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Letters

TO THE EDITOR

The AVOID-HF Trial: Points to Consider

The large-scale AVOID-HF (Aquapheresis Versus Intravenous Diuretics and Hospitalization for Heart Failure) trial compared ultrafiltration and medical treatment in acute heart failure (HF) (1). A major advantage of this study was the use of adjustable, rather than fixed, treatment regimens in both arms. The study was terminated early but still could demonstrate a nonsignificant trend for longer time to first HF event in the ultrafiltration group. We think there are a number of points that, if addressed in future studies, could help further elucidate the role of ultrafiltration in this setting.

First, more patients in the ultrafiltration group experienced adverse events, some of which appear to be related to venous access complications (e.g., bleeding, infection, venous thrombosis). The portable ultrafiltration devices are marketed as having the possibility of using peripheral venous access, and the investigators of AVOID-HF also mention that the ultrafiltration could be performed through the use of a variety of peripheral, midline, and central catheters (2). However, the number and types of venous access that were used for these patients are not reported in the article. This could have been helpful in characterization of the potential link between the type of venous access and the pertinent complications.

Second, diuretics are widely used for management of patients with HF and the previous ultrafiltration studies have reported between 90% and 100% of patients receiving diuretics at the time of admission (3,4). Although the inclusion criteria, the baseline characteristics (e.g., patients' weight), and the outcomes imply that the study population in AVOID-HF has been comparable to other trials, it is not clear why only 55% of the patients were receiving diuretics. A key indication for the use of ultrafiltration in HF is diuretic-refractory volume overload; therefore, this point merits clarification by the investigators.

Third, in acute HF, there exists substantial discrepancy between the amount of fluid removed and weight loss. In AVOID-HF, too, the patients in the ultrafiltration group had significantly greater net and total fluid removal, whereas weight loss was found to be comparable in both arms. This lends support to the previously proposed notion that ultrafiltration has a higher efficacy for decongestion, but it also raises the question of whether "equivalent" fluid removal would portend similar beneficial effects for ultrafiltration.

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Please note: Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REPLY: The AVOID-HF Trial: Points to Consider

The investigators of the AVOID-HF (Aquapheresis Versus Intravenous Diuretics and Hospitalizations for Heart Failure) trial are grateful to Drs. Marenzi and Kazory for the opportunity to clarify some important aspects of the AVOID-HF trial's primary results paper (1).

Of the 106 patients assigned to the ultrafiltration (UF) arm, 55 subjects (52%) had central and 50 (47%) had peripheral venous access. The type of venous access was unknown in 1 patient. Forty-one central and 31 peripheral venous access patients experienced at least 1 adverse event (1). Therefore it is not possible to conclude that 1 type of venous access is safer than the other. However it should be noted that neither the initial nor the final sponsor of the trial provided

consistent technical support to the study's sites. The AVOID-HF investigators believe that stronger technical support, more rigorous site personnel training, and standardized venous access procedures would be very helpful in minimizing the adverse events associated with UF therapy.

We agree with Drs. Marenzi and Kazory that the table describing the study's population baseline characteristics is unclear regarding the meaning of the 55% value of the patients receiving diuretic agents. All patients enrolled in the AVOID-HF trial were taking oral loop diuretic agents. Indeed therapy with daily oral loop diuretic agents constituted 1 of the inclusion criteria for the AVOID-HF trial (2). Fifty-five percent is the proportion of patients given ≥2 doses of intravenous diuretic agents before randomization to either adjustable UF or adjustable loop diuretic therapy.

As Drs. Marenzi and Kazory note, there was a discrepancy between weight loss, which was similar in the 2 treatment arms and net fluid loss, which was greater in the adjustable UF arm. Regardless of this discrepancy, the adjustable UF patients had a trend toward a longer time to first hospitalization for heart failure in 90 days and a significant reduction in 30-day heart failure and cardiovascular rehospitalizations. This reduction may be a marker of effective decongestion superior to either weight or net fluid loss. Indeed, more than 2 decades ago, Dr. Marenzi coauthored a study in which by design, patients randomized to intravenous furosemide or UF had similar fluid loss. The study found that, compared with patients given intravenous diuretic agents, those receiving UF had sustained weight loss, lower neurohormonal activation, and better functional capacity up to 90 days (3). Therefore, the results of the AVOID-HF trial are consistent with the notion that UF may provide more effective decongestion than intravenous loop diuretic agents do.

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