EDITORIAL COMMENT

Ultrafiltration in End-Stage Heart Failure
Too Little, Too Late?*
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Heart failure and renal failure commonly coexist; the prevalence of chronic kidney disease in heart failure patients is nearly 25% and is associated with poor prognosis (1–3). A substantial proportion of patients with decompensated heart failure show further worsening of renal function during hospitalization, increasing the risks of morbidity and mortality (4–6), particularly among those with residual congestion (7). Several factors, including renal hypoperfusion, neurohormonal activation, immune-mediated damage, and nephrotoxic effects of diuretics and neurohormonal antagonists, have been implicated in the pathogenesis of the cardiorenal syndrome (8).

Although it seems intuitive that hemodynamic factors may be primarily responsible for worsening renal function in acute heart failure, this does not seem to be the case (9). The ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Catheterization Effectiveness) trial found no link between invasively measured hemodynamic parameters (including cardiac output) and serum creatinine in 194 patients with advanced heart failure (10); only right atrial pressure correlated weakly with renal function, suggesting a possible role for renal congestion, but not hypoperfusion, in the pathogenesis of cardiorenal failure. These observations have fueled increasing interest in nonloop diuretic approaches for the management of venous congestion in acute heart failure. To date, however, pharmacological therapies targeted at management of worsening renal function or diuretic resistance in the context of heart failure, including adenosine-receptor antagonists (11), natriuretic peptides (12), inotropes (13), and vasopressin antagonists (14), have provided disappointing results.

An alternative approach to decongestion is the direct mechanical removal of salt and water through ultrafiltration (15). Conventional dialysis, particularly peritoneal dialysis, frequently has been used clinically for this purpose, although evidence supporting the routine use of this approach is lacking. The development of technology for bedside aquapheresis through peripheral venous catheters has fueled enthusiasm for this approach as an upfront alternative to diuretic treatment for patients with acute decompensated heart failure, with data from recent randomized controlled clinical trials supporting the potential benefits of this approach on weight loss, exercise capacity, hemodynamics, and hospitalizations for heart failure (16,17).

In this issue of the Journal, Patarroyo et al. (18) present data that illuminate the position of slow continuous ultrafiltration in the management of decompensated and recalcitrant heart failure. The population studied included a highly selected group of 63 patients with advanced heart failure, worsening renal function, and congestion refractory to intensive attempts at hemodynamically guided medical therapy using a pulmonary arterial catheter. The selection criteria identified an extremely ill population of patients with left ventricular ejection fraction of 26 ± 15%, serum sodium of 133 ± 6 mEq/l, baseline creatinine of 1.9 ± 0.8 mg/dl, mean central venous pressure of 20 mm Hg, mean pulmonary capillary wedge pressure of 30 mm Hg, and cardiac index of 1.8 l/min/m² defining hemodynamics consistent with cardiogenic shock (18% were treated with inotropes at baseline). After 48 h of ultrafiltration, a reduction in filling pressures and an increase in cardiac index were noted, but without significant improvement in blood urea nitrogen or serum creatinine levels. After initiation of ultrafiltration, 59% of these advanced HF patients required conversion to continuous dialysis during the hospital course, and 14% were dependent on dialysis at discharge. Despite effective decongestion, as perhaps may be expected for this population with advanced disease refractory to conventional therapy, in-hospital mortality was high, with 19 (30%) of 63 patients dying before discharge and 6 additional patients discharged to terminal care in hospice.

Although this is a small patient sample from a single center, these sobering data clearly highlight the limitations of ultrafiltration as salvage therapy for patients with worsening renal function in the setting of advanced, medically refractory heart failure. The study presents a counterpoint to recent studies highlighting potential short-term benefits to ultrafiltration in acute decompensated heart failure and earlier observations regarding the usefulness of dialysis in patients with refractory heart failure (19–21). As the au-

*Editorials published in the Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

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authors concede, renal replacement was offered in this population as a therapy of desperation in the face of failure of conventional methods, in the hope that effective decongestion might provide sufficient hemodynamic benefit to reverse the downward spiral of cardiorenal deterioration. The observation that volume removal improved hemodynamic parameters without a major influence on clinical outcomes and may have accelerated deterioration in renal function for a substantial subset of patients is an important cautionary note about the limitations of medical therapy in the setting of end-stage disease.

Although limited data regarding baseline renal function are provided in this report, the aggregate experience suggests that those with creatinine clearance of less than 20 ml/minute would be at particularly high risk for permanent dialysis after rescue ultrafiltration, whereas those with creatinine clearance of more than 40 ml/minute may be managed successfully with recovery of native kidney function. Better risk stratification algorithms incorporating formal assessment of glomerular filtration rate as well as other clinical and laboratory parameters may add precision to the decision-making process. Whether patients with a lesser severity of heart failure might benefit from ultrafiltration as an upfront or salvage approach to diuretic resistance or cardiorenal syndrome is the subject of ongoing clinical trials (22). However, the notion that some patients with heart failure may be beyond salvage even with heroic efforts involving mechanical support resonates with observations from the ventricular assist device literature highlighting the lack of benefit with urgent implantation of durable mechanical circulatory support in refractory cardiogenic shock (INTERMACS [Interagency Registry for Mechanically Assisted Circulatory Support] Profile 1) (23).

As the arsenal of available therapies for management of end-stage heart failure expands, it becomes increasingly important to define the margins of medical futility to prevent unnecessary prolongation of the dying process for patients and their families and exposure of patients to risk and discomfort with possible unrealistic expectations that they will return to an acceptable health status. A recent statement from the American Heart Association, on decision making in advanced heart failure highlights the importance of considering the overall trajectory of illness and patient preferences in the selection of medical treatments near the end of life (24). Therapies (e.g., defibrillation, dialysis resynchronization) that may improve quality or duration of life during the early phases of disease may be less effective and desirable as disease nears the end stage. In the oncology population, earlier introduction of palliative care considerations has been shown to improve quality of life for patients and families without shortening survival (25). Recognition and acknowledgment of disease progression similarly may facilitate early introduction of palliative approaches for symptom management in a heart failure population with a similar symptom burden and prognosis. Physicians caring for heart failure patients increasingly must take responsibility for helping patients to make the deliberate choice not to engage high-risk therapies that are unlikely to influence the ultimate outcome and indeed may impair quality of life during the limited time that remains.

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Key Words: acute decompensated heart failure • cardiorenal syndrome • prognosis • slow continuous ultrafiltration.