Editorial

# Assessment of renal function in the critically ill - Shall we look beyond predictive equations?

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Acute Kidney Injury (AKI) affects up to 20% of critically ill patients[1] and is an independent predictor of mortality.[2] Measurement of serum creatinine levels has been in use from the 1940s to detect renal dysfunction.[3] However, it is clear that creatinine level is an imperfect tool in assessing kidney function. Creatinine levels are influenced by extraneous factors such as age, gender, race, muscle mass, and the extent of volume resuscitation; besides, levels begin to rise only after the glomerular filtration rate (GFR) falls to 60% of baseline.[4] Once a day creatinine levels, as practiced in many intensive care units (ICUs), bear little real time correlation with renal function in the dynamic milieu typical of critically ill patients.[5] The RIFLE [6] and its modification, the AKIN criteria,[7] have been validated as tools to assess the severity of AKI. However, they too require baseline creatinine levels, which may not always be known. Clearly, we need better tools to diagnose AKI sufficiently early and follow its course more precisely to enable appropriate therapeutic interventions.

Renal function may be accurately assessed by measuring GFR; use of exogenous markers such as inulin and $^{125}$I-iothalamate are cumbersome and not feasible in routine clinical practice. Creatinine clearance (Cr Cl) may be measured as a surrogate marker of GFR. Although conventionally performed on a 24-hour urine sample, much shorter collection times have been shown to be of comparable accuracy.[8,9]

Equations commonly employed to calculate Cr Cl include the Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) formulae. The CG equation was formulated on creatinine measurements in an inpatient cohort of Caucasian males with mild renal dysfunction[10] while the MDRD study was conducted on outpatients with a variable degree of chronic renal impairment.[11] Neither of these predictive equations has been rigorously evaluated in critically ill patients.

In this issue of the *Indian Journal of Critical Care Medicine,* Kharbanda *et al*.,[12] estimated GFR using the CG and MDRD formulae in a mixed group of patients admitted to the intensive therapy unit (ITU) and compared it with 24-hour Cr Cl to assess renal function. Although there was correlation between these predictive equations and 24-hour Cr Cl, the degree of bias seems to suggest that they are imprecise tools for clinical use in an intensive care setting.

What was the degree of renal dysfunction of the patients studied? The mean serum creatinine level was 1.06 mg/dl and the mean 24-hour urine output was close to 2.0 liters without diuretics. The mean 24-hour Cr Cl was 79.76 ml/min/1.73 m$^2$. Is it possible that these patients had relatively preserved renal function at the time of testing? If so, could it be that the positive correlation that the investigators found between both predictive equations and 24-hour Cr Cl was due to the reasonably "steady state" renal function in these subjects?

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Hoste *et al.*, conducted a similar study on 28 patients admitted to the ICU with normal serum creatinine (<1.5 mg/dl).[13] Neither the CG nor the MDRD equation showed significant correlation with a 1 hour Cr Cl. Although these patients had a "normal" creatinine level, the 1 hour urinary Cr Cl was below 80 ml/min/1.73 $m^2$ in 71% of patients, suggesting poor sensitivity of these predictive equations to detect renal function in critically ill patients. In another prospective cohort study in critically ill patients, MDRD and CG estimates of GFR were compared with 4 hour urinary Cr Cl. MDRD estimates were performed by 4 and 6 variable equations; however, the degree of bias and percentage error were unacceptably high for clinical use in this subgroup of patients.

The weight of evidence seems to suggest that the CG and MDRD predictive equations have limited value in nonsteady state conditions, characterized by rapidly changing renal function that is characteristic of critically ill patients with AKI. Given the poor correlation that creatinine levels bear with renal function in AKI, it is perhaps understandable that equations based on it are also likely to have similar drawbacks. Urinary Cr Cl based on timed urine collection may be preferable to predictive equations to assess renal function more precisely in sick ICU patients. Although conventionally performed on a 24-hour sample, this is rarely feasible in an ICU setting; much shorter collection times may be appropriate in critically ill patients. Biomarkers such as cystatin C and neutrophil gelatinase associated lipocalcin (N-GAL) are being investigated and will perhaps, in the future, offer us more precise tools to estimate renal function in the critically ill.[14,15]

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