Reconsidering Ultrafiltration in the Acute Cardiorenal Syndrome

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Aggressive diuretic therapy in a patient who is hospitalized for acute decompensated heart failure often leads to progressive renal dysfunction despite persistent congestion. The underlying mechanisms of this so-called acute cardiorenal syndrome are complex and not fully understood.\(^1,2\) As initial therapy in this setting, ultrafiltration as compared with diuretic therapy may result in a higher rate of sodium and volume removal, with greater weight loss and less frequent rehospitalizations.\(^3,4\) These findings have suggested that ultrafiltration can provide more effective relief of congestion than pharmacologic therapy can, particularly in the setting of cardiorenal compromise. Ultrafiltration may also reduce diuretic-induced neurohormonal activation, restore responsiveness to diuretics, and improve outcomes.

As now reported in the Journal, the results of the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) directly challenge our understanding of the effectiveness of ultrafiltration. In this well-designed and well-executed study, ultrafiltration did not result in greater weight loss or improved renal function as compared with pharmacologic therapy and was associated with a similar rate of death or rehospitalization for acute decompensated heart failure.\(^5\) The use of an elaborate drug algorithm (involving continuous infusion of diuretics with the addition of metolazone, vasoactive therapy, or both) to overcome resistance to diuretics may have made it unnecessary for clinicians to lower diuresis targets in response to the acute cardiorenal syndrome, thus eliminating the potential confounder of inadequate pharmacologic management. Furthermore, there was an unexpected overall decrease in serum creatinine level in the pharmacologic-therapy group, rather than the anticipated increase, thus refuting the claim that ultrafiltration is less harmful to renal function. It is difficult to argue that ultrafiltration provides “diuretic sparing” benefits in patients with acute cardiorenal syndrome when a well-managed pharmacologic approach provided equivalent clinical outcomes with fewer serious adverse effects.

How do we reconcile the promising results from previous ultrafiltration studies with the somewhat unanticipated findings from CARRESS-HF? CARRESS-HF investigated a patient population that had persistent congestion with a rising serum creatinine level. This population may have an attenuated response to standard pharmacologic therapy as compared with patients receiving ultrafiltration as initial therapy. There has been recent appreciation that worsening renal function during treatment of acute decompen-sated heart failure may reflect underlying diminished renal reserve rather than treatment effects.\(^6\) In fact, CARRESS-HF illustrates the overall dismal outcomes in patients in whom the acute cardiorenal syndrome develops. Regardless of treatment strategy, only approximately one tenth of the patients had adequate decongestion at 96 hours, and more than a third of the patients died or were readmitted to the hospital for acute decompensated heart failure within 60 days, despite substantial overall weight loss. Hence, the results of CARRESS-HF may be consistent with the findings of single-center studies of ultrafiltration in patients with the acute cardiorenal syndrome, which have shown a low rate of renal recovery despite effective volume removal and favorable hemodynamic effects.\(^7,8\)

We simply do not know whether a rise in serum creatinine level during treatment represents desired effects of hemoconcentration (when ther-
apy is efficacious) or undesired deterioration of renal function (when therapy is ineffective). In fact, transient changes in serum creatinine levels during therapy for acute decompensated heart failure may not necessarily reflect substantial underlying renal injury or adverse long-term consequences if congestion is adequately relieved.  

The effect of therapy on the bivariate primary end point of change in weight and change in serum creatinine level may be dependent on the rate at which congestion is being relieved. Previous studies have used similar ultrafiltration rates with shorter treatment durations. It is conceivable that a slower but steady ultrafiltration rate may help maintain an adequate plasma refill rate. This may result in longer duration of ultrafiltration and greater volume removal without inducing azotemia. It is important to remember that the ultimate goal is to relieve congestion safely and not to show how promptly the excess volume can be removed. Therefore, future studies are needed to determine the safest and most effective rate, duration, and amount of sodium and volume removal with ultrafiltration to achieve the best possible clinical outcomes in patients with the acute cardiorenal syndrome.

There is a pressing need to continue the search for better strategies to manage the acute cardiorenal syndrome, and we may have to challenge our preconceptions. Once touted as a promising option for cardiorenal rescue therapy, ultrafiltration as performed in CARRESS-HF can no longer be considered to be a favorable choice for routine therapy in patients with the acute cardiorenal syndrome. CARRESS-HF reminds us that we need to refine the use of ultrafiltration in treatment for acute decompensated heart failure and also to devote much effort to determining how best to prevent the acute cardiorenal syndrome in the first place. We may even have to confront the possibility that the pressure to reduce hospital length of stay with a strategy of initial aggressive diuresis in patients with acute decompensated heart failure may actually result in an increased incidence of the acute cardiorenal syndrome and cause unwanted consequences. Perhaps slow and steady may ultimately win the race after all.