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Prospectives and limitations by a novel algorithm

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Title: Prospectives and Limitations by a novel algorithm.

Reply to the letter " " by

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Dear colleagues,

we have recently proposed a novel algorithm to be more accurate to calculate individual GFR in cancer patients over a broad range of constitutive GFR than conventionally used formulas [1]. In order to proof potential translation of our results in clinical practice, we chose carboplatin as a very useful anticancer drug because the agent undergoes extensive glomerular filtration as unchanged drug. Carboplatin AUC measured by the limited sampling method according to Sorensen et al. was used as a reference to compare calculated and real carboplatin pharmacokinetics by the Calvert formula and GFR values of varying origin in more detail [2].

During the study, our centralized IV admixture service used a carboplatin target AUC of 5 mg/ml x min and GFR based on creatinine clearance (CrCl) via 24-hour urine collection (n=15) and the Jelliffe formula (n=14). Based on additional tubular secretion of creatinine [3], CrCl values are constitutively higher than corresponding GFR values with higher AUC-values as a consequence calculated by the Calvert formula which is in accordance to our observation: 5.8 ± 1.1 mg/ml x min. However, this difference does not appear to be of clinical relevance.

Our algorithm has been based on the MDRD-6 formula in order to include more patient specific parameters, e.g. blood urea and albumin. We retrospectively assessed the validity of the MDRD-4 IDMS (data not shown), however its accuracy appeared to be lower with a mean MPE of -12% (SD \pm 17%) and a precision of 16% (SD \pm 12%). As a consequence, we did not favour the use of the MDRD-4 furthermore. Whether the CKI-EPI formula, which has not been included in our calculations so far, may be of increasing value needs further clinical investigation [4].

Undoubtedly, clinical experience with anticancer drugs in obese cancer patients remains scarce. Whereas the use of the unmodified Cockcroft-Gault formula cannot be recommended in obese patients receiving carboplatin based on the severely increased risk for overdosage, modification of the original formula by inclusion of body surface area (BSA) as a reference or by the use of adjusted ideal (AIBW) rather than current body weight has not yet been clearly evaluated [5]. Our algorithm has not been developed with a special focus on obese cancer patients, however, those who were valuable revealed to be accurately assessed. As a consequence, the novel algorithm can also be used in patients with

increased body mass index (BMI) without further limitations. Possibly, the inclusion of the Salazar-Corcoran formula within the algorithm may be of some advantage in this context, because it has been originally developed for non cancer patients with obesity.

In conclusion, we totally agree that more intensified studies may be warranted to evaluate the usefulness of the MDRD-4 formula in more detail and to focus obese patients with their underlying renal function in more detail in the near future.

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