Editorial

Challenges in Assessing the Burden of Hospitalized Heart Failure in End-Stage Kidney Disease

KATHERINE M. WANG, MD, AND GLENN M. CHERTOW, MD, MPH

Stanford, California

A diagnosis of end-stage kidney disease (ESKD) confers significant risk for cardiovascular disease, which accounts for nearly one-half of all deaths in this patient population, and at rates ranging roughly 5- to 30-fold higher than unaffected persons depending on age.[1] Heart failure, with a prevalence of 40% and an annual incidence rate of 7%−14% in patients on hemodialysis, is a leading cause of hospitalization and death.[2,3] Admission rates for heart failure and fluid overload were 20.5 per 100 patient-years for patients initiating dialysis in 2010. For prevalent patients on dialysis in 2011, admission rates were 17.7 per 100 patient-years.[4] Typical symptoms of heart failure, including fatigue, dyspnea, lower extremity edema, and ascites, may be difficult to differentiate from volume overload owing to inadequate ultrafiltration during dialysis, making heart failure a challenge to diagnose and manage in the ESKD population.

In this issue of the *Journal of Cardiac Failure*, Inampudi et al investigate the trends, outcomes, and costs of hospitalized heart failure in patients with ESKD from 2001 to 2014. Hospitalizations were classified as primary if heart failure was listed as the principal discharge diagnosis, or secondary if heart failure was listed at any other position in the list of diagnosis codes. The authors observed an initial increase in primary heart failure hospitalizations, peaking in 2006, followed by a steady decrease thereafter. Meanwhile, they noted that secondary heart failure hospitalizations (presumably, hospitalizations complicated by heart failure, or where heart failure was present, or where heart failure was not an active issue but was included among other comorbid conditions) showed a steady increase. Although the rates of inpatient mortality and length of stay declined over time, more patients experienced nonroutine discharges to health care facilities versus routine discharges home. These latter findings are consistent with hospitalized heart failure trends characterized within the general population.[5]

The trajectory of primary hospitalizations likely reflects a combination of improved clinical care practices along with introduction of performance and quality measures. Medicare began tracking hospital performance in the late 1980s and proceeded to expand available data on quality and outcomes measures in cardiovascular care.[6] In 2002, the Joint Commission established standardized heart failure measures, releasing performance data to the public in 2004.[7,8] The decrease in primary heart failure hospitalization temporally coincides with more uniform adherence to evidence-based practices in heart failure management, and instated penalties for heart failure readmission to deter premature discharges and poorly coordinated transitions of care. Since 2012, the Centers for Medicare and Medicaid Services have levied compounding penalties against hospitals who exceed expected 30-day readmission rates and/or report increased mortality rates for certain conditions including heart failure (even if readmission rates decrease).[9] These payment rules have undoubtedly changed clinical and coding practices.

With respect to secondary heart failure hospitalizations (ie, hospitalizations in which heart failure was coded as a nonprimary diagnosis), the authors are challenged to reach definitive conclusions because the National Inpatient Sample is an admission-level, rather than a patient-level, dataset. As such, one cannot distinguish initial versus rehospitalization by patient. More than 1 in 3 patients with ESKD are readmitted within 30 days of hospital discharge.[1] These high readmission rates undoubtedly influence hospitalization trends; however, in scenarios where heart failure is not the primary discharge diagnosis, there is uncertainty as to what role if any heart failure played preceding or during the hospitalization. Similarly, although higher scores on the Elixhauser comorbidity index might suggest an increase in medical complexity, if physicians and/or other personnel were to include more secondary diagnosis codes, or select diagnosis codes that result in enhanced remuneration to a hospital or physician practice, case mix might only appear to be more complex, an activity often referred to as code creep.

From the Division of Nephrology, Department of Medicine, Stanford University School of Medicine, Stanford, California.

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Reprint requests: Katherine M. Wang, MD, Division of Nephrology, Stanford University School of Medicine, 777 Welch Road, Suite DE, Palo Alto, CA 94034. E-mail: wangkm@stanford.edu

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We offer a different interpretation with respect to the reported (and emphasized) finding that patients on peritoneal dialysis hospitalized for heart failure experienced poorer outcomes than patients on hemodialysis. Although the authors show that patients on peritoneal dialysis hospitalized for heart failure are more likely to die during hospitalization, it is noteworthy that more than 97% of heart failure admissions in patients with ESKD occurred in patients receiving hemodialysis; fewer than 3% occurred in patients receiving peritoneal dialysis. Yet the proportion of the ESKD population treated with peritoneal dialysis was roughly 10% across the years included in the study conducted by Inampudi et al. Thus, hospitalized heart failure was far less common in patients receiving peritoneal dialysis.

Heart failure remains a common and consequential diagnosis in patients with ESKD; hospitalized heart failure places an enormous burden on the ESKD population and on the health care delivery system at large. Based on current evidence, we recommend the following strategies be used to optimize the outcomes of patients with ESKD and heart failure. Careful attention to diet and the judicious use of selected cardiovascular drugs can and will improve outcomes among patients with acute decompensated heart failure, as well as those with more stable heart failure. Dietary salt restriction should be adopted by all patients with heart failure in the setting of ESKD. For patients on dialysis with residual kidney function, the continued use of loop diuretics can help to control hypervolemia and ameliorate hyperkalemia and metabolic acidosis, while lessening the degree of ultrafiltration required of intermittent hemodialysis or cycler-based peritoneal dialysis. A recent study suggested that the continued use of diuretics was associated with lower interdialytic weight gain and lower rates of all-cause hospitalization.[10] In a placebo-controlled trial of patients on hemodialysis with heart failure and a left ventricular ejection fraction of less than 35%, those randomized to carvedilol (in addition to standard therapy in both groups) showed improved left ventricular function in 6 months, lower all-cause hospitalization rates, and lower cardiovascular and all-cause mortality at the 2-year follow-up.[11,12] Drug removal during dialysis should be considered; β-blockers such as metoprolol and atenolol have dialyzability rates exceeding 70%.[13] We prefer carvedilol, which is negligibly removed by dialysis, and thus may offer cardioprotective effects against sudden cardiac death and myocardial stunning, both well-established complications of dialysis therapy.[14] Patients with chronic kidney disease including ESKD have been excluded from large randomized clinical trials of inhibitors of the renin−angiotensin−aldosterone system (RAAS), although subgroup analyses from the same clinical trials and other observational studies suggest a clinical benefit in this population. In patients with variable degrees of impaired kidney function, randomization to ramipril after myocardial infarction[15] and captopril in those at high risk[16] showed risk reduction in cardiovascular outcomes and mortality. Observational analyses of patients receiving dialysis demonstrate that use of RAAS blockade associates with lower all-cause mortality.[17−19] A meta-analysis showed that patients on dialysis who received RAAS blockade experienced reductions in left ventricular mass.[20] Notably, patients with little or no residual kidney function generally do not experience higher rates of hyperkalemia related to the use of RAAS inhibitors.

Two placebo-controlled, randomized trials profiled the safety and efficacy of the mineralocorticoid receptor antagonist spironolactone in patients receiving hemodialysis. Rates of hyperkalemia were modest and similar in both groups in both trials. Although limited in sample size and statistical power, neither study demonstrated improvement in parameters of cardiac structure (left ventricular mass index) or function (eg, diastolic function, ejection fraction, functional class, or 6-minute walk distance).[21,22] Finally, several studies have suggested that more frequent hemodialysis can reduce left ventricular mass and may decrease cardiovascular event rates.[4] A randomized clinical trial comparing more frequent with conventional thrice weekly hemodialysis showed that more frequent hemodialysis resulted in a significant improvement in the composite coprimary endpoints of death or change in left ventricular mass and death or change in self-reported physical health[23] and longer term follow-up showed a 46% decrease in the risk of death among patients randomized to frequent hemodialysis.[24]

As shown by Inampudi et al, hospitalized heart failure remains a major burden for the ESKD population, even if rates of hospitalization with a primary discharge diagnosis of heart failure have declined over the past decade. Given the inextricable connection between ESKD and heart failure, and with more than 124,000 patients initiating dialysis annually, it is imperative that providers across all disciplines work cooperatively to tackle this problem.

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