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EDITORIAL

# Blood urea nitrogen and creatinine in in-hospital cardiac arrest patients

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When unexpected clinical deterioration, such as in-hospital cardiac arrest (IHCA) or sudden death, occurs in hospitalization patients, especially for those patients who have not been recognized with a terminal disease (a clinical situation showing an irreversible and continuously deteriorated patient's health accompanied with an expectedly shortly lifespan) or who do not sign the do-not-resuscitate (DNR) orders, regardless whether the cause is, poses a biggest and extraordinary challenge for a psychosocial emergency, which may result in many uncertainties, including the decision to withhold and withdraw life-sustaining treatment or the following legal issues.[1,2] Therefore, many efforts will be initiated immediately for those IHCA patients to save their lives, if DNR orders are not obtained. Some patients may prolong life due to giving the presence of technological advances, but post-resuscitation outcomes may be critical. Therefore, more powerful and accurate biomarkers and/or clinical parameters are urgently needed to determine what situations may be associated with mortality as well as with developing post-resuscitation morbidity while surviving.[3–5] In theory, similar to all other diseases,[5–9] an early identification of risk factors associated with IHCA and an offering the prompt and effective treatment may decrease the IHCA -related morbidity and mortality. The recent publication in the last October issue of the *Journal of the Chinese Medical Association* entitled "Prognostic significance of the blood urea nitrogen to creatinine ratio in in-hospital cardiac arrest after targeted temperature management," attempted to use the simple parameters of blood urea nitrogen (BUN) to creatinine (Cr) ratio (BCR) to predict the neurological outcome at discharge among IHCA patients receiving targeted temperature management (TTM).[10] The authors found that elevated post-TTM BCR was a significant predictor (adjusted odd ratio [aOR], 1.081; 95% confidence interval [CI], 1.002-1.165) and elevated intra-arrest BCR was a marginal predictor (aOR, 1.067; 95% CI, 1.000-1.138) for worse neurological outcomes at discharge among IHCA patients.[10] Additionally, the authors found a cutoff value of 16.7 for a post-TTM BCR with a sensitivity of 61.9% and a specificity of 70.0% to predict poor neurological outcome at discharge among IHCA patients.[10] The current article is interesting and worthy of further discussion.

First, it should clarify what does the item, such as BUN, Cr, or BCR, means. The authors considered the aforementioned parameters as a biomarker, especially for BCR for renal function (acute kidney injury [AKI]), based on showing a promising indicator (BCR) reflecting more than patients' fluid or nutritional status and a positive association with mortality in heart failure, renal disease, COVID-19, and stroke.[10] Similarly, after ischemic stroke, lower BCR was associated with better neurological function.[10] All suggest that a higher BCR (poor renal function or severity of AKI) may be associated with worse outcomes, especially for patients with a poor neurological prognosis. We agree with the authors' opinion; however, some concerns should be announced. Biochemistry and simple complete blood counts may be one of the most frequently used tests in clinical routine practice, and besides history and physical examination, both parameters are considered more convenient and less costly with rapid availability to help physicians clarify what the urgency of a patient's condition is.[7,8,11] However, these simple tests are often influenced by many confounding factors, and all may result in misinterpretation easily, leading to misjudgment in the diagnosis and severity of diseases in patients,[12–14] and contributing to the uncertainty of the roles of biochemistry and simple complete blood counts. In fact, as shown by the authors, the role of BCR was inconformity.[10]

Although BUN and Cr concentrations are easily available biomarkers of renal function in clinic, BUN and Cr concentrations of patients could not be totally reflective of real renal function.[14] Many factors influence both BUN and Cr concentrations. The nutrition status, such as dietary protein supply, rate of amino acid incorporation into tissue, amino acid release from tissue, and liver capacity to form urea, significantly influences the production of BUN, resulting in fluctuation of serum levels independently from renal function.[15] Although measurement of serum Cr may be more constant compared to measurement of serum BUN, at least three factors influence Cr concentration beyond renal function, including variation in Cr production, tubular secretion, and analytical measurement issues.[15] Based on

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the metabolic end products of nitrogen-containing substances in human bodies, any alternation in these metabolic pathways leads to disproportional BUN, Cr, and BCR dissociation.[15] If both BUN and Cr could not clearly or accurately reflect the renal function, it is hard to believe that BCR can.

As shown by the authors, BCR was a laboratory biomarker frequently used for determining the dehydration, and adequate hydration may prevent adverse neurological recovery in stroke patients with a BCR greater than 15.[10] However, no gold standard method could be applied for measuring hydration status objectively, contributing to a biggest challenge for targeted rehydration treatment suggestively.[16] We are wondering how to share the authors' experience with other patients if IHCA patients are stated to have a BCR greater than 16.7,[10] since rehydration therapy is relatively difficult in the context of airway compromise and fluid overload in patients with co-existing cardiac diseases, especially heart failure.[16] Unfortunately, up to two-fifths of patients were found in Dr. Meng's study.[10] Did these patients with underlying heart failure presented as IHCA also have the similar correlation between BCR and worse neurological outcome?

Due to the diversity of patients with underlying diseases, it may be particularly difficult to determine the cause of IHCA. Hypovolemic shock related with IHCA may be beneficial with early recognition of dehydration, such as a high BCR level. By contrast, cardiogenic shock may be not. Dr. Sun et al investigated the prognostic effectiveness of BCR on cardiogenic shock, and the results showed high CBR was correlated with improved in-hospital survival for patients with cardiogenic shock, regardless of the presence or absence of AKI status, as compared to low BCR.[17] Similar to Dr. Sun's study,[17] Dr. Meng's study also could not prove causality.[10]

Although Dr. Meng's effort was done on the identification of the critical prognostic factor to predict the neurological outcomes in IHCA patients, many confounding factors and possible biases could not be completely avoided, contributing to the uncertain role of BCR in the prediction of neurological outcomes in patients in IHCA patients after resuscitation. However, at least, these parameters are checked routinely and are easily available in hand. We hope more and more studies will be conducted to establish a more powerful and reproducible model to offer useful information about the outcome of IHCA patients. All efforts are attempted to save lives and diminish the post-resuscitation sequelae in these critically ill patients.

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