Cardiorenal Syndrome

By Peter A. McCullough

The complex interplay between the kidney and the heart where one organ dysfunction can initiate or accelerate the decline of the other was recently addressed at a KDIGO Controversies Conference on the prevention, diagnosis, and management of heart failure in kidney disease (1). Since cardiorenal syndrome (CRS) is often observed in the setting of heart failure, CRS continues to be one of the highest topics of interest among those caring for medical patients in the hospital and for those in ambulatory primary and medical subspecialty care (2, 3). In 2019, Rangaswami et al. (4) published the first American Heart Association (AHA) Scientific Statement on the topic. This well-written document goes a long way in explaining what we know and how much more we don’t know about CRS.

For type 1 CRS, which is most commonly acute heart failure (HF), followed by azotemia in response to intravascular diuresis, the important message is that the biomarkers of tubular injury in general are not elevated, which suggests that it is not a form of bona fide acute kidney injury (AKI) (5). Additionally, multiple studies have found that withdrawing renin-angiotensin-aldosterone system inhibitors (RAASIs) because of clinical concern for the azotemia is associated with higher rates of readmission and death. Thus, one may take the view that in the absence of superimposed sepsis or shock, type 1 CRS is a problem of insufficient plasma refill and relative arterial underfilling in the setting of excess venous congestion. Because RAASs lowers cardiac filling pressures acutely and antagonizes the maladaptive effects of angiotensin II in the kidney, it is mechanistically attractive to continue these agents in the setting of acute HF unless there is a compelling indication (hypotension, hyperkalemia, or drug intolerance) to withdraw them. Contextual cessation of RAASs because of azotemia does not appear to be well supported, and nephrologists should reconsider this common approach.

Type 2 CRS is chronic HF contributing to the progression of chronic kidney disease (CKD), and this certainly happens in the setting of type 2 diabetes and macroalbuminuria (6, 7). HF itself may contribute to proteinuria, and the combined effect on peripheral edema leads to escalating doses of diuretics. Whereas the principles of decongestion and a narrow therapeutic window for cardiac volume loading are manifest, observational data suggest that patients with HF who are receiving the highest doses of diuretics have the worst outcomes. One study has shown as one size fits all high/low-dose loop diuretics in HF or intravenous infusions have failed to shed light on the optimal approach. However, when diuretic management is guided by the use of blood biomarkers such as B-type natriuretic peptide (BNP) in the office or implantable pulmonary pressure monitors, HF outcomes including hospitalization and death can be improved.

Type 3 CRS is AKI that leads to HF (8). This can certainly happen in an elderly hospitalized patient; the AKI usually must be anuric and the patient be predisposed to diastolic or systolic dysfunction. Few data exist on this problem; however, observational studies suggest that inadvertent intravenous fluid administration may make it worse. Thus, our use of intravenous crystalloid must be goal directed, and “maintenance” parental fluid approaches should be discouraged.

Type 4 CRS is progressive CKD that leads to left ventricular hypertrophy and dysfunction (9, 10). It is important to realize that 20% of CKD patients carry a diagnosis of HF before they start renal replacement therapy, and there is a wealth of opportunity upstream in CKD to prevent HF and/or decrease the risk for hospitalization or death (11, 12). For patients who are receiving dialysis, the choice of frequent home dialysis 5 or 6 days a week appears to be the most beneficial in preventing the development or worsening of HF (13).

Finally, type 5 CRS is simultaneous heart and kidney failure in the setting of an overwhelming systemic illness such as influenza, sepsis, or multiple trauma (14). The principles here are supportive care to allow the opportunity for organ recovery (15). Avoidance of superimposed ischemic or chemotoxic injury to either organ is a high priority. The data suggest that maintaining mean arterial pressures > 65 mm Hg is essential to organ preservation and survival. In this setting, biomarkers of cardiac injury and failure (troponin, BNP) and also AKI (TIMP2 × IGFBP7, NGAL, L-FABP) can be extremely useful in distinguishing transient hemodynamic effects from acute tubular injury (16). The AKI biomarkers strongly predict the development of stage 2/3 AKI (doubling or more of serum creatinine) over the following 12 to 48 hours (17). This can be enough time to change clinical strategies, including use of hemodynamic monitoring, inotropic agents, and withdrawal of nephrotoxins such as certain antibiotics or the use of iodinated contrast material.

In summary, the work of the AHA Scientific Committee has been extremely valuable in moving this field forward, and to find this piece in a cardiology journal is a welcome sight for cardionephrologists, who are working so hard to care for these patients. To learn more about this topic, please consider attending the annual meeting of the Cardiorenal Society of America, to be held in Phoenix, Arizona, March 6–7, 2020, www.cardiorenalsociety.org.

Peter A. McCullough, MD, MPH, is Professor of Medicine and Vice Chair of Internal Medicine at Baylor University Medical Center, Dallas, Texas.

References