Vascular calcification is not an independent predictor of mortality in pre-dialysis adult patients

To the Editor:

It has been established that vascular calcification is predictive of mortality in haemodialysis patients [1]. Among pre-dialysis patients, in a study recently published in *Nephrol Dial Transplant*, Hanada et al. have stated that aortic calcification is associated with a greater risk of cardiovascular events [2]. Furthermore, positive associations between coronary calcification with both cardiovascular events and mortality rate have been reported in the pre-dialysis setting [3]. However, these latter studies were limited by the fact that either mortality was not evaluated [2] or adjustment for possible confounders was not performed [3]. To further investigate this issue, we performed a prospective study of a cohort of 92 pre-dialysis patients (mean ± SD age: 68 ± 12 years) at different chronic kidney disease (CKD) stages (12.5% at stage 2, 37.5% at stage 3, 41% at stage 4 and 9% at stage 5). Abdominal aortic and coronary calcifications were evaluated by multi-slice spiral computed tomography. Eighteen patients died during the follow-up period (mean ± SD duration: 794 ± 244 days). In crude survival analyses, a coronary calcification score >259 AU and an aortic calcification score >1.53 predicted overall mortality (P = 0.01 and P = 0.04, respectively). These cut-off values were estimated by maximizing sensitivity and specificity in ROC curves for predicting mortality. However, the associations were no longer statistically significant after adjustment for age in multivariate Cox regression analyses. In conclusion, vascular calcification was not an independent predictor of mortality in pre-dialysis adult patients. Other factors such as endothelial dysfunction [4] may prevail over vascular calcification in early-stage CKD. Further investigation in a prospective study with a larger sample size is required to address this issue.

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Reply

Sir,

In their letter, Swapnil and Brar correctly point at additional reasons such as co-medication potentially contributing to heterogeneity, an observation that was practically found in all meta-analyses performed until now. However, as recent investigations [1,2] as well as a meta-analysis addressing this issue specifically [3] indicate, adding NAC to bicarbonate does not significantly alter bicarbonate's effect on contrast-induced AKI. Consequently, excluding an investigation using different doses of NAC might not be necessary. The power of a study actually addresses the probability of overseeing existing differences rather than finding a difference by chance, the type I error of usual statistics in any published trial. In short of that, truly, we cannot find any disguising homogeneity by demonstrating in our comment [4] that even inclusion of all studies (published and unpublished) known to that point did not get rid of excess variability among study results. We are well aware of the importance of unpublished studies with regard to publication bias [5,6], but as we have demonstrated, this does not help the case with regard to contrast-induced AKI studies, and consequently, publication bias does not also appear to be the major source of heterogeneity in this context. Finally, this ongoing discussion just even clearer demonstrates the urgent requirement of additional large adequately powered multicentre trials investigating on clinical end points and the effects of bicarbonate in preventing contrast-induced AKI.

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Reply

To the Editor,

We thank Barreto et al. for their interest in our publication and for their important comments. The association of vascular calcification with mortality in pre-dialysis CKD remains incompletely understood because of the limited amount of information. The study described in the letter showed that vascular calcification was not an independent predictor of mortality in subjects with pre-dialysis CKD mainly of stages 2–4. We were unable to evaluate the association of abdominal aortic calcification with mortality because of the small number of deaths in our patient population during the follow-up period. Recently, Watanabe et al. [1] showed a significant association of coronary artery calcification (CAC) with mortality in pre-dialysis CKD patients, but again, the small number of deaths did not permit a multivariate analysis. This prevented confirmation of an independent association of the CAC score with mortality. In contrast, Chiu et al. [2] found an independent relationship between the severity of CAC and all-cause mortality in patients with early-stage CKD due to diabetic nephropathy. Given these findings, we agree that prospective studies with larger sample sizes are needed to address this issue adequately.

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