Table 3. Evidence Table of RCTs Comparing Pharmacological Therapy for Fluid Overload and Ultrafiltration in Patients With Acute Decompensated HF

Study	Subjects, n	Primary End Point	UF Protocol	Diuretics Protocol	Effect on Renal Function	Effect on Weight Loss	Adverse Events
RAPID-CHF[133]	40	Weight loss at 24 h	Single 8-h UF session to maximum rate of 500 mL/min per 1.73 m^2	Clinician based	NS	Similar in both groups; trend toward higher weight loss in UF arm	…
UNLOAD[134]	200	Weight loss and dyspnea at 48 h	Time and rate of UF flexible; maximum rate of 500 mL/min per 1.73 m^2	Clinician based	NS	UF>DT	…
CARRESS-HF[135]	188	Change in SCr and weight at 96 h	Fixed UF rate of 200 mL/min per 1.73 m^2	Prespecified stepped-up algorithm	Significant increase in SCr with UF	Similar in both groups	Higher SAEs in UF arm
CUORE[136]	56	Hospitalization for HF at 1 y	Time and rate of UF flexible; maximum rate of 500 mL/min per 1.73 m^2	Clinician based	Significant increase in SCr with DT at 6 mo	Similar in both groups	…
AVOID-HF*[137]	224	Time to HF <90 d after discharge	Time and rate of UF flexible; maximum rate of 500 mL/min per 1.73 m^2	Prespecified algorithm	NS	Similar in both groups	Higher SAEs in UF arm

AVOID-HF indicates Aquapheresis Versus Intravenous Diuretics Hospitalizations for Heart Failure; CARRESS-HF, Cardiorenal Rescue Study in Acute Decompensated Heart Failure; CUORE, Continuous Ultrafiltration for Congestive Heart Failure; DT, diuretic therapy; ellipses (…), data not available or reported.; HF, heart failure; NS, not significant; RAPID-CHF, Relief for Acutely Fluid Overloaded Patients With Decompensated Congestive Heart Failure; RCT, randomized controlled trial; SAE, serious adverse event; SCr, serum creatinine; UF, ultrafiltration; and UNLOAD, Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure.

*Trial terminated early. Data as reported on subjects enrolled until trial termination.

SECRET of CHF trial (Short Term Clinical Effects of Tolvaptan in Patients Hospitalized for Worsening Heart Failure With Challenging Volume Management) trial did not show significant improvement in dyspnea in patients with AHF who were selected for greater potential benefit from tolvaptan.[143]

Although patients with AHF have elevated natriuretic peptides, the vasodilatory and natriuretic effects of the endogenous release of these substances are often not enough to overcome the hemodynamic effects of the other neurohormones mentioned. Nesiritide is a recombinant BNP with venous, arterial, and coronary vasodilatory properties that reduce afterload and increase CO without inotropic effects. It also causes natriuresis, improves the GFR, and suppresses the RAAS axis.[144,145] The ASCEND-HF trial (Acute Study of Clinical Effectiveness of Nesiritide and Decompensated Heart Failure) randomized 7141 patients with AHF to 1 to 7 days of intravenous nesiritide or placebo. The primary end point of dyspnea improvement, rehospitalization, or death was not statistically different between groups. The coprimary end point of dyspnea improvement at 6 and 24 hours was statistically higher in the nesiritide group, but this group also had more hypotension, and there were no differences in renal function.[146] The ROSE-AHF trial randomized 360 patients with AHF independent of LVEF and eGFR of 15 to 60 mL/min per 1.73 m^2 at 1:1 to low-dose nesiritide or dopamine and, within each randomization, randomized them further at 2:1 into either active treatment or placebo infusions for 72 hours. Low-dose nesiritide had no significant effect on the coprimary end points of cumulative urine volume and change in serum CysC at 72 hours and no effect on the secondary end points reflective of decongestion, renal function, or clinical outcomes.[116]

Although theoretically attractive, neurohormonal modulation in the AHF setting has failed to improve hard clinical and renal end points in large randomized studies. Because of this, only tolvaptan and nesiritide have been approved for use by the US Food and Drug Administration, and their use is limited to specific clinical situations.

Inotropes have the potential to improve type 1 CRS by improving CO and reducing venous congestion. Specific inotropes such as dopamine have direct renal effects that may additionally result in improvement of type 1 CRS, but clinical data are mixed. A common theme in studies of inotropic therapy for AHF and reduced EF is that although favorable acute hemodynamic effects are achieved, long-term cardiovascular outcomes are not affected because of the presence of arrhythmias, ischemia, and worsening long-term myocardial function.[147]

Dopamine is a catecholamine with effects on the β- and α-adrenergic receptors, as well as the renal dopaminergic receptors, resulting in cardiac inotropy, systemic vasoconstriction, and improved renal blood flow.[148] Early studies supported the renal protective effects of low-dose