

## Cystatin C-based equations: don't repeat the same errors with analytical considerations

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Sir,

We read with interest the paper published by Zahran *et al.* on the cystatin C-based equations for the estimation of glomerular filtration rate (GFR) in renal transplanted patients [1]. The paper and the topic are certainly of interest. However, we would like to formulate some remarks that appear relevant to us, regarding the methodology and the discussion, before accepting the conclusions of this paper. In their discussion, Zahran *et al.* insisted on the lack of standardization for serum creatinine as a limitation of their study. This is an 'analytical limitation' of the study but there is another important 'analytical' limitation that concerns the determination of cystatin C used in this study. In fact, there are two major methods to measure cystatin C : particle-enhanced immunoturbidimetric immunoassay (PETIA) and immunonephelometric immunoassay (PENIA) [2,3]. In the 10 cystatin C-based equations studied by Zahran *et al.*, 6 have been elaborated from the PENIA method and 4 from the PETIA one. There are clear analytical differences between the two methods, and results obtained with the PENIA method are clearly different from those obtained with the PETIA [2,3]. Using PENIA cystatin C results in a PETIA-elaborated equation is thus potentially misleading. Moreover, Zahran *et al.* have measured cystatin C with another 'old' method (ELISA). Once again, the cystatin C results obtained with this ELISA kit cannot be used in a formula elaborated with the PENIA or the PETIA. Asserting that ELISA results are strongly correlated with the two other methods is not sufficient. A strong correlation exists between the PENIA and the PETIA cystatin C results ( $r = 0.97$ ) but this fact does not exclude a significant bias between the results, as can be shown by Bland and Altman analysis [2].

Moreover, the ELISA kit used by Zahran *et al.* has poor performance in terms of the analytical coefficient of variation (CV): 6 to 9% for ELISA and 4 to 5% for the PENIA (the fact that the interassay CVs are better than the intrassay CVs is also rather questionable). As the relationship between GFR and cystatin C is exponential, such differences in the analytical precision of cystatin measurement can obviously explain the lack of precision observed for the cystatin C-based equations in this study. As it is the case for the creatinine-based equations, precision of the cystatin C determination has great importance for the precision of the cystatin C-based equations results [4]. We admit that usefulness of cystatin C-based equations for the estimation of GFR in transplanted patients remains questionable [5], but more studies seem necessary on this topic, with improved methodology, notably from an analytical point of view. We would like to have the authors' point of view on this comment.

### References

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