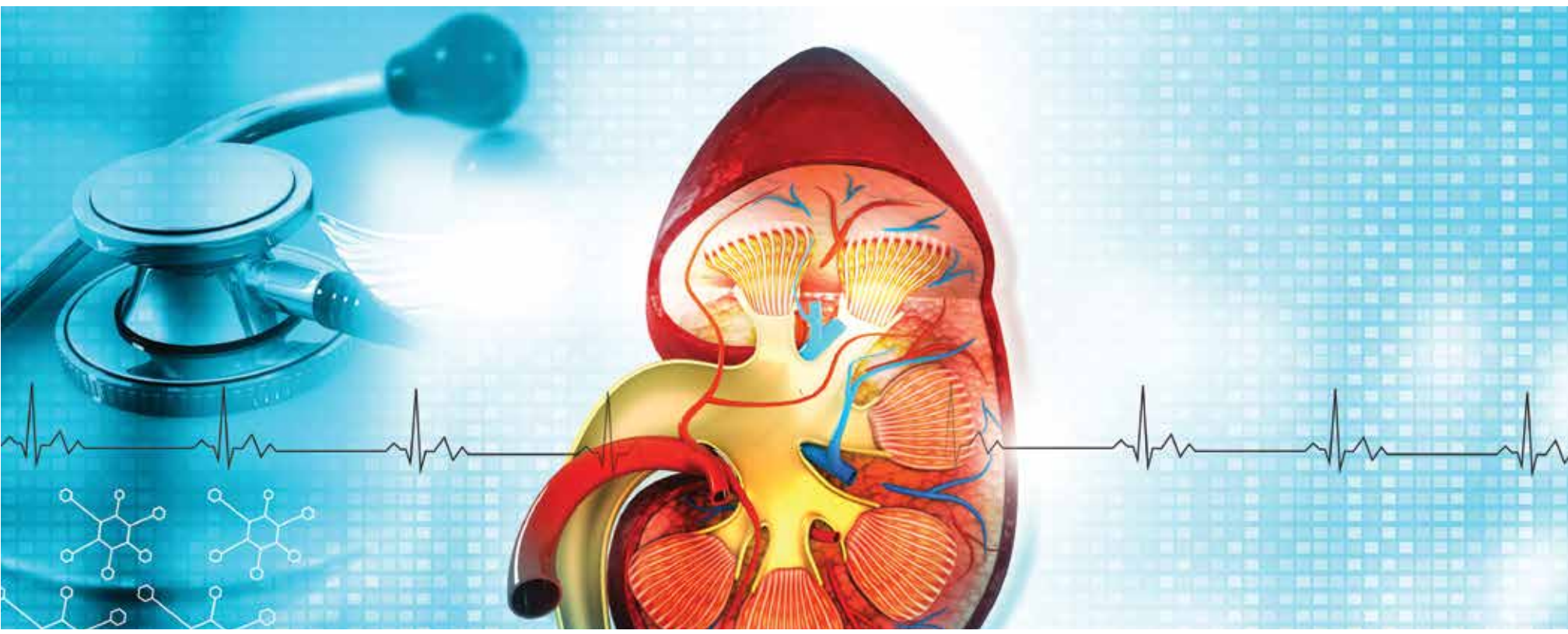

KIDNEY AND CARDIOVASCULAR DISEASES

Exploring Cardiorenal Developments

The heart and the kidney share immense metabolic demands, overlapping stressors, and devastating diseases. Cardiovascular disease remains the predominant cause of death for people with kidney diseases. In turn, the development of chronic kidney disease portends poor outcomes and may limit guideline-directed medical therapies for people with cardiovascular disease.

Thankfully, kidney and cardiovascular diseases are also joined by a growing number of therapeutic options: angiotensin-converting enzyme inhibitors, angiotensin receptor blockers (alone or in combination with neprilysin inhibitors), glucagon-like peptide 1 receptor agonists, mineralocorticoid receptor antagonists, and of course, sodium-glucose cotransporter-2 inhibitors. Nephrologists and cardiologists now welcome our shared patients to the kitchen of many cooks. However, the need for dedicated cardio-nephrologists rises with the growing complexities of advanced heart failure management, cardiothoracic surgery, and other cardiovascular disease treatments.

In this special issue of *Kidney News*, we explore cardiorenal topics for the nephrologist that range from the common (e.g., loop diuretic choice in heart failure) to the critical (e.g., combined kidney-heart transplant and complications of left ventricular assist devices). We also highlight the experience of model cardio-nephrology clinical and training centers across the United States. ■

Kidney News *thanks Daniel Edmonston, MD, MHS, for editing this special issue. Dr. Edmonston is assistant professor of medicine (nephrology), Duke University School of Medicine, and faculty member, Duke Clinical Research Institute, in Durham, NC.*

The author reports no conflicts of interest.

LVADs and the Kidney

By Carl P. Walther and Sankar D. Navaneethan

When the heart is chronically failing to provide adequate circulation despite numerous evidence-based medical and procedural options, left ventricular assist devices (LVADs) can be placed. Implantation of these devices is usually permanent (destination therapy), although some recipients may go on to receive heart transplants (bridge to transplant) (1); rarely is there sufficient heart recovery to enable LVAD removal (bridge to recovery) (2).

Although kidney health and function are important and affected across the spectrum of heart disease and cardiovascular procedures, perhaps nowhere is the kidney more challenged than in LVAD recipients. First, consider the kidney substrate: Kidney damage may accrue at each stage of the life course leading to advanced heart failure and LVAD implantation. Diabetes and atherosclerosis injure both the heart and the kidney; the aging process causes fibrosis in both organs; acute kidney injury (AKI) episodes accumulate from prior cardiovascular procedures and surgeries; and chronic heart failure, punctuated with acute decompensations, causes congestive nephropathy and later, with failure of forward flow, ischemia.

From this environment, the kidney enters the perioperative period. LVADs are placed once all less-invasive measures have been exhausted; prior to implantation, many patients require one or more inotropes or even temporary mechanical circulatory support with a balloon pump, a percutaneous microaxial pump, or veno-arterial extracorporeal membrane oxygenation. From this state of chronic and acute stress and damage, the kidney is then put through the prototypical insult of major cardiac surgery. Ischemia-reperfusion injury, inflammatory cascade activation and oxidative stress, hemolysis, and nephrotoxic exposures may all be at play (Table 1). Once the LVAD is in place, macrocirculation usually normalizes, with cardiac output returning to normal and elevated central venous pressures declining (except when the feared complication of right ventricular failure develops). This usually increases estimated kidney function (at least for a time and with the caveat that kidney function estimates are likely to be highly confounded in these patients), and in some people, this results in persistent normalization of estimated kidney function (in the majority, there is no evidence of persistent kidney function improvement) (3). Potential mechanisms for beneficial and harmful effects on the kidney with LVAD support are shown in Figure 1.

Nephrology expertise is essential for accurate etiologic and prognostic deconstruction of AKI syndrome. This may require integration of relevant information ranging from distant kidney events to operating room details and potentially gathering information with tools from manual urine microscopy to interpretation of tissue inhibitor of metalloproteinases-2 (TIMP-2) ·

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insulin-like growth factor-binding protein 7 (IGFBP7) scores to image-based venous congestion assessments. Kidney replacement therapy (KRT) decisions (need, timing, and therapy parameters) are the most conspicuous nephrology service, and these decisions necessarily use subjective judgment on the part of the nephrologist and close collaboration with intensivists. KRT management throughout the recovery course is a challenge requiring close collaboration as well, particularly when the patient no longer has invasive hemodynamic monitors. Fluid removal in this case requires consideration of the pump speed, flow rate, and pulsatility index, along with appropriate hemodynamic measurements based on whether the aortic valve opens (in which case usual oscillometric or auscultatory measurements can be used) or does not (requiring measurement using Doppler ultrasound and a manual sphygmomanometer) (4).

The era of precision nephrology holds great promise for individualized diagnoses and targeted therapies in many areas. The realm of durable mechanical circulatory support will be a particular challenge, given the extreme clinical complexity of kidney insults and the limited access to kidney tissue for study because of the tenuousness (and anti-coagulation) of the patients. Despite these challenges, noninvasive diagnostic and investigative tools—primarily being developed in other realms—should enable improvements in kidney diagnostic and prognostic precision and even provide mechanistic insights soon. Precise pathophysiologic diagnostics, plus effective targeted therapies for cardiac surgery-associated AKI, are urgently needed to improve the health of LVAD recipients. ■

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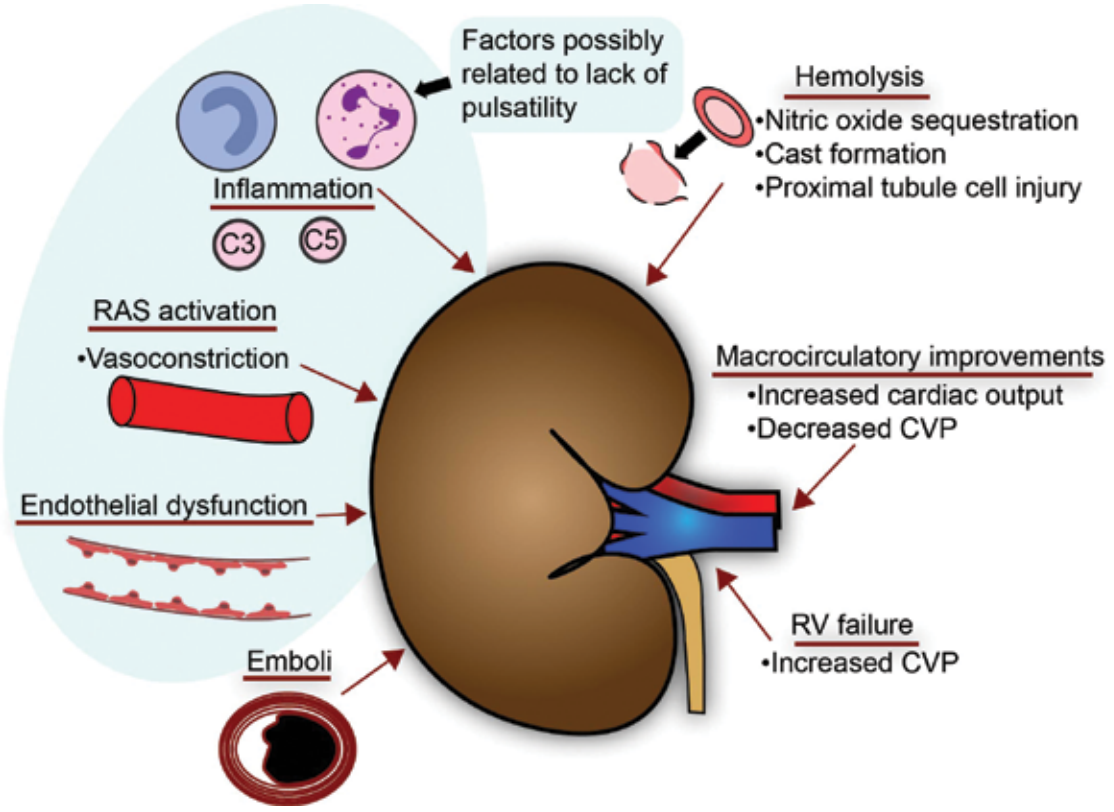
The authors report no conflicts of interest.

Figure 1. Potential mechanisms for LVAD effects (beneficial and harmful) on the kidneys



CVP, central venous pressure; RAS, renin-angiotensin system; RV, right ventricle. The figure is reprinted from Walther et al. (4).

Table 1. Categories and mechanisms of potential AKI with LVAD implantation

Category of injury	Causes
Ischemia and ischemia-reperfusion injury	CPB initiation and discontinuation, microcirculatory dysfunction, temperature changes, intraoperative bleeding, aortic cross clamping for additional procedures
Inflammation	CPB, surgical tissue injury
Hemolysis	CPB, LVAD pump
Microemboli	Cholesterol emboli, thromboemboli, gaseous emboli with CPB
Nephrotoxic exposures	Antibiotics

CPB, cardiopulmonary bypass.

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