First, this was a single-dialysis-unit study and thus could not represent the outcomes of all patients in our nationwide cohort. Second, although GNRI consists of simple objective measurements, the calculated parameter of weight/WLo (Lorentz equations) should be adjusted according to different values for GNRI, albumin, and weight loss.[7] It could not be clearly determine whether any modification of the equation through the detailed description was necessary. Third, erythropoietin resistance index is defined as the erythropoietin dose administered per

http://dx.doi.org/10.1016/j.jcma.2016.01.004

kilogram body weight per week. However, in many studies it has been suggested that the average value be monitored over a 3-month period to determine whether there is any possibility of correctable blood loss or illness.[1] Moreover, the erythropoietin responsiveness index with the same calculation was also used.

The quality of dialysis has greatly improved in Taiwan. We observed the same and improved patterns and percentages of cumulative survival between elderly dialysis patients with a GNRI of $\geq$ 92 and those with pure frailty without dialysis.[10,11] However, the mean age of the pure frailty group was comparatively higher.[10] Dialysis may reverse uremia, but residual metabolic derangements, inflammation, comorbid conditions, and the dialysis procedure itself may allow PEW to develop or worsen. Furthermore, it is possible that weight gain may occur while losing muscle, a phenomenon known as sarcopenic obesity, which is an important issue that needs to be addressed.[12,13] The time-averaged serum creatinine concentration is a more appropriate surrogate of muscle mass, and changes of serum creatinine over time may represent parallel changes in skeletal muscle mass.[13] Nutritional recommendations for the management of sarcopenic obesity are similar to those for PEW, which include exercise (aerobic and resistance), anti-inflammatory strategies, and adequate protein intake.[6,14]

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

References

1. Kalantar-Zadeh K, McAllister CJ, Lehn RS, Lee GH, Nissenson AR, Kopple JD. Effect of malnutrition−inflammation complex syndrome on EPO hyporesponsiveness in maintenance hemodialysis patients. *Am J Kidney Dis* 2003;**42**:761−73.
2. Kalantar-Zadeh K, Block G, Humphreys M, Kopple J. Reverse epidemiology of cardiovascular risk factor in maintenance dialysis patients. *Kidney Int* 2003;**63**:793−803.
3. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int* 2008;**73**:391−8.
4. 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**:337−51.
5. Tsai MT, Chen YT, Lin CH, Huang TP, Tarng DC, Taiwan Geriatric Kidney Disease Research Group. U-shaped mortality curve associated with platelet count among older people: a community-based cohort study. *Blood* 2015;**126**:1633−5.
6. Carrero JJ, Stenvinkel P, Cuppari L, Ikizler TA, Kalantar-Zadeh K, Kaysen G, et al. Etiology of the protein-energy wasting syndrome in chronic kidney disease: a consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM). *J Ren Nutr* 2013;**23**:77−90.
7. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr* 2005;**82**:777−83.
8. Kinugasa Y, Kato M, Sugihara S, Hirai M, Yamada K, Yanagihara K, et al. Geriatric nutritional risk index predicts functional dependency and mortality in patients with heart failure with preserved ejection fraction. *Circ J* 2013;**77**:705−11.
9. Tsai MT, Hu FH, Lien TJ, Chen PJ, Huang TP, Tarng DC. Interaction between geriatric nutritional risk index and decoy receptor 3 predicts mortality in chronic hemodialysis patients. *Am J Nephrol* 2014;**40**:191−9.
10. Bao Y, Dalrymple L, Chertow GM, Kaysen GA, Johansen KL. Frailty, dialysis initiation, and mortality in end-stage renal disease. *Arch Intern Med* 2012;**172**:1071−7.
11. Tsai MT, Liu HC, Huang TP. The impact of malnutritional status on survival in the elderly hemodialysis patients. *J Chin Med Assoc* 2016;**79**:309−13.
12. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;**56**:M146−56.
13. Kalantar-Zadeh K, Streja E, Kovesdy CP, Oreopoulos A, Noori N, Jing J, et al. 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.
14. Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, Deutz NE, et al. Nutritional recommendations for the management of sarcopenia. *J Am Med Dir Assoc* 2010;**11**:391−6.

Shuo-Chun Weng
Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC

Center for Geriatrics and Gerontology, Division of Nephrology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

Der-Cherng Tarng*
Department and Institute of Physiology and Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC

Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

*Corresponding author. Dr. Der-Cherng Tarng, Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: dctarng@vghtpe.gov.tw (D.-C. Tarng).