Comparison of Iohexol Plasma Clearances Calculated From 5 Early-Compartment Correction Equations With Urinary Clearance of Iohexol

To the Editor: We read with great interest the publication of Delanaye *et al.*[1] comparing 5 early-compartment correction equations for glomerular filtration rate (GFR) measurements. The authors concluded that most equations (Bröchner-Mortensen, Fleming, Jodal-Bröchner-Mortensen, and Ng) were concordant, except for Chantler's equation that deviated from others; however, the lack of comparison with urinary clearance of exogenous tracers was underscored as a major limitation.

In our department, iohexol plasma clearance is systematically determined in association with urinary clearance. We retrospectively investigated the bias and precision of the 5 equations in 369 consecutive patients, using iohexol urinary clearance as a common comparator. The results were stratified according to GFR ranges (Figure 1).

Because iohexol urinary clearance is known to underestimate GFR by approximately 15%,[2,3] plasma clearance of iohexol should overestimate the urinary clearance in the same range. For the 4 equations validated by Delanaye *et al.*,[1] this hypothesis was confirmed for GFR >60 ml/min per 1.73 m^2, whereas the mean bias appeared >15% for GFR <60 ml/min per 1.73 m^2. Conversely, in this low GFR range, Chantler's equation had the expected bias (approximately 15%), and a precision similar to the other equations. The overestimation of GFR by plasma clearance of iohexol for low ranges of GFR is well known[4] and can be prevented by late blood sample, which is not always easily achieved in clinical practice. Our data suggest that Chantler's equation may remain relevant and not necessarily be abandoned for patients with GFR <60 ml/min per 1.73 m^2, because it is unbiased even in the absence of late blood sample.

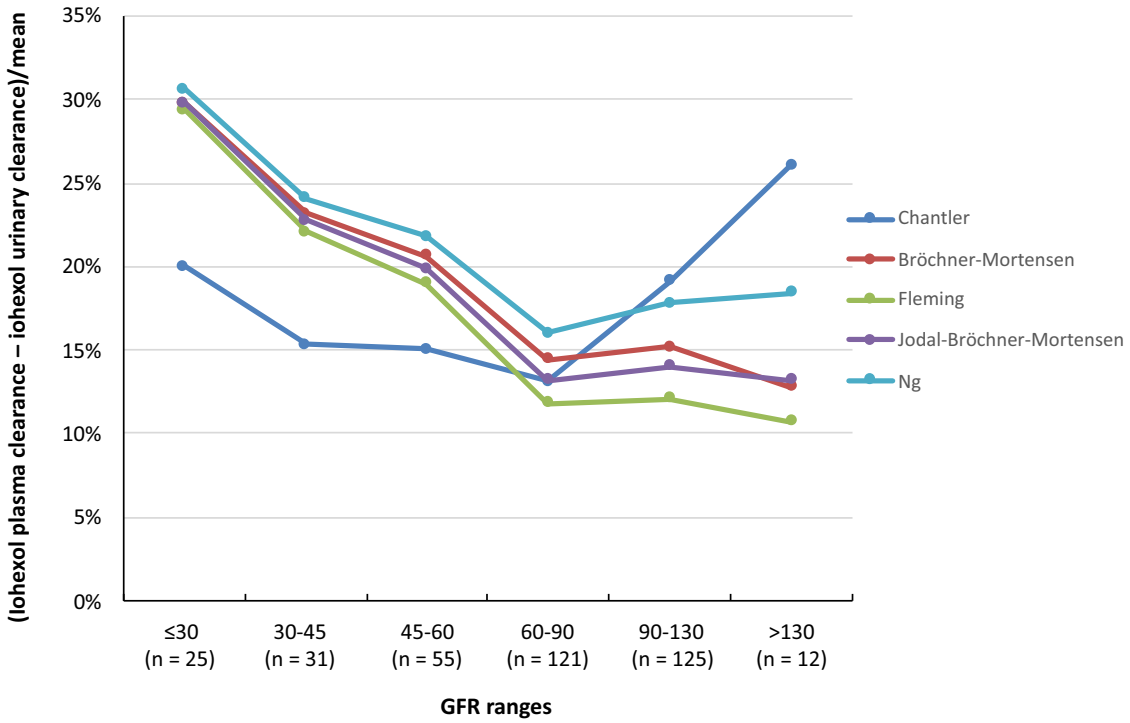

Figure 1. The figure illustrates the biases among the 5 iohexol plasma clearances (based on the 5 early-compartment correction equations for glomerular filtration rate [GFR]measurements) and the iohexol urinary clearance. The results are stratified according to GFR ranges. Iohexol plasma clearance was determined from 4 to 6 blood samples, between 120 and 270 minutes after iohexol injection, and urinary clearance was the mean of 4 to 6 clearance-period values. Bias was defined as the mean of the relative differences between plasma and urinary clearances. Precision was the SD of the bias. Precisions of the different equations were between 20.9% and 21.0%, 13.8% and 13.9%, 12.3% and 12.5%, 10.4% and 10.7%, 10.8% and 11.2%, and 12.9% and 16.0% when GFR was respectively ≤30, 30–45, 45–60, 60–90, 90–130, and >130 ml/min per 1.73 m^2.

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The Authors Reply: Results proposed by Stehlé *et al*. regarding our article on the different methods to correct for the early-compartments for the determination of GFR by plasma clearances[1] is of interest because data comparing plasma versus urinary clearances are relatively rare.[2] In our article, we fairly stated that we had no urinary clearances, and thus our analysis was just a comparison of current equations to correct for the early-compartment.[1] Stehlé *et al*. perfectly confirmed what we showed: a high concordance of the results given by the Bröchner-Mortensen, Fleming, Jodal-Bröchner-Mortensen, and Ng, whereas the Chantler correction gave different results. However, we are more careful in our interpretation of the results by Stehlé *et al*., who suggest to consider the Chantler method in low glomerular filtration rate (GFR) ranges. First, their sample in this GFR range is relatively low. Second, as acknowledged by the authors, the difference between urinary and plasma clearances in low GFR is due to the timing of the last sample, which is (like in our own study) probably too early (270 minutes). The role of the equation to correct for the early-compartment has no role in this discrepancy. Several data suggested that concordance between plasma and urinary clearances are higher in low GFR when the last sample is later (6 to 24 hours).[3,4] We have no proof that the Chantler correction would be "better" in terms of GFR if plasma clearance would be obtained with an adequate late sampling. Last, in our opinion, it remains difficult to recommend a method that is (maybe) "better" in low GFR range, but that is "worse" in high GFR ranges.

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