Randomized Trial of Ultrafiltration versus Pharmacologic Care in Patients with Acute Decompensated Heart Failure and Cardiorenal Syndrome:
Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF)

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on behalf of the
NHLBI Heart Failure Clinical Research Network
Background

- Relief of congestion is an important treatment goal in patients with acute decompensated heart failure (ADHF)
- Acute (type 1) cardiorenal syndrome occurs in 25% to 33% of such patients coincident with increasing doses of loop diuretics
- Venovenous ultrafiltration (UF) is a potential therapy in this setting, but little is known about the safety and efficacy of UF compared to pharmacologic care in ADHF complicated by acute cardiorenal syndrome and persistent congestion
Aim

To compare the effects of ultrafiltration with stepped pharmacologic care algorithm on renal function and weight loss in patients hospitalized with ADHF, worsened renal function, and persistent congestion
Study Design

Admitted to hospital for ADHF with worsened renal function and persistent congestion

Pharmacologic care  
Ultrafiltration

Treatment stops when optimal volume status is reached

Primary endpoint assessed 96 hours after randomization

Outcomes assessed at 60 days
Patient Selection

Inclusion
- Age 18 or older
- Admitted to hospital with ADHF
- Worsened renal function with increase in creatinine $\geq 0.3$ mg/dL
- Persistent congestion

Exclusion
- Creatinine $> 3.5$ mg/dL
- Alternate explanation for worsening renal function
- Systolic blood pressure $< 90$ mm Hg
- Hematocrit $> 45$
- Need for IV vasoactive drugs
Randomized Treatment Arms

Ultrafiltration

- IV access
- Stop all diuretics for duration of UF
- Heparin for PTT 2.0–2.5 x normal
- UF rate 200 mL/hr
- Use of IV inotropes or vasodilators prohibited
Randomized Treatment Arms

Stepped Pharmacologic Care

First 2 days
- Adjust diuretics to maintain 3–5 liters urine/day

After 48 hours if urine output still inadequate
- Consider dopamine or dobutamine if SBP < 110 mm Hg and EF < 40%
- Nitroglycerin or nesiritide if SBP > 120 and severe symptoms

After 72 hours if urine output still inadequate
- Consider hemodynamic guided IV therapy, crossover to UF, or dialysis
Primary Endpoint

Change in serum creatinine AND change in weight between randomization and 96 hours, considered as a bivariate response

- Intention to treat
- Multivariate linear regression model, adjusting for baseline values of weight and creatinine
## Baseline Features

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pharmacologic Care (N = 94)</th>
<th>Ultrafiltration (N = 94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — years</td>
<td>66</td>
<td>69</td>
</tr>
<tr>
<td>Male</td>
<td>72%</td>
<td>78%</td>
</tr>
<tr>
<td>White race</td>
<td>71%</td>
<td>72%</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>35%</td>
<td>30%</td>
</tr>
<tr>
<td>HF hospitalization in past year</td>
<td>79%</td>
<td>75%</td>
</tr>
<tr>
<td>Ischemic etiology</td>
<td>51%</td>
<td>70%*</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>67%</td>
<td>65%</td>
</tr>
<tr>
<td>H.O. hypertension</td>
<td>84%</td>
<td>85%</td>
</tr>
<tr>
<td>Serum creatinine — mg/dL</td>
<td>2.09</td>
<td>1.90</td>
</tr>
<tr>
<td>Qualifying creatinine inc — mg/dL</td>
<td>0.46</td>
<td>0.43</td>
</tr>
</tbody>
</table>

*p-value < 0.05
Results: Primary Endpoint
Mean changes in creatinine and weight at 96 hours

<table>
<thead>
<tr>
<th>Weight Loss (lbs)</th>
<th>Creatinine Increase (mg/dL)</th>
<th>Creatinine Decrease (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Gain (lbs)</td>
<td>-----------------------------</td>
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</tbody>
</table>

- **Ultrafiltration (N = 92)**: P = 0.003
- **Pharmacologic Care (N = 94)**
Change in Weight

Mean Weight Change from Baseline (lbs)

-20 -15 -10 -5 0

24 hr 48 hr 72 hr 96 hr 7 days 30 days 60 days

Pharmacologic Care
Ultrafiltration
Change in Creatinine

Mean Creatinine Change from Baseline (mg/dL)

Pharmacologic Care

Ultrafiltration

*P < 0.05
60-day Event Rates

Death or HF Rehospitalization

- HR = 1.50 (1.05, 2.15)
- P = 0.0260

Death or Serious Adverse Event

- HR = 1.01 (0.62, 1.64)
- P = 0.9556

Pharmacologic Care

Ultrafiltration
Conclusions

- Pharmacologic care was superior to ultrafiltration at 96 hours for preservation of renal function with similar weight loss
- Ultrafiltration, as administered in this study, had higher rates of adverse events and therefore offers no advantage to stepped pharmacologic care in patients with ADHF, worsened renal function, and persistent congestion
- Treatment of these patients remains a challenging clinical problem in need of better therapy