Supplementary information

Proteinuria as a Therapeutic Target in Advanced Chronic Kidney Disease: a Retrospective Multicenter Cohort Study

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Supplementary Discussion

Definition of the change in proteinuria

There was no consensus on the definition of an early change in proteinuria[1]. Quartile decrease or percent decrease in proteinuria during a certain period of time was used by many studies[1-4]. One recent meta-analysis using both absolute and relative change in proteinuria concluded that proteinuria reduction from baseline to the first follow-up measurement between 2.5 and 13 months was associated with lower risk of the doubling of serum creatinine level, end-stage renal disease or death. The use of percent change by baseline albuminuria might be insufficient to separate the effects of the two correlated variables[5]. For example, one study showed that patients with higher baseline proteinuria benefits more from RAS blockade because of greater reduction in proteinuriain this group (relative risk of 0.2 per 1 g/day)[6]. This effect might be obscure if using percent changes. By using absolute changes in proteinuria, our study demonstrated that more proteinuria reduction resulted in slower GFR decline and lower risk of renal death[7].

Associated Risk Factors

Age predicted renal death but did not associate with the decline of GFR in the present study. The effects of age on GFR decline are still controversial[8,9].

The NKF KDOQI guideline had illustrated the conflicting results regarding age and progression rate in different studies[10]. Age <46 years as a risk factor might reflect a clinical fact that these younger patients with advanced CKD might have a more progressive underlying disease. Conversely, more participants >72 years died to reach the outcome of renal death than did those patients <46 years. This result echoed the result of a previous study that death is a competing risk for end stage renal disease in elderly patients with CKD[8]; therefore, the importance of multidisciplinary care is to decrease mortality in the aged group[11].

Baseline albumin levels of 3.2–4.4 g/dL and phosphate levels of 3.7–7.2 mg/dL predicted mortality in our study, and this finding was not consistent with the previous literature. A higher serum phosphorus level was associated with mortality in CKD[12], and hypoalbuminemia was a strong predictor of death in both, dialysis and non-dialysis CKD populations[13,14]. The small number of participants with baseline albumin levels <3.2 g/dL (n = 32) and phosphate levels >7.2 mg/dL (n = 7) would distort the effects of these two parameters. However, the protective effects of albumin level >4.4 g/dL and phosphate level <3.7 mg/dL would be in accordance with the aforementioned literature.

Herbal medicine use was also associated with faster renal progression.

Herbal medicine is popular in Taiwan and is associated with CKD risk[15]. We also demonstrated that herbal medicine use was a predictor of renal death in our study, and the KDIGO guideline advocated for not using herbal remedies in patients with CKD[16].

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