

# 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*<sup>1</sup> 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 (eGFR<sub>creat</sub>) and cystatin C (eGFR<sub>cys</sub>). The authors demonstrate a significant negative correlation between the prednisolone dose and the eGFR<sub>cys</sub>/eGFR<sub>creat</sub> 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 eGFR<sub>cys</sub>/eGFR<sub>creat</sub> 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 eGFR<sub>cys</sub>/eGFR<sub>creat</sub> 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 eGFR<sub>cys</sub>/eGFR<sub>creat</sub> ratio < 0.60-0.70 without any non-renal

influences on eGFR<sub>cys</sub> or eGFR<sub>creat</sub>, and that is associated with a substantial increase in morbidity and mortality.<sup>2,3</sup>

The authors excluded a large group of patients with presumed low muscle mass (creatinine < 0.6 mg/dl, BMI < 18.5 or > 25 kg/m<sup>2</sup>). However, the underlying pathophysiology should be the same and correction of the eGFR<sub>creat</sub> 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,<sup>4</sup> but might also be endogenously increased in specific diseases (eg in lung fibrosis).<sup>5</sup> Considering these influences, treatment of the underlying condition with corticosteroids would decrease elevated serum cystatin C, as has been reported among patients with asthma.<sup>6</sup>

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.

## FUNDING INFORMATION

Open Access funding enabled and organized by ProjektDEAL. WOA Institution: KLINIKUM DER UNIVERSITAET MUNCHEN Blended DEAL : ProjektDEAL

## KEYWORDS

cystatin C, glomerular filtration rate, prednisolone

## CONFLICT OF INTEREST

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


## DATA AVAILABILITY STATEMENT

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

First published: 23 July 2020 <https://doi.org/10.1111/jcpt.13235>

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Journal of Clinical Pharmacy and Therapeutics* published by John Wiley & Sons Ltd

Isaac Lean MD<sup>1</sup>  
 Michael Paal MD, PhD<sup>2</sup>  
 Yana Suttmann MD<sup>1</sup>  
 Christina Dengler MSc<sup>1</sup>  
 Ulf Schönemarck MD<sup>1</sup> 

<sup>1</sup>Department of Medicine IV, University Hospital, LMU Munich,  
 Munich, Germany

<sup>2</sup>Institute of Laboratory Medicine, University Hospital, LMU  
 Munich, Munich, Germany

#### Correspondence

Ulf Schönemarck, Department of Medicine IV, University  
 Hospital, LMU Munich, Marchioninistrasse 15, 81377  
 Munich, Germany.

Email: Ulf.Schoenermarck@med.uni-muenchen.de

#### ORCID

Ulf Schönemarck  <https://orcid.org/0000-0002-3266-9791>

#### REFERENCES

1. Tsushita H, Tanaka R, Suzuki Y, et al. Effects of dose and type of corticosteroids on the divergence between estimated glomerular filtration rates derived from cystatin C and creatinine. *J Clin Pharm Ther.* 2020;45:1-8.
2. Grubb A. Shrunken pore syndrome - a common kidney disorder with high mortality. Diagnosis, prevalence, pathophysiology and treatment Options. *Clin Biochem.* 2020;83:12-20.
3. Åkesson A, Lindström V, Nyman U, et al. Shrunken pore syndrome and mortality: a cohort study of patients with measured GFR and known comorbidities. *Scand J Clin Lab Invest.* 2020;80:412-422.
4. Naka M, Kadoya M, Kosaka-Hamamoto K, et al. Overestimation of glomerular filtration rate calculated from serum creatinine as compared with cystatin C in patients with subclinical hypercortisolism: Hyogo Adrenal Metabolic Registry. *Endocr J.* 2020;67:469-476.
5. Kasabova M, Joulin-Giet A, Lecaille F, et al. Human cystatin C: a new biomarker of idiopathic pulmonary fibrosis? *Proteomics Clin Appl.* 2014;8:447-453.
6. Cimerman N, Brguljan PM, Krasovec M, et al. Serum cystatin C, a potent inhibitor of cysteine proteinases, is elevated in asthmatic patients. *Clin Chim Acta.* 2000;300:83-95.

**How to cite this article:** Lean I, Paal M, Suttmann Y, Dengler C, Schönemarck U. 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.* *J Clin Pharm Ther.* 2021;46:547-548. <https://doi.org/10.1111/jcpt.13332>