# Management of Heart Failure in Advancing CKD: Core Curriculum 2018

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Heart failure and chronic kidney disease have increasing incidence and prevalence owing in part to the aging population and increasing rates of hypertension, diabetes, and other cardiovascular and kidney disease risk factors. The presence of one condition also has a strong influence on the other, leading to greater risks for hospitalization, morbidity, and death, as well as very high health care costs. Despite the frequent coexistence of heart failure and chronic kidney disease, many of the pivotal randomized trials that guide the management of heart failure have excluded patients with more advanced stages of chronic kidney disease. In this Core Curriculum article, management of a challenging, yet not unusual, case of heart failure with reduced ejection fraction in a patient with stage 4 chronic kidney disease provides an opportunity to review the relevant literature and highlight gaps in our knowledge.

*Complete author and article information provided before references.*

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***Case:*** *An 82-year-old man is referred for steadily worsening kidney function in the setting of chronic congestive heart failure (HF). His history is remarkable for long-standing hypertension and a myocardial infarction in his late 60s with Canadian Cardiovascular Society grade I stable angina. Coronary angiography shows no lesions believed to be amendable to percutaneous or surgical revascularization. He has been treated for HF with reduced ejection fraction (HFrEF) for approximately 5 years and has noted slowly increasing serum creatinine concentrations. His current medications include acetylsalicylic acid, 81 mg; bisoprolol, 2.5 mg; furosemide, 40 mg; candesartan, 8 mg; and atorvastatin, 40 mg, all once daily. He has no drug allergies, although treatment with an angiotensin-converting enzyme (ACE) inhibitor was discontinued due to cough. He still works 6 days per week running his own small business. He experiences at worst New York Heart Association (NYHA) class II symptoms and has edema to the shins, mostly by the end of the day and improved by morning.*

*Physical examination reveals an elderly man with mild kyphoscoliosis, no distress, appearing his stated age. Blood pressure is 118/72 mm Hg with a heart rate of 64 beats/min, regular rhythm, and normal respiratory rate. He has no carotid bruits, and jugular venous pressure is ~4 cm above the sternal angle. Chest auscultation reveals some scattered crackles in the bases, and heart sounds are somewhat distant with a soft pansystolic murmur radiating to the left axilla and no extra heart sounds. Examination of the abdomen has unremarkable findings, and he has mild pitting edema to the lower shins with some chronic venous stasis changes to the skin. His extremities feel warm and are well perfused.*

*Laboratory tests reveal serum creatinine concentrations of 1.2 to 1.5 mg/dL for many years, but during the past 2 years, they have slowly increased to 2.0 to 2.2 mg/dL. Estimated glomerular filtration rates (eGFRs) are between 27 and 30 mL/min/1.73 m². Serum potassium concentrations are consistently <5.0 mEq/L, hemoglobin concentration is 12.0 g/dL, other chemistry results are normal, and urinary albumin-creatinine ratio (UACR) is 45 mg/g with no hematuria. An ultrasound of the kidneys shows poor corticomedullary differentiation, some cortical thinning, and no obstruction, consistent with chronic medical kidney disease. An echocardiogram reveals mild to moderate mitral regurgitation, mild aortic valve sclerosis with no gradient, and left ventricular ejection fraction (LVEF) of 38% with wall motion abnormalities consistent with ischemic heart disease.*

**Question 1: How common is it for a patient with HFrEF to have or develop concomitant chronic kidney disease (CKD) with eGFR < 60 mL/min/1.73 m²?**

a) <5%
b) 5%-25%
c) 45%-65%
d) >90%

**Question 2: Which one of the following statements is most correct?**

a) With more severe stages of CKD, the risk for death in patients with HF increases significantly
b) Cardiac resynchronization therapy (CRT) is indicated in all patients with HFrEF, regardless of kidney function
c) CRT is indicated in all patients with CKD stages 1 to 3
d) Most studies of HFrEF included patients with CKD stages 1 to 4

*For answers, see the following text.*



*The Core Curriculum aims to give trainees in nephrology a strong knowledge base in core topics in the specialty by providing an overview of the topic and citing key references, including the foundational literature that led to current clinical approaches.*

## Epidemiology of Combined HF and CKD

The patient described in this scenario is unfortunately one of a growing number who live in the intersection of 2 increasingly prevalent diseases, HF and CKD. Both conditions have increasing incidence and prevalence owing in part to the aging population, but also due to increasing rates of hypertension, diabetes, or other cardiovascular and kidney disease risk factors. The presence of one condition also has a strong influence on the other, leading to greater risks for hospitalization, morbidity, and death, as well as very high health care costs. HF is very common, projected to affect more than 8 million Americans by 2030, and currently is implicated in 1 of every 9 deaths in the United States. There are approximately 1 million hospitalizations for HF each year in the United States, at a total cost of nearly $30.7 billion; this cost is projected to reach nearly $70 billion by 2030. CKD is also very common, with estimates suggesting that nearly 500 million people worldwide have CKD stage 3 or greater (eGFR < 60 mL/min/1.73 $m^2$). Due to declining death rates globally from such diseases as human immunodeficiency virus (HIV)/AIDS, malaria, and other infectious diseases, as well as cardiovascular diseases and many cancers, CKD has increased dramatically as a cause of both morbidity and mortality worldwide.

Individuals with heart disease as a primary disorder can experience reduced kidney function as a secondary disorder, and vice versa, or both can coexist based on shared risk factors or systemic disorders, so called cardiorenal syndromes (CRSs). CRSs are generally defined as disorders of the heart and kidneys in which acute or chronic dysfunction in one organ triggers acute or chronic dysfunction of the other. Box 1 presents the 5 phenotypes and their definition. Figure 1 shows a proposed schematic by which the heart and kidneys interact with one another, and disease of one organ can produce progressive dysfunction through hemodynamic, neurohormonal, and other modulating processes.

**Box 1.** Classification and Definitions of Cardiorenal Syndromes

**General Definition of Cardiorenal Syndromes**
Disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other.

**Acute Cardiorenal Syndrome (Type 1)**
Acute worsening of cardiac function leading to decreased kidney function.

**Chronic Cardiorenal Syndrome (Type 2)**
Long-term abnormalities in cardiac function leading to decreased kidney function.

**Acute Renocardiac Syndrome (Type 3)**
Acute worsening of kidney function causing cardiac dysfunction.

**Chronic Renocardiac Syndrome (Type 4)**
Long-term abnormalities in kidney function leading to cardiac disease.

**Secondary Cardiorenal Syndromes (Type 5)**
Systemic conditions causing simultaneous dysfunction of the heart and kidney.

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Estimates of the prevalence of the coexistence of HF and CKD are challenging and subject to bias. For instance, observational studies typically collect a cohort of patients characterized by the presence of one of the diseases and then determine the prevalence of the other, leading to large variations in the estimates of coexisting CKD and HF. The Acute Decompensated Heart Failure National Registry (ADHERE) analyzed data from nearly 120,000

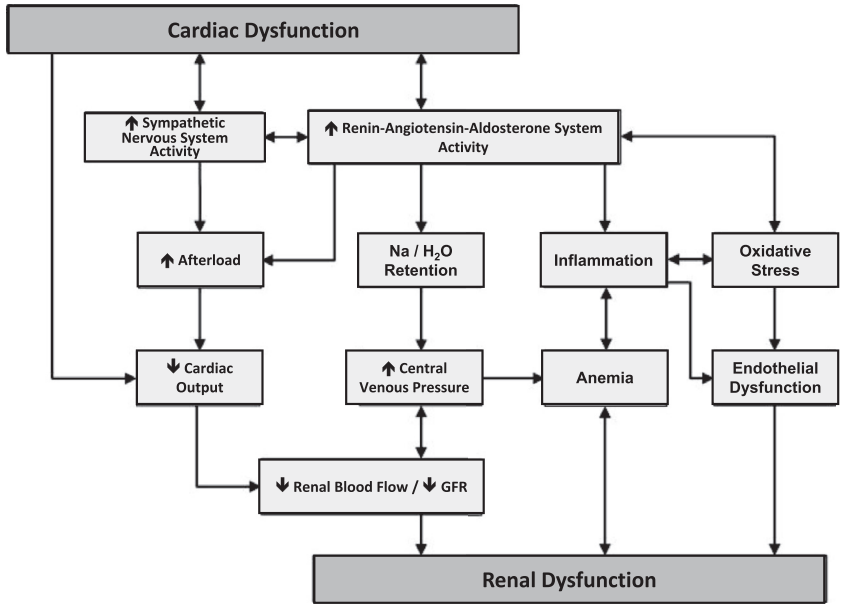


**Figure 1.** Postulated mechanisms underlying the interactions between the heart and kidneys. Arrows indicate pathways by which heart failure may lead to chronic kidney disease and vice versa. The relative importance of these and other mechanisms is not known, and many of these relationships are based on animal models. Abbreviation: GFR, glomerular filtration rate. Reproduced from Szymanski et al (*Heart Fail Rev.* 2012;17(3):411-420), which is copyright of the authors and was released under a CC BY-NC license by Springer Publishing.