Since the mean eGFR at baseline was 73.6 mL/min/1.73 m², the mean time to reach CKD stage 5 with dual RAS blockade would be 106 years. Finally, 8502 patients were exposed to dual RAS blockade in the ONTARGET Study, for a median follow-up of 56 months. During this 39 676 patient-year follow-up, the claimed significant increased risk of renal failure requiring renal replacement therapy was due to an excess of 15 cases of acute renal failure, without any difference in the incidence of chronic dialysis [2]. This excess risk of <4 events for 1000 patients treated per year is in fact a rather good tolerance profile for patients with a strong RAS blockade. Nevertheless, we should be aware that treatment strategies aiming at further decreasing glomerular pressure and proteinuria, with optimization of either RAS blockade or diuretic dosage, requires cautious monitoring to prevent pre-renal failure.

The second comment suggests that RAS blockade in combination with diuretics may increase urine volume and subsequently increase fluid intake via drinking, contributing to microalbuminuria reduction [6]. Indeed, the suppression of vasopressin (AVP) by increased water ingestion reduces proteinuria, glomerulosclerosis and tubulointerstitial fibrosis in 5/6 nephrectomized rats [7]. The AVP receptor antagonists also decrease proteinuria in animal models via haemodynamic and non-haemodynamic effects of AVP blockade, but without increasing urinary output because of AVP-resistant downregulation of aquaporin-2 and aquaporin-3 in CKD [8]. Indeed, a defective urine concentrating capacity is a manifestation of CKD. This may explain a post hoc analysis of the Modification of Diet in Renal Disease (MDRD) Study that found an association between high urine volumes and rates of GFR decline, suggesting that high fluid intakes make CKD progression worse [9]. Therefore, the safety and efficacy of increased water intake have yet to be confirmed in a prospective randomized controlled study. Nevertheless, loop diuretics increase diuresis only during the first 2–3 days following treatment institution, until a new equilibrium is attained [10], and may not increase water intake in the long term.

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Serum levels of proANP and albumin are independent predictors of mortality in the high-risk patients (elderly and diabetics) treated by haemodialysis (HD) and continuous peritoneal dialysis in 4-year prospective observation

Sir,

Recently, Locatelli and Vigano [1] discussed the significance of natriuretic peptides as the marker for mortality in ESRD patients. They referred to the results published by Paniagua et al. [2] who noticed in a large cohort of CAPD, AD and HD patients that the N-terminal fragment of B-type natriuretic peptide (NT-proBNP) was a predictor of death risk independently of fluid volume overload and dialysis modality. The independency from fluid overload is explained by the relation of NT-proBNP elevation to both fluid overload and myocardial damage. In context of this observation, we would like to present the results of an as yet unpublished study performed in 86 dialysis patients (46 on maintenance HD and 40 treated by CAPD).

The clinical characteristics of the study group were the following: median age 73.5 years (41 females and 45 males), 71% diabetics, 59% elderly, 30% of patients with both risk factors, median time on dialysis before inclusion 17 months, and a median residual diuresis of 550 mL. There were no differences between HD and CAPD patients in these features. However, the distinctive elements between HD and CAPD subgroups were lower albumin concentration (P < 0.002) and higher cholesterol levels (P < 0.001) in CAPD patients. In addition, the following laboratory parameters were determined in all patients at the onset of the observation: plasma proANP (amino terminal 1–98
ANP fragment), NT-proBNP concentration, serum CRP and IL-6 values. In the prospective observation, 53 patients (62%) survived 20 months, and 27 patients 50 months (the last point of the observation). No effect of dialysis modality (HD vs. CAPD) on the survival was discerned. In the univariate linear model, the survival was significantly associated with elevated CRP (P = 0.05), higher plasma proANP (P = 0.05) and lower albumin concentration (P = 0.013). The effect of higher plasma proANP (P = 0.018) and lower albumin concentration (P = 0.013) was left as an independent variable in the Cox regression model. In conclusion, in the studied group of particularly fragile dialysis patients, the elevated proANP level appeared to be an independent predictor of mortality, whereas the NT-proBNP concentration did not exhibit a significant effect.

This difference could be caused by distinctive mechanisms of proANP and NT-proBNP synthesis. ANP is secreted mainly by the right atrium, while BNP is produced by cardiac ventricles. ANP has been found to be more sensitive to changes in intravascular volume, whereas BNP level is more related to left ventricular mass and function [1,3]. Therefore, the association between higher plasma proANP and mortality, found in our study, could emphasize the crucial importance of volume control in diabetic and elderly ESRD patients, independent of modality of dialysis.

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