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LETTER

# High serum potassium levels after using losartan can reflect more severe renal disease

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**Keywords** Hyperkalaemia · Inhibitors of the renin–angiotensin system · Renal disease progression · Tubulointerstitial damage

**Abbreviations**

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| RAS | Renin–angiotensin system |
| RENAAL | Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan |
| TI | Tubulointerstitial |

*To the Editor:* We read with great interest the paper by Miao et al. [1] showing in a post hoc analysis of the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study [2] that increased serum potassium levels affect renal outcomes. The authors' observations are intriguing as they show that not all the patients in the study benefited from using inhibitors of the renin–angiotensin system (RAS); in fact, some may have suffered adverse events, including an acceleration of renal disease progression, most notably in those with hyperkalaemia. Miao and colleagues argue that the changes in potassium levels are dependent on losartan therapy, but its effect on risk for renal events is independent of the use of losartan (Table 3 in Miao et al. [1]). This is intriguing, as the percentage of patients on potassium-sparing diuretics is quite small and most of the other antihypertensive medications are not commonly associated with hyperkalaemia.

Miao et al. state that changes in potassium levels could reflect the severity of tubulointerstitial (TI) damage. This is supported by the observation that the high potassium group also had lower baseline haemoglobin levels, which is compatible with more severe interstitial damage. It is well established that the hyporeninaemic hypoaldosteronism syndrome and low levels of erythropoietin are associated, probably reflecting damage to the juxtaglomerular apparatus and interstitial cells, respectively [3].

Diabetic nephropathy is a heterogeneous disease in patients with type 2 diabetes [4]. Proteinuria does not always predict progression [4]. It would be interesting to know whether in the RENAAL patients there was a relationship between the changes in the albumin to creatinine ratio and potassium levels. There are different histological patterns in diabetic kidney disease: most patients have typical glomerular basement membrane thickening and mesangial expansion, while some have significant glomerulosclerosis and others have severe TI scarring. In fact, it is TI scarring that correlates best with the severity of renal impairment and predicts the progression of diabetic kidney disease [5]. It comes as no surprise, at least

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to us, therefore, that hyperkalaemia as a possible indicator of more severe TI damage is associated with faster progression of diabetic nephropathy.

Should we then continue the use of inhibitors of RAS in hyperkalaemic patients with potentially progressive diabetic kidney disease? The continued use of inhibitors of RAS in such patients is associated with worse outcomes [6, 7].

With this in mind, we disagree with the authors' conclusion that increased serum potassium levels dampen the renoprotective effect of losartan. We believe that it is more likely that those patients with high serum potassium levels and increased risk of adverse renal outcomes are either those who have received higher doses of inhibitors of RAS, have increased sensitivity to a similar dose, or have more severe TI disease, and hence faster progression of their underlying nephropathy.

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**Duality of interest statement** The authors declare that there is no duality of interest associated with this manuscript.

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