ASSESSMENT OF KIDNEY STATUS AND GENDER SPECIFICITY IN CHRONIC HEART FAILURE

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HF and CKD represent concurrent chronic disease epidemics.*1*, *2* Both conditions have increasing incidence and prevalence in older age groups as well as persons with hypertension, diabetes mellitus, or other cardiovascular and kidney disease risk factors.*3* The presence of one condition appears to accelerate the presentation and progression of the other; having both conditions increases the risk of hospitalization, rehospitalization, need for intensive care or kidney replacement therapy, and death.*4*, *5*, *6*, *7*, *8*, *9* In addition, patients with HF and CKD may fail to respond as predicted to conventional therapies or experience increased toxicity to them.

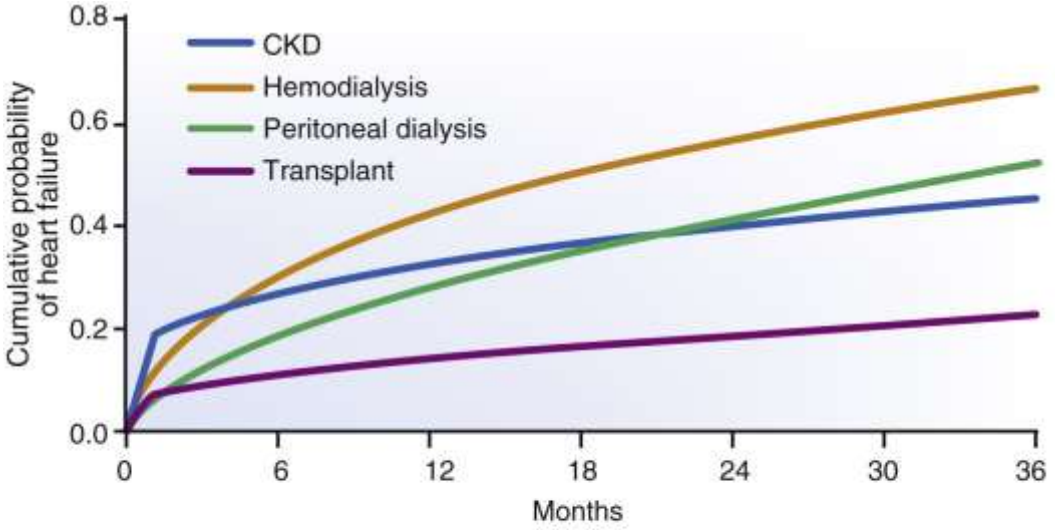
Definitions, Pathophysiology, and Epidemiology

The 2016 European Society for Cardiology guidelines for managing HF define it on the basis of signs and symptoms owing to structural and/or functional cardiac abnormalities, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.*12* Subsets of HF include preserved ejection fraction, ≥50% (HFpEF); reduced ejection fraction, <40% (HFrEF); and mid-range ejection fraction, 40% to 49% (HFmrEF). Comorbid conditions make the diagnosis challenging, such as CKD and end-stage kidney disease (ESKD), as sodium and water retention contribute to HF manifestations.*13*

CKD is defined on the basis of persistently reduced estimated glomerular filtration rate (eGFR) of <60 ml/min per 1.73 m2 or at least 1 marker of kidney damage for >3 months.*14* The latter markers include albuminuria, urine sediment abnormalities, histological, or structural abnormalities. HF as the primary syndrome can experience secondary CKD, and vice versa, or both can coexist on the basis of shared risk factors or systemic disorders. The distinction of which disease is primary and which is secondary may be challenging.

The incidence of de novo HF in known CKD is in the range of 17% to 21%.*15* The emergence of HF varies depending on the degree of CKD and the modality of kidney replacement therapy, including transplantation (*Figure 1*). Reduced eGFR is associated with increased risk of all-cause mortality, cardiovascular mortality, and hospitalization in patients with HFpEF or HFrEF.*16*, *17*, *18* Elevated urine albumin is prognostic for HF outcomes, albeit to a lesser extent than reduced eGFR. Both reduced

eGFR and albuminuria can develop as a result of HF. Thus, HF and CKD occur in a bidirectional fashion with considerable overlap. A large meta-analysis of patients with HFrEF and HFpEF found that ~55% of both groups had CKD G3a or higher (eGFR < 60 ml/min per 1.73 m2), with a stepwise increase in mortality risk with the stage of CKD.*19* As severity of CKD increases, so does the prevalence of HF. An estimated 44% of patients on hemodialysis have HF (10% with HFpEF, 13% with HFrEF, and 21% with unspecified).*20* The complex and integrated pathophysiology is depicted in *Figure 2*.



CKD: Incident general Medicare CKD patients, age 66 & older, 2001–2003 combined
ESKD: Incident ESKD patients, age 20 & older
Patients with CHF at baseline excluded. Probabilities unadjusted

Figure 1. Cumulative probability of heart failure in populations with chronic kidney disease (CKD), dialysis, and a kidney transplant. CHF, congestive heart failure; ESKD, end-stage kidney disease. Reproduced with permission from Collins AJ, Foley R, Herzog C, et al. Excerpts from the United States Renal Data System 2007 annual data report. Am J Kidney Dis. 2008;51(1 suppl 1):S1–S320.130

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