Comment on: ‘Effects of dose and type of corticosteroids on the divergence between estimated glomerular filtration rates derived from cystatin C and creatinine’ by Tsushita et al

To the Editor:

In their important study, Tsushita et al add further information to the clinically important observation that corticosteroid therapy can increase cystatin C serum levels without influencing kidney function. The study shows that treatment with corticosteroids (dependent on the dose) has an impact on the divergence between the estimated glomerular filtration rate (eGFR) calculated from serum creatinine (eGFRcreat) and cystatin C (eGFRcys). The authors demonstrate a significant negative correlation between the prednisolone dose and the eGFRcys/eGFRcreat ratio for doses of more than 0.170 mg/kg/day. This nicely corresponds to the threshold dose of glucocorticoid-adverse effects and the endogenous cortisol production. However, this observation could not be demonstrated when patients were treated with hydrocortisone and methylprednisolone. As discussed in the paper, the latter was due to the lack of power as most patients who were taking these medications were treated with doses below this cut-off.

Unfortunately, but for understandable reasons, the authors excluded approximately 75% of the patients with simultaneous measurement of serum creatinine and cystatin C and corticosteroid therapy, limiting the results to a small but well-defined patient group. However, several questions might be answered within this patient population.

Is the effect of corticosteroids comparable and stable within the different CKD stages? Patients with eGFR < 30 ml/min were excluded because cystatin C plateaus in patients with end-stage kidney disease, but what about patients in CKD stages 1, 2 and 3?

When looking at Figure 2B, it is interesting to note that a small proportion of patients presents with an eGFRcys/eGFRcreat ratio > 0.79 despite a prednisolone dose > 0.170 mg/kg/day. Could the authors find any specific patient characteristics to explain this observation?

On the contrary, several patients show an eGFRcys/eGFRcreat ratio < 0.79 with much lower prednisolone doses (<0.170 mg/kg/day). The latter finding could represent patients with the recently described ‘shrunken pore syndrome’, which describes patients with an eGFRcys/eGFRcreat ratio < 0.60-0.70 without any non-renal influences on eGFRcys or eGFRcreat, and that is associated with a substantial increase in morbidity and mortality.2,3

The authors excluded a large group of patients with presumed low muscle mass (creatinine < 0.6 mg/dl, BMI < 18.5 or > 25 kg/m²). However, the underlying pathophysiology should be the same and correction of the eGFRcreat to the true patient body surface might be helpful when analysing these patients.

Finally, one has to bear in mind that cystatin C levels are not only altered in several clinical conditions such as hyperthyroidism and hypercortisolism,4 but might also be endogenously increased in specific diseases (eg in lung fibrosis).5 Considering these influences, treatment of the underlying condition with corticosteroids would decrease elevated serum cystatin C, as has been reported among patients with asthma.6

In conclusion, estimation of the GFR using creatinine or cystatin C are both limited due to different influences on the endogenous production of these parameters rather than the kidney function itself. Therefore, interpretation of eGFR values should take place within the individual clinical context. In the future, better parameters will be needed for an independent assessment of the true GFR.

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CONFLICT OF INTEREST
None of the authors have any potential conflicts of interest associated with this research.

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Data sharing is not applicable to this article as no new data were created or analysed in this study.

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