Defining the role of Renal Replacement Therapy in Cardiorenal Syndrome

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No disclosure
Agenda

- Defining and classifying cardiorenal syndrome
- Defining and classifying heart failure
- Treatment options for HF based on pathophysiology
- Diuretics in HF
- Mechanical fluid removal in HF
- Role of RRT in HF
- Conclusion
Definition of Cardiorenal Syndromes

- Pathophysiologic disorders of the heart and the kidney whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other organ
  - highlights the bidirectional nature of organ dysfunction
  - defines the temporal relationship between the primary and secondary disease organ
  - recognizes variations that exist between subtypes in terms of predisposing factors, identification, natural history and outcomes
  - acknowledges that patients may move between subtypes during the course of the disease
  - further sub-classification based on transient or reversible, acutely or chronically progressive or stable disease is avoided

7th ADQI Conference CRS, NDT 2010; 25:1416-1420
<table>
<thead>
<tr>
<th>Type</th>
<th>Phenotype description</th>
<th>Definition</th>
<th>Clinical scenarios (examples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acute cardio-renal syndrome</td>
<td>Acute worsening of heart function leading to kidney injury and/or dysfunction</td>
<td>Acute decompensated heart failure, Cardiac surgery, Acute coronary syndrome, Contrast associated AKI</td>
</tr>
<tr>
<td>2</td>
<td>Chronic cardio-renal syndrome</td>
<td>Chronic abnormalities in heart function leading to kidney injury and/or dysfunction</td>
<td>Chronic heart failure, Congenital heart disease, Ischemic heart disease</td>
</tr>
<tr>
<td>3</td>
<td>Acute reno-cardiac syndrome</td>
<td>Acute worsening of kidney function leading to heart injury and/or dysfunction</td>
<td>Acute pulmonary edema in AKI, Arrhythmias in AKI, Contrast associated AKI with adverse cardiac outcomes, Post-inflammatotary GN, Rhabdomyolysis</td>
</tr>
<tr>
<td>4</td>
<td>Chronic reno-cardiac syndrome</td>
<td>Chronic kidney disease leading to heart injury, disease and/or dysfunction</td>
<td>Left ventricular hypertrophy in CKD, Adverse cardiovascular events in CKD, APKD with cardiac manifestations</td>
</tr>
<tr>
<td>5</td>
<td>Secondary cardio-renal syndromes (Acute/ Chronic)</td>
<td>Systemic conditions leading to simultaneous injury and/or dysfunction of heart and kidney</td>
<td>Acute: Sepsis, malaria, leptospirosis, SLE, cocaine, methotrexate, pheochromocytoma, Chronic: Diabetes, hypertension, SLE, chronic liver disease, amyloidosis, sickle cell disease</td>
</tr>
</tbody>
</table>
# Classification of Heart Failure

<table>
<thead>
<tr>
<th>Type of heart failure</th>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFP EF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criteria</strong></td>
<td></td>
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<tr>
<td>1</td>
<td>Symptoms ± Signs (may not be present in early HF or in patients treated with diuretics)</td>
<td>Symptoms ± Signs (may not be present in early HF or in patients treated with diuretics)</td>
<td>Symptoms ± Signs (may not be present in early HF or in patients treated with diuretics)</td>
</tr>
<tr>
<td>2</td>
<td>Left ventricular ejection fraction &lt;40%</td>
<td>Left ventricular ejection fraction 40-49%</td>
<td>Left ventricular ejection fraction &gt;50%</td>
</tr>
</tbody>
</table>
| 3                     | 1. Elevated levels of natriuretic peptides (BNP >35 pg/mL and/or NT-pro-BNP >125 pg/mL)  
2. At least one additional criterion:  
a. Relevant structural heart disease (LVH or LAE)  
b. Diastolic dysfunction | 1. Elevated levels of natriuretic peptides (BNP >35 pg/mL and/or NT-pro-BNP >125 pg/mL)  
2. At least one additional criterion:  
a. Relevant structural heart disease (LVH or LAE)  
b. Diastolic dysfunction | 1. Elevated levels of natriuretic peptides (BNP >35 pg/mL and/or NT-pro-BNP >125 pg/mL)  
2. At least one additional criterion:  
a. Relevant structural heart disease (LVH or LAE)  
b. Diastolic dysfunction |
Pathophysiology of HF and management options

- Beta-blockers
- SNS
- Inflammation (IL-1, IL-6, TNF-α)
- RAAS
  - Ang II
  - Vasopressin
  - Endothelin
- Adenosine R activation
- Aldosterone production
- Na & H₂O retention
- Vasoconstriction
- Vasopressin antagonists
- Endothelin antagonists
- Adenosine-1 R antagonists
- Aldosterone antagonists

Heart
- Ventricular wall stress and dilatation (remodeling) → LVH
- Inotropes
- Cardiac resynchronization
- Cardiac devices

Kidney
- Hypoperfusion
- Apoptosis
- Sclerosis and fibrosis
- Progression of CKD

Adenosine R antagonists
Aldosterone antagonists
Diuretics
Vasodilators
<table>
<thead>
<tr>
<th>Hypoperfusion -</th>
<th>Congestion -</th>
<th>Congestion +</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Warm-Dry</td>
<td>Warm-Wet (Systolic BP N/↑)</td>
</tr>
<tr>
<td></td>
<td>Discordantly reduced renal blood flow, intrarenal microvascular dysregulation</td>
<td>Renal venous pressure ↑, discordantly reduced renal blood flow, impaired autoregulation</td>
</tr>
<tr>
<td></td>
<td>Adjust oral therapy</td>
<td>Vascular type (hypertension predominates): vasodilators, diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiac type (congestion predominates): diuretics, vasodilators, consider ultrafiltration if diuretic resistant</td>
</tr>
<tr>
<td>Hypoperfusion +</td>
<td>Cold-Dry</td>
<td>Cold-Wet</td>
</tr>
<tr>
<td>Cold sweated extremities</td>
<td>Renal blood flow ↓, impaired autoregulation</td>
<td>Renal venous pressure ↑, renal blood flow ↓, impaired autoregulation</td>
</tr>
<tr>
<td>Oliguria</td>
<td>Consider fluid challenge, consider inotropic support if still hypoperfused</td>
<td>SBP &gt;90 mm Hg: vasodilators, diuretics, consider inotropic agents in refractory cases</td>
</tr>
<tr>
<td>Mental confusion</td>
<td></td>
<td>SBP &lt;90 mm Hg: inotropic agents, consider vasoressors in refractory cases, diuretics (once perfusion is corrected), consider mechanical circulatory support if no response to drugs</td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narrow pulse pressure</td>
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</tbody>
</table>
Patients with HF require a higher serum diuretic concentration to elicit the same diuretic response (diuretic resistance) and have diminished responses to ceiling doses of loop diuretics.
After oral diuretic ingestion, the time to maximum diuretic concentration is delayed in ADHF, compared with compensated state in the same patient. This may allow for the same percentage of drug to be absorbed but not achieve a concentration that will cross the threshold necessary for diuresis.
Diuretics in ADHF

Cox ZL, J Card Fail 2014; 20(8):611-622
Diuretics in ADHF

Felker GM, JACC 2012; 59(24):2145-2153
Diuretics versus UF for HF

Decreased cardiac output due to chronic heart failure

Cardio-renal syndrome:
Abnormal hemodynamics, neurohormonal activation, excessive tubular sodium reabsorption, inflammation, oxidative stress and nephrotoxic medications

Decreased water clearance and increased sodium reabsorption

LOOP DIURETICS to eliminate hypotonic urine

- Unpredictable elimination of sodium and water
- Development of diuretic resistance
- Risk of hypokalemia (low potassium levels) and hypomagnesemia (low magnesium levels)
- Insufficient symptom relief: Persistent congestion, failure to lower sodium levels
- Worsening heart failure, increased mortality after discharge, increase in re-hospitalization rates

ULTRAFILTRATION to remove isotonic plasma water

- Predictable removal of sodium and fluids
- Restoration of diuretic responsiveness
- No change in electrolytes, particularly potassium and magnesium
- More effective decongestion and fewer heart failure events compared to loop diuretics
- Improved glomerular filtration rate
- Efficacy, and improved outcomes

Costanzo MR, JACC 2017; 69(19):2428-2445
## 2016 ESC Guidelines for management of HF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies.</td>
<td>IIb</td>
<td>B</td>
<td>578–580</td>
</tr>
<tr>
<td>Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury.</td>
<td>Ila</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

2016 ESC HF Guidelines, Eur Heart J 2016; 37:2129-2200
8.5. Renal Replacement Therapy—Ultrafiltration: Recommendations

**CLASS IIb**

1. Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight (752). (Level of Evidence: B)

2. Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy. (Level of Evidence: C)
<table>
<thead>
<tr>
<th>Study/ Year</th>
<th>Patient number</th>
<th>Primary efficacy point</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNLOAD, 2007</td>
<td>200</td>
<td>Weight loss and dyspnea 48 hours after randomization</td>
<td>Costanzo MR, JACC 2007; 49:675-683</td>
</tr>
<tr>
<td>CARESS-HF, 2012</td>
<td>188</td>
<td>Bivariate response of change in SCr and change in weight 96 hours after randomization</td>
<td>Bart BA, NEJM 2012; 367:2296-2304</td>
</tr>
<tr>
<td>CUORE, 2014</td>
<td>56</td>
<td>HF rehospitalization after 1 year</td>
<td>Marenzi G, J Card Fail 2014; 20:9-17</td>
</tr>
<tr>
<td>AVOID-HF, 2016</td>
<td>224</td>
<td>Time to first HF event within 90 days of hospital discharge (rehospitalization or unscheduled outpatient or emergency treatment with loop diuretic)</td>
<td>Costanzo MR, JACC HF 2016; 4:95-105</td>
</tr>
</tbody>
</table>
## UF for HF: UNLOAD Trial, 2007

<table>
<thead>
<tr>
<th>Study Name, Publication Year (Ref. #)</th>
<th>Study Group</th>
<th>UF Arm</th>
<th>Comparison Arm</th>
<th>Primary Efficacy Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNLOAD, 2007 (33)</td>
<td>N = 200</td>
<td>Aquadex System 100†</td>
<td>Standard care: IV diuretic agents. For each 24-h period, at least twice the pre-hospitalization daily oral dose</td>
<td>Weight loss and dyspnea assessment at 48 h after randomization</td>
</tr>
<tr>
<td></td>
<td>Hospitalized with HF, ≥2 signs of fluid overload</td>
<td>Mean fluid removal rate 241 ml/h for 12.3 ± 12 h</td>
<td></td>
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</tr>
</tbody>
</table>

### Primary Endpoint Result
- Weight loss: 5.0 ± 3.1 (UF) vs. 3.1 ± 3.5 kg (standard care); p = 0.001
- Dyspnea score: 5.4 ± 1.1 (UF) vs. 5.2 ± 1.2 (standard care); p = 0.588

### Reported Clinical Outcomes*
- 90 days: HF rehospitalization:
  - 18% (UF) vs. 32% (standard care), p = 0.022; HR 0.56; 95% CI: 0.28-0.51; p = 0.04
  - Unscheduled clinic/emergency visits: 21% (UF) vs. 44%, p = 0.009

### Mortality
- 90 days: 9 (9.6%) UF vs. 11 (11.6) standard care

### Adverse Events
- No significant between-group differences, except bleeding (1 UF vs. 7 standard care, p = 0.032).
- UF group: 1 catheter infection, 5 filter clotting events, 1 patient transitioned to hemodialysis due to insufficient response to UF.

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Costanzo MR, JACC 2017; 69(19):2428-2445
## UF for HF: CARESS-HF Trial, 2012

### Study Name, Publication Year (Ref. #)
- **CARESS-HF, 2012 (32)**

### Study Group
- **N = 188**
  - Hospitalized with HF, ≥2 signs of congestion, and recent ≥0.3 mg/dl sCr increase

### UF Arm
- Aquadex System 100† at a fixed rate of 200 ml/h
- Median duration 40 h

### Comparison Arm
- SPT with intravenous diuretic agents dosed to maintain urine output 3-5 l/day

### Primary Efficacy Endpoint
- Bivariate response of change in sCr and change in weight 96 h after randomization

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### Primary Endpoint Result
- **Mean sCr change:** +0.23 ± 0.70 mg/dl (UF) vs. −0.04 ± 0.53 mg/dl (SPT)
- **Mean weight loss:** 5.7 ± 3.9 (UF) vs. 5.5 ± 5.1 kg (SPT); p = 0.58

### Reported Clinical Outcomes*
- **Crossover:** STP: 6 patients STP: (6%) also received UF (2 before 96 h)
- **UF:** 8 patients (9%) received diuretic agents instead of UF; 28 patients (30%) also received diuretic agents before 96 h.
- **7 days:** no difference in death, worsening or persistent HF, hemodialysis, SAE, or crossover (23% UF vs. 18% SPT, p = 0.45)
- **60 days HF hospitalization:** 26% (UF) vs. 26% (SPT) p = 0.97

### Mortality
- **60 day:** 17% UF vs. 13% SPT; p = 0.47

### Adverse Events
- **60-day SAE:** 72% UF vs. 57% SPT; p = 0.03, attributed to renal failure, bleeding, or catheter complications

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Costanzo MR, JACC 2017; 69(19):2428-2445
# UF for HF: AVOID-HF Trial, 2016

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<th>Comparison Arm</th>
<th>Primary Efficacy Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVOID-HF, 2016 (56)</td>
<td>N = 224</td>
<td>AUF with Aquadex FlexFlow System®; adjustments per protocol guidelines on the basis of vital signs and renal function</td>
<td>ALD with adjustments per protocol-guidelines on the basis of vital signs and renal function</td>
<td>Time to first HF event (HF rehospitalization or unscheduled outpatient or emergency treatment with intravenous loop diuretic agents or UF) within 90 days of hospital discharge</td>
</tr>
<tr>
<td></td>
<td>Hospitalized with HF; ≥2 criteria for fluid overload; receiving daily oral loop diuretic agents</td>
<td>Mean fluid removal rate 138 ± 47 ml/h for 80 ± 53 h</td>
<td>Mean furosemide-equivalent dose 271.26 ± 263.06 mg for 100 ± 78 h</td>
<td></td>
</tr>
</tbody>
</table>

**Primary Endpoint Result**

- 25% AUF vs. 35% ALD (p = 0.11); HR: 0.66; 95% CI: 0.4-1.1

**Reported Clinical Outcomes**

- Length of index hospitalization: median 6 (AUF) vs. 5 (ALD) days, p = 0.106
- 30-day HF rehospitalizations/days at risk: 11 of 2,876 (AUF) vs. 24 of 2,882 (ALD), p = 0.06
- 30-day CV rehospitalizations/days at risk: 17 of 2,882 (AUF) vs. 33 of 2,891 (ALD), p = 0.037
- For both HF and CV events: fewer patients rehospitalized; fewer number of days rehospitalized/days at risk

**Mortality**

- 90 days 15% AUF vs. 13% ALD, p = 0.83

**Adverse Events**

- At least 1 SAE: 66% (AUF) vs. 50% (ALD), p = 0.4
- SAEs of special interest: 23% (AUF) vs. 14% (ALD); p = 0.122
- Related SAEs: 14.6% (UF) vs. 5.4% (ALD), p = 0.026

*Costanzo MR, JACC 2017; 69(19):2428-2445*
UF for HF: AVOID-HF Trial, 2016

Consider Completion of Therapy if ONE of the following:

- Resolution of congestion (all of the following):
  - JVP < 4 cm H2O
  - No orthopnea
  - Trace or no peripheral edema

- Best achievable "dry weight" has been achieved
- Hemodynamic evidence of poor tolerance of fluid removal by persistent hemodynamic changes
- Net negative <1 L/24 h

Persistent elevation in sCr > 1.0 mg/dL above baseline at start of IV diuretic treatment (B)

Persistent hemodynamic instability (C)

After Completion of IV Loop Diuretic Therapy

If satisfactory "dry weight" has been reached
AND sCr is stable
- Initiate loop diuretic therapy with goal to keep net even
- GDMT

If sCr, hemodynamics or UO are NOT stable
- Hold diuretics until sCr is stable for a minimum of 12 h and then initiate oral diuretics as above
- If elevated sCr or hemodynamic instability present, then consider a bolus of IV fluid

(B) Guidelines for the completion of adjustable loop diuretic agents. (C) Guidelines for management after completion of adjustable loop diuretic agents (see also references 52 and 53).
UF for HF: AVOID-HF Trial, 2016

(A) Guidelines for the adjustment of UF therapy. (B) Guidelines for the completion of ultrafiltration therapy: 40 mg of furosemide = 1 mg bumetanide or 10 mg of torsemide (52,53). b.i.d. = twice daily; GDMT = guideline-directed medical therapy; IV = intravenous; JVP = jugular venous pressure; LV = left ventricular; QD = once daily; RV = right ventricular; SBP = systolic blood pressure; sCr = serum creatinine; UO = urine output; other abbreviations as in Figure 1.
### Pertinent exclusion criteria for UF in HF

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>- SCr &gt;3 mg/dL (255 micromol/L)</td>
<td>- SCr &gt;3.5 mg/dL (300 micromol/L)</td>
<td>- SCr &gt;3 mg/dL (255 micromol/L) or planned RRT</td>
</tr>
<tr>
<td>- Hct &gt;45%</td>
<td>- Hct &gt;45%</td>
<td>- Hct &gt;45%</td>
</tr>
<tr>
<td>- SBP &lt;90 mm Hg</td>
<td>- SBP &lt;90 mm Hg</td>
<td>- SBP &lt;90 mm Hg</td>
</tr>
<tr>
<td>- Use of vasoactive drugs (inotropes or vasodilators)</td>
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<tr>
<td></td>
<td>- ACS within 4 weeks</td>
<td>- Severe concomitant disease expected to cause death in &lt;90 days</td>
</tr>
<tr>
<td></td>
<td>- Sepsis</td>
<td>- Need for MV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Liver cirrhosis</td>
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<tr>
<td></td>
<td></td>
<td>- Previous SOTx</td>
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Mechanical fluid removal

Fluid overload

- Does the patient need solute clearance?
- Does the patient have life threatening fluid overload?
- Is diuresis resistance present or likely?

Diuretics +/- fluid restriction

- No
  - Regular review:
    - Adequate fluid removal?
    - Absence of serious side effects from diuretics?
  - Yes: Mechanical fluid removal: RRT or UF +/- fluid restriction
  - No: Diuretics +/- fluid restriction

- Yes
  - Mechnical fluid removal: RRT or UF +/- fluid restriction

Ostermann M; Chapter 137, Crit Care Nephrol; Pages 835-837
CVVH versus SCUF in HF

- Prospective longitudinal follow-up study

- 120 patients with CRS Type 1 or CRS Type 2 admitted to the ICU for HF

- Compared CVVH to SCUF

- Received IV diuretics >24 hours

- UOP >125 mL/hour and eGFR >30 mL/min: initiated in SCUF

Premuzic V, Ther Apher and Dial 2017; 21(3):279-286
CVVH versus SCUF in HF

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>CVVH</th>
<th>SCUF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR, mL/min</td>
<td>21.3 ± 2.2</td>
<td>21.4 ± 2.6</td>
<td>39.6 ± 4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SCR, micromol/L</td>
<td>278.1 ± 10.2</td>
<td>279.7 ± 11.9</td>
<td>166.4 ± 5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>133.8 ± 9.9</td>
<td>133.6 ± 9.4</td>
<td>132.2 ± 9.7</td>
<td>0.40</td>
</tr>
<tr>
<td>Survival, days</td>
<td>192.5 ± 17.7</td>
<td>194.8 ± 17.8</td>
<td>109.6 ± 2.91</td>
<td>0.003</td>
</tr>
</tbody>
</table>

120 patients

Follow-up: 24 months

82 CVVH

28/82 (34.1%) died

38 SCUF

15/38 (39.4%) died

Premuzic V, Ther Apher and Dial 2017; 21(3):279-286
CVVH versus SCUF in HF

Premuzic V, Ther Apher and Dial 2017; 21(3):279-286
Cardiorenal outcomes in HF patients on SCUF

- Retrospective cohort study of 63 consecutive adult patients with HF admitted to HF ICU at Cleveland clinic between 2004 – 2009

- Patients refractory to SMT and having worsening oliguria or anuria

- SCUF at 100 – 400 mL/hour

Pattaroyo M, JACC 2012; 60(19):1906-1912
Cardiorenal outcomes in HF patients on SCUF

PAP decrease by >20%
CVP <8 cm H2O
PCWP <18 mm Hg
CI increase ≥2.2 L/min/m²
MAP >65 mm Hg

<table>
<thead>
<tr>
<th></th>
<th>Before SCUF</th>
<th>48 hours after SCUF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mg/dL)</td>
<td>60 ± 31</td>
<td>61 ± 21</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>2.2 ± 0.9</td>
<td>2.4 ± 1.0</td>
</tr>
</tbody>
</table>

Pattaroyo M, JACC 2012; 60(19):1906-1912
Cardiorenal outcomes in HF patients on SCUF

Patients with advanced HF underwent SCUF, (N=63)

CVVHD conversion recommended (N=37)
- Discharged to hospice (N=4)
- In-Hospital mortality (N=16)
- Discharged on RRT (N=9)
- Discharged without RRT (N=8)

No CVVHD conversion needed (N=26)
- Discharged without RRT (N=23)
- In-Hospital Mortality (N=3)

SBP at admission and 30-d mortality

- SBP ≤ 110 mmHg: 50%
- SBP > 110 mmHg: 75%

- 59% switched to CVVHD
- 43.2% died in hospital
- 14% RRT dependent on discharge
- Overall 1-year mortality 70%

Pattaroyo M, JACC 2012; 60(19):1906-1912
CRRT as a rescue strategy in CRS Type 1

- Retrospective cohort study of 37 patients, admitted between 2005 – 2013, who were on inotropes and/or vasopressors

- Studied in hospital mortality

- 65% inotropes; 5% on vasopressors and 32% on both

- CVVHDF with RCA, QB 200 mL/min, Effluent dose 25-30 mL/kg/hour

Prins KW, Clin Kidney J 2015; 8:87-92
In-hospital mortality was 62%

Age >70 years was associated with 100% in-hospital mortality
Median survival was 15.5 days after CRRT initiation

Median survival was 10 months post-hospital discharge

Prins KW, Clin Kidney J 2015; 8:87-92
CRRT as a rescue strategy in CRS Type 1

Survivors | Non-survivors
---|---
LVEF, % | 36.0 ± 15.8 | 25.9 ± 15.9
Vasopressor | 4 (21%) | 21 (91%)
RRT in refractory CRS Type 1

- Retrospective cohort study from China reported on the outcome of refractory CRS Type 1 patients treated with RRT

- 52 patients: divided into 3 groups
  - Survivors: RRT dependent
  - Survivors: RRT independent
  - Death

- The median SCr and BUN at RRT initiation were 307 micromol/L and 25.8 mmol/L

Wu B, Cardio Renal Med 2017; 7:118-127
RRT in refractory CRS Type 1

- 30-day mortality: 59.6%
- 90-day mortality: 65.4%
- 90-day RRT dependency: 17.3%

Wu B, Cardio Renal Med 2017; 7:118-127
# RRT in refractory CRS Type 1

<table>
<thead>
<tr>
<th></th>
<th>All (n = 52)</th>
<th>RRT independence (n = 9)</th>
<th>RRT dependence (n = 9)</th>
<th>Death (n = 34)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>APACHE II scores</strong></td>
<td>14.4 ± 4.2</td>
<td>12.8 ± 3.6</td>
<td>13.4 ± 2.4</td>
<td>15.1 ± 4.6</td>
<td>0.358</td>
</tr>
<tr>
<td><strong>SOFA scores</strong></td>
<td>8.7 ± 4.7</td>
<td>6.3 ± 4.6</td>
<td>6.3 ± 2.1</td>
<td>10 ± 6.2</td>
<td>0.028*</td>
</tr>
<tr>
<td><strong>NYHA classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.210</td>
</tr>
<tr>
<td>Class II</td>
<td>6 (11.5)</td>
<td>3 (50.0)</td>
<td>0 (0)</td>
<td>3 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>18 (34.6)</td>
<td>3 (16.7)</td>
<td>3 (16.7)</td>
<td>12 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>28 (53.9)</td>
<td>3 (16.7)</td>
<td>6 (21.4)</td>
<td>19 (67.9)</td>
<td></td>
</tr>
<tr>
<td><strong>AKI stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.031</td>
</tr>
<tr>
<td>No AKI</td>
<td>6 (11.5)</td>
<td>3 (33.3)</td>
<td>2 (22.2)</td>
<td>1 (2.9)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>14 (26.9)</td>
<td>3 (33.3)</td>
<td>2 (22.2)</td>
<td>9 (26.5)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>13 (25.0)</td>
<td>2 (22.2)</td>
<td>2 (22.2)</td>
<td>9 (26.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19 (36.5)</td>
<td>1 (11.1)</td>
<td>3 (33.3)</td>
<td>15 (44.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Drugs before RRT initiation during 24 h</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressors</td>
<td>23 (44.2)</td>
<td>1 (11.1)</td>
<td>2 (22.2)</td>
<td>20 (58.8)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>15 (28.9)</td>
<td>4 (44.4)</td>
<td>4 (44.4)</td>
<td>7 (20.6)</td>
<td>0.202</td>
</tr>
<tr>
<td>Inotropes</td>
<td>21 (40.4)</td>
<td>1 (11.1)</td>
<td>4 (44.4)</td>
<td>16 (47.1)</td>
<td>0.148</td>
</tr>
<tr>
<td>Antiarrhythmic</td>
<td>11 (21.1)</td>
<td>1 (11.1)</td>
<td>0 (0)</td>
<td>10 (29.4)</td>
<td>0.119</td>
</tr>
<tr>
<td>Furosemide, mg/day</td>
<td>160 (80–240)</td>
<td>80 (60–140)</td>
<td>140 (60–240)</td>
<td>175 (100–260)</td>
<td>0.065</td>
</tr>
<tr>
<td>Spirolactone, mg/day</td>
<td>0 (0–20)</td>
<td>0 (0–20)</td>
<td>0 (0–20)</td>
<td>0 (0–20)</td>
<td>0.947</td>
</tr>
</tbody>
</table>

Wu B, Cardio Renal Med 2017; 7:118-127
## RRT in refractory CRS Type 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval days(^a)</td>
<td>1.031 (0.982–1.083)</td>
<td>0.213</td>
</tr>
<tr>
<td>Diuretic resistance</td>
<td>1.337 (0.605–2.954)</td>
<td>0.473</td>
</tr>
<tr>
<td>Diuretic efficiency</td>
<td>0.900 (0.810–0.998)</td>
<td>0.048(^*)</td>
</tr>
<tr>
<td>Use of vasopressors</td>
<td>2.949 (1.471–5.913)</td>
<td>0.002(^*)</td>
</tr>
<tr>
<td>Severe metabolic acidosis</td>
<td>2.392 (1.136–5.035)</td>
<td>0.022(^*)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>1.337 (0.605–2.954)</td>
<td>0.364</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>0.888 (0.270–2.914)</td>
<td>0.884</td>
</tr>
<tr>
<td>SCr, µmol/L</td>
<td>1.000 (0.999–1.002)</td>
<td>0.687</td>
</tr>
<tr>
<td>BUN, mmol/L</td>
<td>1.019 (0.991–1.047)</td>
<td>0.183</td>
</tr>
<tr>
<td>Urine volume, per 100 mL/24 h</td>
<td>0.895 (0.814–0.985)</td>
<td>0.023(^*)</td>
</tr>
<tr>
<td>Fluid balance, per 100 mL/24 h</td>
<td>1.043 (1.011–1.075)</td>
<td>0.008(^*)</td>
</tr>
</tbody>
</table>

Wu B, Cardio Renal Med 2017; 7:118-127
**Advanced HF**

**NYHA** New York Heart Association classifications define the extent of heart failure based on physical limitations.

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>I</td>
<td>Cardiac disease but no symptoms</td>
</tr>
<tr>
<td>II</td>
<td>II</td>
<td>Mild symptoms and slight limitation during ordinary activity</td>
</tr>
<tr>
<td>III</td>
<td>III</td>
<td>Marked limitation during any activity; comfortable only at rest</td>
</tr>
<tr>
<td>IIIB/IV</td>
<td>7</td>
<td>Advanced NYHA III symptoms</td>
</tr>
<tr>
<td>IV</td>
<td>6</td>
<td>Exertion limited</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Exertion intolerant</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Resting symptoms</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Inotrope dependent</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Progressive decline on inotropic support</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Critical cardiogenic shock</td>
</tr>
</tbody>
</table>

**INTERMACS‡ Registry** The Interagency Registry for Mechanically Assisted Circulatory Support is a US clinical registry that categorizes the clinical characteristics of device recipients.

INTERMACS‡ Registry provides even further detail on the advanced heart failure patient profile.

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*Slide Courtesy: Dr David Sim NHC Singapore*
### Table 13.3 Patients potentially eligible for implantation of a left ventricular assist device

- Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:
  - LVEF <25% and, if measured, peak VO₂ <12 mL/kg/min.
  - ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause.
  - Dependence on i.v. inotropic therapy.
  - Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mmHg and SBP ≤80–90 mmHg or CI ≤2 L/min/m²).
  - Absence of severe right ventricular dysfunction together with severe tricuspid regurgitation.

Cl = cardiac index; HF = heart failure; i.v. = intravenous; LVEF = left ventricular ejection fraction; PCWP = pulmonary capillary wedge pressure; SBP = systolic blood pressure; VO₂ = oxygen consumption.
Clinical effects of RRT in treatment-resistant CHF

- Prospective observational non-randomized study in 23 patients with CRS Type 2 treated with HD or PD

- CKD Stage 5: 14 patients; CKD Stage 4: 7; CKD Stage 3: 2

- Mean eGFR $14.6 \pm 12.1$ mL/min

- 11/23 (48%) received HD and 12/23 (52%) received PD

Cnossen TT, NDT 2012; 27:2794-2799
Clinical effects of RRT in treatment-resistant CHF

7/23 (30%) died
Median survival 16 months

<table>
<thead>
<tr>
<th></th>
<th>Pre-dialysis</th>
<th>Post-dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>1.8 ± 1.6</td>
<td>2.1 ± 2.9</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1.4 ± 0.6</td>
<td>0.4 ± 0.6</td>
</tr>
<tr>
<td>(days/patient/month)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>0.27 ± 0.29</td>
<td>0.23 ± 0.23</td>
</tr>
<tr>
<td>(number of hospitalizations)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0.19 ± 0.25</td>
<td>0.03 ± 0.06</td>
</tr>
<tr>
<td>(number of hospitalizations)*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Decreased CV hospitalizations
Increased all-cause hospitalizations
62% improved NYHA – 2 classes after 4 months
QOL improved in 75%

Cnossen TT, NDT 2012; 27:2794-2799
High Volume PD (HVPD) in CRS Type 1

- Outcome of High Volume Peritoneal Dialysis (HVPD) in 64 patients with CRS Type 1

- 54.7% needed inotropic agents and/or IV vasodilators

- Median LVEF was 38%

- UF 2.5 L/day

Ponce D. PDI 2017; 37(5):578-583
High Volume PD (HVPD) in CRS Type 1

Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysate volume per cycle (mL)</td>
<td>2,000</td>
</tr>
<tr>
<td>Inflow time (min)</td>
<td>10</td>
</tr>
<tr>
<td>Dwell time (min)</td>
<td>30–60</td>
</tr>
<tr>
<td>Outflow time (min)</td>
<td>20</td>
</tr>
<tr>
<td>Cycle duration (min)</td>
<td>60–90</td>
</tr>
<tr>
<td>Total exchanges per session</td>
<td>16–22</td>
</tr>
<tr>
<td>Session duration (h)</td>
<td>24</td>
</tr>
<tr>
<td>Total dialysate volume per session (L)</td>
<td>32–44</td>
</tr>
<tr>
<td>% glucose</td>
<td>1.5–4.25</td>
</tr>
<tr>
<td>Kt/V</td>
<td></td>
</tr>
<tr>
<td>Prescribed per session/weekly</td>
<td>0.5/3.5</td>
</tr>
<tr>
<td>Delivered per session/weekly</td>
<td>0.43±0.1a/2.9±0.41a</td>
</tr>
</tbody>
</table>

76 eligible CRS type 1 patients treated by HVPD

12 patients were excluded

64 patients included

9 septic shock
3 CKD stage 4 or 5

21 died (32.8%)
43 survival (67.2%)

48 recovery of kidney function (75 %)
16 without recovery of kidney function (25%)

Ponce D, PDI 2017; 37(5):578-583
Conclusion

- Extracorporeal/mechanical UF has a role in the management of CHF. It relieves congestion, decreases readmission and improves QOL. However, no evidence of any long-term benefits.

- Mechanical UF is reserved for patients with severe fluid overload in whom diuretics have failed or are unlikely to be effective or are unsafe.

- The decision between UF and RRT depends on whether fluid removal alone or additional clearance is required.

- In patients with advanced HF, on inotropes and/or vasopressors, who have no destination therapy of LVAD or Heart Tx, the role of rescue RRT, goals and extent of care should be discussed before commencing RRT.
Thank you for your attention