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Survival and body fat in hemodialysis patients: true association or effects of concomitant therapy? Reply

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Survival and body fat in hemodialysis patients: true association or effects of concomitant therapy?

Dear Sir:

The article by Kalantar-Zadeh et al (1) addresses a very important aspect of current cachexia research, particularly the phenomenon of “reverse epidemiology,” by reporting a close relation between a higher and increasing percentage of total body fat and better survival in maintenance hemodialysis (MHD) patients.

This finding adds to a growing body of literature that shows a surprising survival advantage of obese patients in chronic diseases, eg, in chronic heart failure (CHF) and aging, sometimes termed the “obesity paradox” (2, 3). Patients with CHF who lose 6% of their previous weight, thereby meeting the criteria of cachexia, have a particularly poor prognosis (4, 5). Notably, this observation is independent of the patient’s high or low baseline body mass index (4). The latter observation supports the view expressed by Kalantar-Zadeh et al, ie, that the advice given to obese patients to lose fat and become catabolic regardless of their limiting underlying disease may not have a solid basis.

Because the 535 patients with end-stage renal disease studied by Kalantar-Zadeh et al are prone to cardiovascular events, the reported survival advantage over the 30-mo follow-up of patients with a percentage body fat of $\geq 24\%$ is even more interesting, particularly if one considers that obesity has been widely viewed as an independent risk factor for cardiovascular diseases. Epidemiologic data for patients with chronic renal failure indicate a 5-y mortality rate of 66%. Cardiovascular events account for 88 deaths per 1000 patient-years at risk and continue to be the single largest cause of mortality (6).

The authors reported 19.8% mortality over a 30-mo follow-up period, which is lower than one would expect (1). Importantly, the precise cause of death was not reported, which could be helpful to highlight the mechanisms behind the “reverse epidemiology.” Without this information, the interpretation of a lower mortality rate is not complete and could also reflect a preselected healthier patient population.

Kalantar-Zadeh et al reported the presence of cardiovascular disease in 292 patients, ie, in 54% of their MHD patients. We assume that these patients were treated with a variety of cardiovascular drugs, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-2-receptor antagonists, β blockers, and statins for the management of hypertension, coronary artery disease (CAD), and CHF. It is well established that all these drugs improve the prognosis of patients with CAD. Moreover, β blockers and ACE inhibitors have also been shown to be associated with a survival advantage in patients with end-stage renal failure (7, 8). ACE inhibitors and β blockers are known to reduce the risk of weight loss (4), and β blockers inhibit lipolysis and increase body fat—at least in CHF (9). Statins have pleiotropic effects, including the ability to exert anti-inflammatory action. This might explain why the authors were

unable to show the expected correlation of body fat with increased proinflammatory cytokines (1). Therefore, it would be interesting to see whether the adjustment for medication use would affect the outcome in this study population.

The study by Kalantar-Zadeh et al focused on dynamic changes in body fat mass with the use of near-infrared (NIR) interactance to assess body composition. No data have validated this technique relative to dual-energy X-ray absorptiometry (DXA). The latter method is the gold standard for measuring body fat. NIR measurements are known to underestimate body fat increasingly as the degree of adiposity increases, especially in grossly obese women (10). Therefore, it would be interesting to see whether the reported association of a 1% increase in NIR-measured percentage body fat and a 3% lower mortality risk would be confirmed if DXA analysis is applied.

The authors observed that a decrease in percentage body fat in MHD patients was associated with a death risk 2 times that in patients who had an increase in percentage body fat over 6 mo. Because the authors did not report body weight changes during that period, the question arises whether a decrease in body fat content is paralleled by a shift toward lean mass.

The article by Kalantar-Zadeh et al clearly indicates the need for further basic and clinical studies with more long-term follow up to identify the pathophysiologic mechanisms leading to the increasingly observed obesity advantage in chronic illness and aging. More work is required to validate recommendations for body-composition targets in different chronic disease settings. Potentially, further insight into the underlying mechanisms could change current nutritional advice to patients. Nowadays, both professional and lay public generally regard overweight as a risk factor for morbidity and mortality irrespective of general health status. Future studies will show whether this will hold true for patients with advanced chronic organ failure.

No conflicts of interest were reported.

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health implications, especially because the current practice of medicine is heavily based on the universal opinion that “losing fat is better in everybody” (5). Many overweight dialysis and CHF patients may not benefit from losing weight. On the contrary, weight loss may be associated with adverse outcomes (6). Clinical trials to increase weight, muscle mass, and even body fat in cachectic dialysis and CHF patients are urgently needed.

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Reply to A Sandek et al

Dear Sir:

We thank Sandek et al for their important comments on our recent paper about the association of body fat and its changes over time with quality of life and prospective mortality in dialysis patients (1). In our study, we focused on all-cause mortality but agree that an examination of cause-specific mortality, including death from cardiovascular disease, may be clinically relevant as well, especially because almost one-half of all causes of death in dialysis patients are attributable to cardiovascular events (2). However, the diagnosis of death due to cardiovascular disease may be subject to ascertainment bias, especially if death certificates are used as the main source of determining the cause of death.

We also agree that the assessment of inflammation in dialysis patients is somewhat challenging, because most dialysis patients take many medications, including those with potential antiinflammatory properties, such as angiotensin-converting enzyme inhibitors or angiotensin-receptor blocker, β blockers, and statins. Hence, the use of a precise medication record may better control for this important confounding, which we plan to pursue in our future studies.

Dual energy X-ray absorptiometry (DXA) is probably more accurate than is near-infrared (NIR) interactance in assessing body composition. However, DXA is a more elaborate method and cannot be readily implemented in large-scale epidemiologic studies with repeated measures. In such studies, NIR appears more practical and user-friendly. We recently found that the accuracy of NIR in the assessment of total percentage body fat in dialysis patients is comparable with DXA (3).

Undoubtedly, more studies are needed in several patient populations with cachexia and reverse epidemiology, including dialysis patients and patients with chronic heart failure (CHF). Both of these groups of patients show similar cardiovascular disease risk paradoxes (4). The growing body of literature pertaining to the reverse epidemiology of conventional cardiovascular disease risk factors, including the “obesity paradox,” may have major clinical and public

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Effect of a high-fat meal on the postprandial ghrelin response

Dear Sir:

Depending on the type of macronutrient, differences in postprandial ghrelin secretion have been shown in lean and obese