Alternative to Loop Diuretics

Ultrafiltration *from page 1*

study involving 200 patients hospitalized for decompensated heart failure and volume overload. Patients were randomized to peripheral ultrafiltration or aggressive use of loop diuretics—the standard therapy—with the goals of getting them stabilized, feeling better, and out of the hospital as quickly as possible.

Patients in the ultrafiltration arm averaged a weight loss of 5.0 kg at 48 hours, with no adverse impact on renal function, compared with 3.1 kg with standard care. The mean net fluid loss of 4.6 L in the ultrafiltration group at 48 hours was also significantly greater than the 3.3 L in the standard care group.

But what really grabbed the attention of heart failure specialists in the audience was the difference in 90-day outcomes. That's because decompensated heart failure is the number one cause of U.S. hospital admission, with 90% of these hospitalizations resulting from volume overload—and health policy officials are desperate to reduce that enormous burden on resources.

Patients in the ultrafiltration group were rehospitalized for heart failure for a collective 123 days during the 3 months after discharge, compared with 330 days in the standard care group. The ultrafiltration group also fared markedly better in terms of other resource-utilization end points (see box).

Dr. Costanzo attributed the sustained benefits of ultrafiltration to three factors: It doesn't activate neurohormonal systems, as do loop diuretics; it is more efficient in that it removes proportionately more sodium per unit fluid removed; and it allows patients to take "a diuretic holiday," as reflected in their lower dose of oral diuretics at discharge, compared with patients who had received loop diuretics.

The use of high-dose intravenous diuretics has been linked to increased short-term morbidity and mortality. Most physicians will be surprised to learn that the safety and efficacy of this long-standard therapy has never been tested in a randomized trial, she added.

Dr. Gregg C. Fonarow called the UNLOAD data "very impressive and something that I think should influence clinical practice now. ... The adverse consequences of high-dose loop diuretics have been underappreciated. Anything we can do to get fluid off while limiting the amount of loop diuretics needed is good from a physiologic standpoint. To have a way to remove fluid efficiently that's safe and rapidly relieves symptoms and potentially prevents hospitalizations is a great therapeutic advance," he said in an interview.

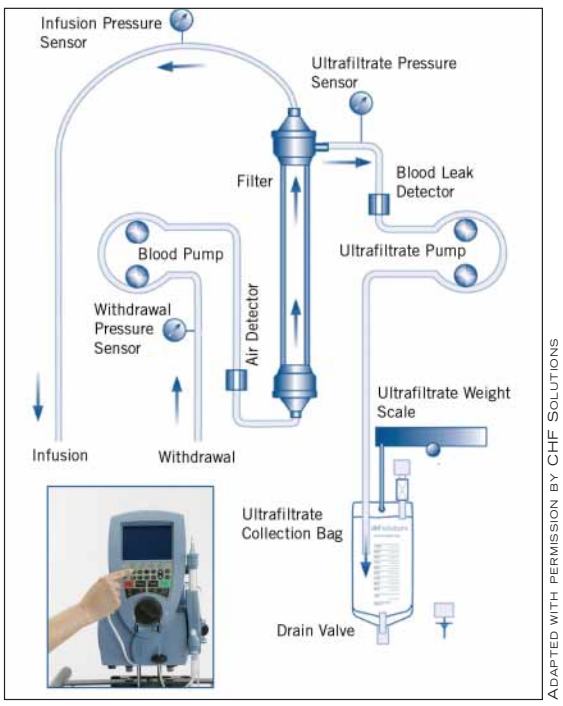
UNLOAD sets the stage for a larger, more definitive outcomes study, added Dr. Fonarow, professor of medicine at the University of California, Los Angeles and director of the Ahmanson-UCLA Cardiomyopathy Center.

Ultrafiltration was accomplished using a Food and Drug Administration–approved device marketed by CHF Solutions Inc. Unlike older ultrafiltration methods, which never caught on because they required central venous access and intensive patient monitoring, the CHF Solutions device is easy to use, requires only peripheral venous access, and takes only 33 mL of blood extracorporeally at any given time. The device can remove up to 500 cc of fluid per hour, with most patients requiring one or two 8-hour treatment sessions.

The single-use filter costs about $800; however, that pales when compared with the potential cost savings through reduced rehospitalization, especially because Medicare won't reimburse for rehospitalization within 30 days, Dr. Costanzo said.

However, results showed that the markedly greater fluid loss achieved with ultrafiltration did not translate into greater symptom relief. Dyspnea scores at 48 hours were similar in the two treatment arms. In fact, change in dyspnea score did not significantly correlate with weight loss at 48 hours. This challenges the traditional practice of using congestive symptoms to decide when to start and stop therapy in decompensated heart failure. Indeed, the observation that symptoms of congestion aren't a sufficiently sensitive guide to fluid volume provides a further boost to ongoing efforts to develop implantable hemodynamic monitors for this clinical application.

Dr. Costanzo is on the medical advisory board of CHF Solutions, which sponsored UNLOAD. ■



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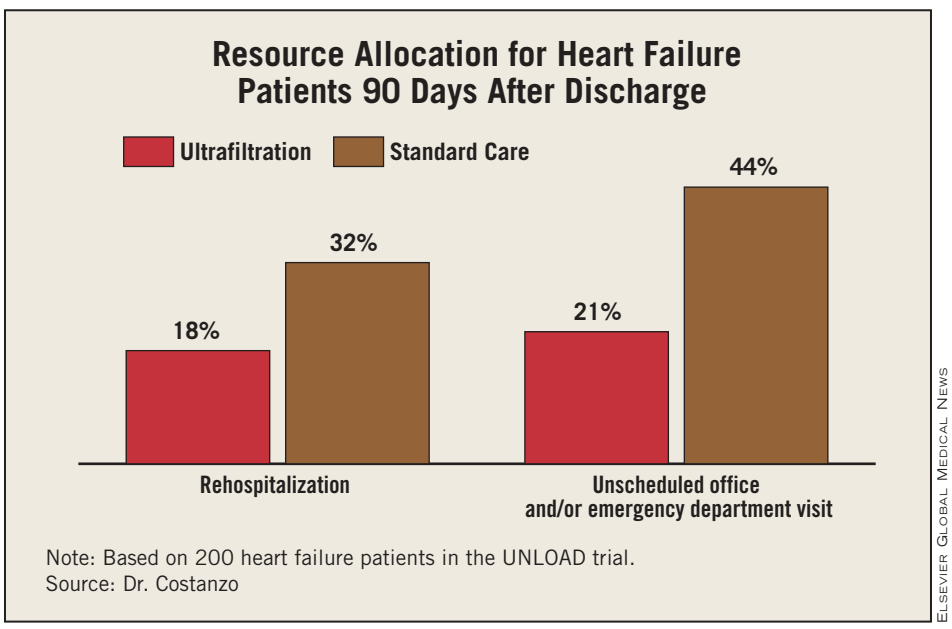
The Aquadex FlexFlow allows fluid to be extracted from a patient's blood at a controlled rate.



Note: Based on 200 heart failure patients in the UNLOAD trial.
Source: Dr. Costanzo

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Patient Selection Key in Using LVADs as Destination Therapy

BY BRUCE JANCIN
Denver Bureau

Atlanta — It is possible to preoperatively identify a small subgroup of candidates for left ventricular assist device implantation as destination therapy, that is, as a permanent alternative to heart transplantation because their poor outcomes would render a transplant futile, said Dr. Katherine Lietz at the annual meeting of the American College of Cardiology.

The long-term outcomes for such a subgroup are remarkably good, she said.

Dr. Lietz presented an analysis of the largest population of LVAD recipients as destination therapy ever described: 311 patients who received the Thoratec HeartMate XVE at 65 hospitals in the United States and who were enrolled in the Food and Drug Administration–mandated Thoratec Destination Therapy Registry, through which they have been followed for a median of 15 months.

The overall group had a 1-month survival of 86%, a 1-year survival of 57%, and a 2-year survival of 38%. But those figures mask a wide range of outcomes. For example, 26% of patients died before they were able to leave the hospital after surgery, with the causes of death being sepsis, multiorgan failure, and right heart failure. The fact that none died of LVAD failure in the first year suggests that patient selection plays a key role in early postoperative outcomes, said Dr. Lietz of the University of Minnesota Medical Center, Minneapolis.

She and her coworkers therefore sought to develop a prospective tool for preoperative risk stratification. They evaluated 65 variables for potential inclusion.

In a multivariate analysis, the significant predictors of poor outcome included malnutrition as reflected by a serum albumin below 3.3 g/dL, low pulmonary artery pressures, a need for ventilatory support, severe renal dysfunction with a creatinine clearance below 30 mL/min, anemia, coagulopathies, any degree of hepatic dysfunction, and an elevated WBC count and other signs and symptoms of infection. Patients who were not on an inotropic agent, a β-blocker, or an ACE inhibitor just before implantation were also at higher risk for early in-hospital mortality.

The investigators assigned each risk factor a weighted relative value and summed them to obtain a cumulative risk score for each patient. On the basis of those scores, they divided the registry cohort into risk categories for in-hospital mortality. The rate of survival to hospital discharge was 100% in the low-risk group, 95% in those at medium risk, 68% in the high-risk group, and 25% in the very-high-risk population.

Overall, 1-year survival was 94%, 73%, and 53% in the low-, medium-, and high-risk groups, respectively, compared with 6% in the very-high-risk subgroup.

This very-high-risk subgroup was composed of just 12% of the total population. By excluding patients in this group, 1-year survival in the remaining 88% of patients in the combined low-, medium-, and high-risk groups was 70%, with a 2-year survival of 50%.

Dr. Lietz stressed that she does not believe that candidates with a very-high-risk score should necessarily be denied destination therapy with an LVAD. After all, many of the risk factors are modifiable—for example, nutritional status and coagulopathies—and could be addressed before surgery to move the patient out of the least-favorable category.

Dr. Marvin A. Konstam, professor of medicine at Tufts University, Boston, and chief of cardiology at New England Medical Center, noted that the decision to resort to destination therapy is driven only in part by the likelihood of device therapy's long-term success. Another key factor in the equation is the patient's prognosis on medical therapy.

"If we can identify a subgroup in which the risk with medical therapy is highest and yet survival with an LVAD is adequate, those might be the ideal destination therapy candidates," he said.

LVADs are most often implanted as a temporary bridge to heart transplantation in patients awaiting a donor organ. But in November 2002, the FDA approved the use of the Thoratec HeartMate XVE as destination therapy in response to the positive results of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial.

Medicare covers the therapy in patients with class IV, end-stage heart failure who otherwise have a life expectancy of less than 2 years and are not candidates for transplantation because of advanced age or comorbidities. ■