Letters and Replies

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Improving the interpretation of protein: creatinine ratios. The impact of creatinine excretion

Sir,

I read with interest the article by Methven et al. [1] comparing albumin:creatinine ratio (ACR), total protein:creatinine ratio (PCR) and 24-hour urine protein. The sensitivity and specificity of PCR values for predicting 24-hour proteinuria have been reported in a number of papers and this constitutes the justification for PCR thresholds in current guidelines. Of particular interest in the study of Methven et al., however, is the finding that in spite of the overall good correlation found between PCR and 24-hour proteinuria, there was a marked change in performance of PCR thresholds across different gender and age groups (attributed to differences in creatinine excretion). It seems that previous publications correlating PCR and 24-hour proteinuria thresholds have obscured the importance of differences in creatinine excretion, leading to guidelines that are potentially flawed. A simple consideration of the Cockcroft-Gault equation makes it clear that creatinine excretion is predicted to be proportional to weight and (140 – age) [2,3]. The impact of gender is given by the appropriate gender-specific Cockcroft-Gault coefficient:

\[
\text{24-hour creatinine excretion in grams} = (140 - \text{age}) \times \text{weight in kg} \\
\times 0.0002 \times 0.85 \text{ for women} 
\]

The different sensitivities of PCR thresholds for different age and gender reported by Methven et al. are consequently just what would be anticipated. The authors are to be commended for highlighting the issue of creatinine excretion; however, I suggest that they could have made further use of the available data. Weight measurements were reported to be available for 83% of the patients. Consequently, the Cockcroft-Gault predicted creatinine excretion could easily have been calculated and the observed PCR adjusted accordingly (i.e. by multiplying by predicted creatinine excretion). Performing such an adjustment should account for differences in muscle mass and remove any need for gender-, age- and weight-specific cut-points. Although adjusting for predicted creatinine excretion removes some of the simplicity of PCR, would this be too high a price to pay for optimizing assessment of proteinuria? Of note, the first reports of PCR assessment demonstrated correlations with 24-hour proteinuria adjusted for Cockcroft-Gault predicted creatinine excretion or body surface area (as an alternative surrogate for muscle mass) [3]. These early studies were in small patient cohorts and seem to have been largely forgotten. Examination of the subsequent larger cohorts such as that of Methven et al. could settle the issue of how much adjusting for predicted creatinine excretion improves performance of PCR/ACR. At a time when the prognostic importance of proteinuria is increasingly emphasized, it is important that this matter be clarified before guidelines are revised [4].

Conflict of interest statement. None declared.

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Reply

Sir,

We thank Dr Ellam for his suggestion. In our article, we demonstrated that sensitivity and specificity of total protein:creatinine ratio (TPCR) and albumin:creatinine ratio (ACR) to predict proteinuria of 1 g/day varied substantially by age, gender and estimated glomerular filtration rate (eGFR) presuming this to be related to muscle mass [1]. He suggests that we adjust TPCR and ACR for predicted 24-h creatinine excretion by using the Cockcroft and Gault formula. In the subgroup of patients with weight available, we have repeated our analyses using adjusted TPCR and ACR measurements (TPCR and ACR multiplied by the predicted creatinine excretion value and divided by 10) [2]. The results are presented in Table 1 and show a positive effect on sensitivity in most subgroups, with the most benefit in patients expected to have higher muscle mass. Overall specificity is unchanged but is improved in groups with lower muscle mass and marginally worse in those with higher