Response to: 'Role of tubulointerstitial injury in ANCA-associated vasculitis is underestimated' by Moiseev *et al*

We thank Dr Moiseev *et al*¹ for their letter about the role of tubulointerstitial injury in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), as a response to our recently published article 'Urinary epidermal growth factor predicts renal prognosis in antineutrophil cytoplasmic antibody-associated vasculitis'.²

Histologically, the typical feature in the kidneys of patients with AAV is pauci-immune necrotising crescentic glomerulonephritis with little immunoglobulin and complement deposition in the glomerular capillary walls.³ Theoretically, glomerular injury is the 'upstream' in ANCA glomerulonephritis, and tubulointerstitial injury is commonly thought to be the 'downstream' of glomerular injury. Therefore, current biomarkers for ANCA glomerulonephritis have been mainly focused on the glomerulus. However, it has been suggested that markers of tubulointerstitial lesions are also important for assessing disease severity and predicting renal prognosis in patients with different renal diseases, even those who have 'glomerulocentric' paradigm. Ju *et al*⁴ found that urinary epidermal growth factor (EGF), as a specific tubular marker, could be a predictor of chronic kidney disease progression in patients with glomerular diseases. Moreover, the role of tubulointerstitial markers was confirmed in several studies in patients with different forms of glomerulonephritis, such as diabetic nephropathy,⁵ IgA nephropathy (IgAN)⁶ and lupus nephritis.⁷ Some studies suggested that interstitial inflammation, interstitial fibrosis and tubular atrophy may have predictive value in detecting the risk of disease progression in patients with AAV.^{8,9}

Although corticosteroid and cyclophosphamide improve the outcome, many patients with AAV experience progression of renal injury despite long-term immunosuppressive therapy. However, there is lack of good tubulointerstitial markers for predicting the renal prognosis in AAV.

We concur with Moiseev *et al*¹ that it is important to evaluate whether biomarkers of tubulointerstitial injury can help the clinical decision-making process for patients with AAV. In our study, we found that tubulointerstitial EGF mRNA expression was significantly associated with estimated glomerular filtration rate (eGFR) at time of biopsy in patients with AAV. Moreover, we found that the ratios of urinary EGF to creatinine (uEGF/Cr) were associated with more severe renal disease, renal resistance to treatment and higher risk of progression to composite outcome in patients with AAV. It should be noted that the predictive value of urinary EGF is not specific for AAV, and some studies showed that it has the ability to predict the development of diabetic nephropathy and IgAN.^{10,11}

In conclusion, urinary EGF/Cr level may be a useful non-invasive biomarker to assess the degree of tubular damage and the potential for transition into chronic progressive kidney disease in patients with AAV. To evaluate the utility of urinary EGF for guiding AAV treatment decision-making, further larger and multicentre cohort studies will be needed.

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