**Blood Urea Nitrogen/Creatinine Ratio in Acute Heart Failure Patients**

Nobuyuki Shiba, MD, PhD

Heart and kidney have a close bidirectional association known as 5 types of “cardiorenal syndrome (CRS)” in the development and worsening of acute and chronic disorders. CRS type 1 appears in 27–40% of patients with acute decompensated heart failure (ADHF) and is characterized by a rapid exacerbation of cardiac function that leads to acute kidney injury (AKI). AKI is the term proposed to reflect the entire spectrum of acute renal failure that occurs in a variety of settings from minimal creatinine (Cr) elevation to anuria.

### Classification of CRS

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<th>CRS subtype</th>
<th>Definition</th>
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<tr>
<td>1</td>
<td>Acute worsening of heart function leading to kidney injury and/or dysfunction</td>
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<tr>
<td>2</td>
<td>Chronic abnormalities in heart function leading to kidney injury or dysfunction</td>
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<tr>
<td>3</td>
<td>Acute worsening of kidney function leading to heart injury and/or dysfunction</td>
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<tr>
<td>4</td>
<td>Chronic kidney disease leading to heart injury, disease and/or dysfunction</td>
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<td>5</td>
<td>Systemic conditions leading to simultaneous injury and/or dysfunction of heart and kidney</td>
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The traditional mechanisms of CRS type 1 are low cardiac output, neurohormonal activation, and release of vasoactive substance leading to low renal perfusion. Additionally, elevated central venous pressure, high intra-abdominal pressure, anemia, and a significant deterioration of immune and somatic cell signaling have been reported as contributors to AKI. The other 4 subtypes of CRS are briefly summarized in Table.

AKI is traditionally divided into 3 categories. Prerenal disease is seen in the context of decreased blood delivery to the kidneys, including HF, shock, acute hemorrhage, severe diarrhea, etc. Intrinsic renal disease includes vascular, glomerular, interstitial, and tubular subcategories. Postrenal or obstructive disease is frequently observed in prostatic disease (hyperplasia or cancer) and metastatic cancer. There is no universally accepted definition of AKI, but 3 definitions have been proposed: RIFLE (Risk, Injury, Failure, Loss of kidney function and End Stage Kidney Disease); AKIN (Acute Kidney Injury Network); and KDIGO (Kidney Disease: Improving Global Outcomes). These 3 definitions include 2 common criteria: decreased urine output or decreased glomerular filtration rate (GFR), which can be assessed by serum Cr level. The etiology of AKI in ADHF patients, other than decreased cardiac output, is multifactorial and complex. Several researchers have reported that HF medication might be associated with AKI development.

Diuretics remain the major treatment in ADHF patients and may lead to a significant decrease in renal perfusion, which may worsen renal function. Furthermore, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are essential for treating ADHF patients, considering the pathogenesis of HF, but the association between such treatments and increasing Cr level has been frequently reported.

Urea production occurs primarily in the urea cycle of the liver as a waste product of protein digestion. Serum Cr is freely filtered at the glomerulus and not reabsorbed, which means Cr clearance can substitute for the true GFR to estimate renal function. Otherwise, the rate of urea excretion is determined mainly by its rate of glomerular filtration and tubular reabsorption.

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reabsorption. Although waste nitrogen is excreted by the kidney primarily as urea (90%), there are several possible mechanisms of increasing urea reabsorption in HF patients. Increased activity of both the renin-angiotensin-aldosterone system and sympathetic nervous system enhances sodium and water absorption and cause passive (“concentration dependent”) reabsorption of urea in the proximal tubules. Furthermore, these activities also facilitate the “flow dependent” reabsorption of urea in the collecting duct (Figure), which is greatly increased in the presence of arginine vasopressin (AVP) via the urea transporter, and AVP-mediated upregulation of such transporters will enhance this process. Because BUN levels are influenced by protein intake, catabolism, and tubular reabsorption, it is not a reliable marker of renal function, but BUN elevation may be a sign of severe HF, which includes low cardiac output and an activated neurohormonal system.

BUN/Cr has been used for the differentiation of prerenal renal dysfunction from intrinsic renal parenchymal disease. Brisco et al reported that elevated admission BUN/Cr identifies ADHF patients with possibly reversible renal dysfunction by HF treatment, but also noted that elevated BUN/Cr was associated with worsened survival in patients with GFR <45 mL/min/1.73 m². The findings reported by Takaya et al support this conclusion and might show more clearly that BUN/Cr is a useful decision-making tool in treating ADHF patients with AKI.

Although BUN/Cr is a useful management tool in ADHF patients, it is a less than ideal measure of renal urea processing or AKI, as discussed earlier. Several novel renal biomarkers recently reported, such as neutrophil gelatinase-associated lipocalin, N-acetyl-β-D-glucosaminidase, kidney injury molecule 1, and cystatin C, may offer a future promising strategy in treating ADHF patients with AKI.

References