Macrocirculation Meets Microcirculation

To the Editor:

Ford et al\(^1\) described in a prospective cohort study that aortic stiffness is independently associated with rate of renal function decline in chronic kidney disease (CKD) stages 3 and 4. Thus, after the original prospective cohort study of Blacher et al\(^2\) in hemodialysis patients (CKD stage 5), this is the first prospective study in renal insufficient patients not being on hemodialysis.

In the meantime, aortic pulse wave velocity (PWV) has emerged as an important blood pressure–independent marker of cardiovascular risk in several other populations.\(^3\) In parallel, patients with CKD stages 3 and 4 are also characterized by advanced cardiovascular risk. However, cross-sectional analysis in CKD 3 and 4 did not show convincing evidence for an association of epidermal growth factor receptor (eGFR) in CKD 3 and 4 and aortic PWV.\(^4,5\) Therefore, the results shown by Ford et al\(^1\) filled the lack of information on this important patient group and demonstrate that the macrocirculation affects the renal function, thus microcirculation.

We mention 2 points, which are remarkable in this study. First, using a rate of renal decline ≥25% as cutoff point is common sense in nephrology. However, the mean eGFR at baseline is given as 32±11 mL/min. Thus, a mean loss of 8 mL/min is reflecting a reached renal end point. In CKD patients at stages 3 and 4, these losses of eGFR can also be reached by adding or intensifying antihypertensive and antiproteinuric therapy using a blocker of the renin-angiotensin system. Moreover, commonly used immunosuppressive agents like calcineurin inhibitors or cyclophosphamide can directly lead to loss of eGFR. These factors do not reflect the association between aortic stiffness and renal function. Ford et al\(^1\) do not mention how far they involved these factors in their study setting.

Second, in Table 5, Ford et al\(^1\) compare 110 patients with a decline in eGFR <25% with those 23 patients with a loss of eGFR ≥25%. However, the hypothesis is built on aortic PWV, but this major readout is measured in 120 patients. Therefore, it is for 13 patients (9.8%) unclear how they would affect the result of the whole cohort. The authors do not mention the distribution of these patients with respect to the decline of renal function. However, this is of importance, because in this moment the \(P\) value for aortic PWV is exactly 0.05. A sensitivity analysis focusing on the missing random values may help clarify the results, because we expect that the patients without aortic PWV measure may rather reflect patients with advanced cardiovascular disease as they have been mentioned as patients with previous aortofemoral grafting. Thus, a sensitivity analysis may further strengthen the results of Ford et al.\(^1\)

Finally, the article described here raises further questions in the context with renal disease and aortic stiffness. In how far does an increase in aortic PWV worsen renal function? Does an enhanced loss of renal function lead to an increase in aortic PWV, thereby offering a partial explanation for increased cardiovascular risk in the CKD patients?

Disclosures

None.

Evangelos Papachristou
Department of Nephrology
University of Patras
Patras, Greece

Marcus Baumann
Department of Nephrology
Klinikum rechts der Isar
Technische Universität München
München, Germany
