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Received for publication: 28.7.10; Accepted in revised form: 4.8.10

Nephrol Dial Transplant (2010) 25: 3812–3814
doi: 10.1093/ndt/gfq454
Advance Access publication 27 July 2010

Baseline creatinine to define acute kidney injury: is there any consensus?

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Acute kidney injury (AKI) is an important clinical problem which is associated with higher mortality, increased health resource utilization and increased risk for chronic kidney disease (CKD) [1–3]. Previously, more than 30 definitions of acute renal failure have been used in the literature, resulting in a wide variation in reported incidence and mortality [4,5]. After the introduction of the consensus criteria Risk Injury Failure Loss End-Stage Renal Disease (RIFLE) [6] and Acute Kidney Injury Network (AKIN) [7,8], there has been a positive move towards the use of more standardized definitions in the literature. Despite their limitations, this has nevertheless been a step forward, allowing meaningful comparisons across studies [9].

The conceptual model of AKI is that of a rapid worsening of kidney function from pre-morbid levels. That said, ideally, a baseline serum creatinine (bCr) value which is reflective of the patient's pre-morbid kidney function should be known, and this is the value to which we compare subsequent creatinine values to diagnose AKI. However, in many cases, bCr value is not readily available to the physician or research team [10]. When no information on prior renal function is available, the Acute Dialysis Quality Initiative has recommended back-estimation from the Modification of Diet in Renal Disease (MDRD) formula, assuming an estimated GFR of 75 mL/min/1.73 m^2 [6]. Various studies have used different ways to define the bCr, such as the creatinine at the time of hospital admission [11–13], the minimum creatinine value during the hospital stay [1,14,15], the creatinine estimated from MDRD [10,16–18] or the lowest value among these. The choice of bCr has a marked effect on the prevalence of AKI, the severity (or stages) of AKI and the mortality that is associated with AKI in various stages [9,19–22]. Moreover, such misclassification can lead to different therapeutic approaches, for example, being inappropriately aggressive in the case of false-positive AKI or misguided complacency in the case of false negatives.

The comparative merits of possible surrogate values for bCr, including MDRD estimation, have been addressed by a number of studies in both adults [19–21] and children [22]. The ideal way to 'validate' the use of estimated bCr (by MDRD) is to take an unselected cohort with known bCr (within the past year, ideally within the previous 3 months). Patients are then classified into RIFLE/AKIN classes based on both the known bCr and the estimated bCr. The misclassification that results from the use of the estimated bCr can then be quantified.

Bagshaw *et al*. performed a comparison of observed *versus* estimated bCr (by MDRD) for determination of RIFLE class in 1314 ICU patients [20]. Use of estimated bCr misclassified 18.8% of patients as having AKI on ICU admission. They concluded that estimated bCr appears to perform reasonably well the determination of the RIFLE categories when pre-morbid renal function was near normal and caution against the use of estimated bCr in patients with suspected CKD. This is clearly logical since the MDRD estimation method assumes that the patient has near-normal pre-morbid renal function, an assumption that obviously cannot be made in the case of suspected CKD,

for example, in patients with long-standing diabetes and proteinuria or patients with multiple risk factors for CKD (older, diabetes, hypertension, African Americans, etc.).

Using the AKIN criteria, Siew and colleagues evaluated three surrogates for bCr in 4863 hospitalized patients: estimated from MDRD, the admission Cr and minimum inpatient serum Cr value [21]. They concluded that all three result in bi-directional misclassifications of the incidence and prognosis of AKI in a hospital setting. In a recent study, Zavada *et al*. compared an estimated bCr by MDRD, an estimated bCr by their newly developed equation using the same anthropometric variables and a gender-fixed bCr [19]. Similar to the above-mentioned findings in the hospital setting, estimates of AKI incidence in the ICU using RIFLE classification was affected by the bias and limited accuracy of all three methods. Specifically, the use of the MDRD equation to estimate bCr would overestimate or underestimate cases of 'risk', but was less likely to misclassify patients in 'injury' and 'failure'. Moreover, neither of the two alternative methods offered a consistent improvement in accuracy compared with MDRD-based estimates.

So, where does this leave us? First, what is clear from all these studies is that any surrogate or estimated bCr will result in some bi-directional misclassification of AKI. This will have an effect on the accuracy of estimates of prevalence, incidence, risk ratios and so forth. It is important to note, however, that such inaccuracy is likely to have greatest significance in mild AKI (e.g. RIFLE Risk or AKIN Stage 1) compared with moderate to severe AKI (e.g. RIFLE Injury/Failure or AKIN Stage 2/3) [19]. Therefore, these factors should be taken into consideration when reading and interpreting the literature [9].

Second, it is crucial for investigators to take every effort to find and use a true bCr before resorting to the use of any surrogate values, particularly since CKD is a key risk factor for AKI.

Third, in recognition of the limitations of estimated bCr, the AKIN group has proposed using the admission serum creatinine as the 'baseline' for hospital-acquired AKI (AKIN Workgroup Statement, personal communication). This is a workable solution particularly for patients with elective hospitalization, for example, elective surgery or cardiac catheterization, and probably reflects the real bCr in those cases. Additionally, if AKI onset is likely to be a consequence of a specific insult, such as surgery or radiocontrast, the 'baseline' can be assumed as the value most proximate to the precipitating event.

Fourth, while the majority of studies have, and likely will, deal with hospital-acquired AKI, the problem of the unknown bCr remains unresolved in the case of community-acquired AKI, for example, a patient who presents to the emergency room with an elevated sCr. In this scenario, only a retrospective diagnosis of AKI is possible, from the trajectory of sCr during the hospitalization. For this issue, AKIN did not have any specific recommendation. Moreover, it recognized that this limitation could potentially introduce significant bias in certain studies.

Despite the known shortcomings of estimating bCr using MDRD, unfortunately, no superior alternative has emerged thus far. More studies and improved methods to estimate bCr are clearly needed. In the interim, perhaps we should err on the side of caution and continue to use it until a definitively better solution comes along. Although RIFLE/AKIN are certainly not perfect, the scientific community has begun to speak more or less the same language when discussing AKI. We should be careful not to take one step forward then two steps backward. We do not want to find ourselves in 2015 with everyone using RIFLE/AKIN, but having 30 more different definitions of baseline creatinine.

Conflict of interest statement. None declared.

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Received for publication: 15.5.10; Accepted in revised form: 5.7.10