Letter to the Editor

Cardiovascular Risk Factors Paradox in Maintenance Dialysis Patients! A Spurious Hypothesis or a Hard Core Reality?

Madam, conventional risk factors of cardiovascular disease and mortality in the general population such as body mass, serum cholesterol, and blood pressure are also found to relate to outcome in maintenance dialysis patients, but often in an opposite direction. Patients with end-stage renal disease (ESRD) whose life prolongation is dependent on maintenance dialysis experience much poorer outcome as compared to the general population[1] Numerous reports indicate that in contrast to the general population, where markers of over-nutrition are associated with increased risk of cardiovascular disease, decreased nutritional measures, such as a low body mass index (BMI) or weight-for-height[2] or a reduced serum cholesterol or creatinine concentration[3], are strongly correlated with increased morbidity and mortality, including a higher risk of cardiovascular events and death in dialysis patients. Similar findings have been reported concerning blood pressure, in that low blood pressure, and not hypertension, appears to be more strongly related to poor outcome in dialysis patients. These findings are in contrast to the well-known association between over-nutrition and poor outcome in the general population. The association between under-nutrition and adverse cardiovascular outcome in dialysis patients, which stands in contrast to that seen in non-ESRD individuals, has been referred to as "reverse epidemiology"[4] or "risk factor paradox".[5]

Publication bias may have handicapped or delayed additional reports with such paradoxical findings in ESRD patients. The etiology of this inverse association between conventional risk factors and clinical outcome in dialysis patients is not clear. Several possible causes are hypothesized. First, survival bias may play a role since only a small number of patients with chronic kidney disease (CKD) survive long enough to reach ESRD. Hence, the dialysis patients are probably a distinctively selected population out of CKD patients and may not represent the risk factor constellations of their CKD predecessors. Second, the time discrepancy between competitive risk factors may play a role. For example, the survival disadvantages of under-nutrition, which is frequently present in dialysis patients, may have a major impact on mortality in a shorter period of time, and this overwhelms the long-term negative effects of over-nutrition on survival. Third, the presence of the "malnutrition-inflammation complex syndrome" (MICS) in dialysis patients may also explain the existence of reverse epidemiology in dialysis patients. Both protein-energy malnutrition and inflammation or the combination of the two are much more common in dialysis patients than in the general population and many elements of MICS, such as low weight-for-height, hypocholesterolemia, or hypocreatininemia, are known risk factors of poor outcome in dialysis patients. The existence of reverse epidemiology may have a bearing on the management of dialysis patients. It is possible that new standards or goals for such traditional risk factors as body mass, serum cholesterol, and blood pressure should be considered for these individuals.

In addition, such terminologies may not necessarily mean that the principles of vascular pathophysiology are different in ESRD patients but may indicate that there are other superimposed and more dominant factors that cause apparent reversal of the relationships between risk factors and outcome. The phenomenon of an established risk factor in the general population having a markedly different and indeed opposite predictive pattern in ESRD may not be unique to the dialysis population. Elderly individuals in nursing homes[6], hospitalized patients[7], patients with malignancy[1], and possibly other subpopulations may have similar epidemiology. Hence, a better understanding of the causes of reverse epidemiology in ESRD may help improve the poor outcome in this and other similar but distinct populations.

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References

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