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ESTIMATED GFR VS CREATININE CLEARANCE FOR DRUG DOSING

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To the Editor:

Stevens et al[1] suggest that the Modification of Diet in Renal Disease (MDRD) Study equation for estimated glomerular filtration rate (GFR) is an acceptable substitute for estimated or measured creatinine clearance (CCr) as an index for adjusting drug doses in patients with chronic kidney disease and acute kidney injury. However, others have raised concerns that injudicious use of estimated GFR as a substitute for CCr could result in significant dosing errors and toxicity, especially for drugs with narrow therapeutic indices.[2-4] Further, their conclusion is not supported by results of 4 studies that showed that using the MDRD Study equation instead of CCr estimates led to recommendations for 30%-60% higher doses of digoxin, amantadine, and various antimicrobials.[5-8] Estimated GFR values have also been shown to overestimate CCr in patients with measured GFRs_60 mL/min/1.73 m^2 (_1 mL/s/1.73 m^2), the population most likely to require dose modification.

Stevens et al used a standard dose for a limited drug subset based on measured GFR to compare doses obtained using 2 estimation methods (MDRD Study equation and CCr). This approach inherently favors the MDRD Study equation, because that formula was derived from iothalamatemeasured GFR. The justification for using measured GFR as the index for determining drug dose categories discounts the many studies relating drug dosing to estimated CCr. Current US Food and DrugAdministration (FDA) guidance on pharmacokinetic studies in chronic kidney disease and product labeling recommend dose modification categories based on CCr, not estimated GFR. The authors also back-corrected the automated estimated GFR result, reported in milliliters per minute per 1.73 m^2, using calculated body surface area (BSA), to yield values in milliliters per minute. This BSA-modified MDRD hasn't been validated and calculating BSA in clinical settings is inconvenient and unlikely to occur. Without back-correction, significant dosing errors might occur.

We believe that until studies are conducted to assess the relationship between GFR estimated by a given methodology and a drug's pharmacokinetic parameters and/or pharmacodynamic end points, traditional methods should be used.

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