Practical Points in Cardiorenal Syndrome

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HFCT Annual Scientific Meeting
June 16, 2017, Eastin Grand Sathorn Hotel, Bangkok
Acute Heart Failure: 
60-Day Readmission: 50%

Patients with **Inadequate Decongestion** at Discharge:

Are Known to be a Higher Risk of Admission and Mortality

Each Readmission: 
Increased *(Doubling)* Mortality!

<table>
<thead>
<tr>
<th>Number of Hospitalizations</th>
<th>Median Survival Time (95% CI), y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.4 (2.3-2.5)</td>
</tr>
<tr>
<td>2</td>
<td>1.4 (1.2-1.5)</td>
</tr>
<tr>
<td>3</td>
<td>1.0 (0.9-1.1)</td>
</tr>
<tr>
<td>4</td>
<td>0.6 (0.5-0.9)</td>
</tr>
</tbody>
</table>

Relief of Congestion is an Appropriate Target in the Treatment of Acute HF

Diuretics

Goal
Adequate Decongestion (Dry and Warm)

Method to Assessment

Biomarker Guided Treatment
NT-proBNP, hsTnT, Hemoconcentration, or Transient Worsening Renal Function

The Swan-Ganz Catheter

“TAILORED THERAPY”
Hemodynamic goals
- PCWP <16 mmHg
- RA <8 mm Hg
- SVR <1200
- Cardiac index >2.0
- BP > 95 mmHg

Current Goals for Decongestion

Congestion Score: Based on Extent of Orthopnea, JVP, Edema (each on scale 0-3)

Adequate Decongestion (Warm & Dry)
- Resolution of Orthopnea
- Trace to No Edema
- JVP of < 8 cm H2O
The Clinical Course and Prognosis Value of Congestion: Finding from EVEREST trial

<table>
<thead>
<tr>
<th>Congestion Score*</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF hospitalization</td>
<td>26%</td>
<td>35%</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>Death</td>
<td>19%</td>
<td>25%</td>
<td>25%</td>
<td>43%</td>
</tr>
<tr>
<td>HF hosp. or Death</td>
<td>36%</td>
<td>46%</td>
<td>46%</td>
<td>60%</td>
</tr>
</tbody>
</table>

*Discharge/Day 7 Congestion score: Based on extent of orthopnea, JVD, edema (each on scale 0-3)

Adequate Decongestion at Discharge is Associated with a Reduction in Readmission and Mortality
Stevenson LW. Eur J Heart Fail. 1999;1:251-57
Sequential nephron blockade
Increasing diuretic dosage

Diuretic Sites of Action

- Mannitol, Acetazolamide
- Thiazide, Metolazone
- Bumetanide, Ethacrynic Acid, Furosemide
- Amiloride, Spironolactone, Triamterene

Congestion is the Main Cause of HF Hospitalization

Traditional Approach to Congestion in Heart Failure

Diuretics (Furosemide)

Relieve Symptom of Congestion and Edema
Diuretics in ADHF

Limitations

The Efficacy of diuretics to decrease mortality in HF *has never bee established*

Diuretic Resistance
Increased Mortality!
Diuretic Resistance in HF

Definition
Persistent Congestion despite adequate diuretic dose
At least 80 mg of furosemide

Cardiorenal Syndrome (CRS) Type 1: Acute CRS
Acute Heart Failure leading to Worsening Renal Function (WRF)

Cardiorenal Syndrome (CRS) Type 2: Chronic CRS
Chronic Heart Failure leading to WRF

Cardiorenal Syndrome (CRS) Type 3: Acute WRF leading to HF
Cardiorenal Syndrome (CRS) Type 4: CKD leading to HF
Cardiorenal Syndrome (CRS) Type 5: Systemic condition leading to simultaneous WRF and HF

Pathophysiology of Cardiorenal Syndrome

Low Cardiac Output?!
Comprehensive analysis of the association between CI and renal function: 575 patients from ESCAPE trial, ESCAPE registry (PAC guided Tx)

Advanced HF with LVEF 23 (+/- 12) %, CI 2.3 (+/- 2.1) L/min/m2
Systolic BP <=125 mmHg, Creatinine <= 3.5 mg/dL
Without Inotropic Drugs (Mirexine, Dopamine, or Dobutamine)

No Positive Association Between CI and Renal Dysfunction

Overall and Specific Subgroup
Low LVEF <35%
High RAP
Low Systolic BP (<100 mmHg, 41%)
More Impaired Renal (GFR <30)

Does Increasing CO improve renal function?

OPTIME-CHF Trial and ROSE-AHF Study that addresses this question
Milrinone 0.5 mcg/kg/min vs Placebo
Low-dose dopamine vs Placebo

No difference in the rate of WRF between groups
Increased CVP is Associated with WRF

Elevated IAP is associated with WRF

CVP but not CI predicted WRF


patients admitted with ADHF Treated with Pulmonary Artery Catheter Guided Therapy
Post hoc analysis
DOSE-AHF trial
ROSE-AHF trial
CARRESS-HF trial

“Stepwise Pharmacological Care Algorithm” (SPCA)
Urine-output-guided diuretic adjustment

VS
Standard Decongestion Therapy

SPCA: Greater in Decongestion, Without WRF

Target = Adequate Decongestion (Warm&Dry)
Dyspnea, Orthopnea: None
Edema: Absent/trace
JVP <= 8 cm H2O

“Stepwise Pharmacological Care Algorithm” (SPCA)

Diuretic Dosing Table

<table>
<thead>
<tr>
<th>Step</th>
<th>Current Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Loop (/day)</td>
<td>Thiazide</td>
</tr>
<tr>
<td>A</td>
<td>≤ 80</td>
<td>±</td>
</tr>
<tr>
<td>B</td>
<td>81 - 160</td>
<td>±</td>
</tr>
<tr>
<td>C</td>
<td>161 - 240</td>
<td>±</td>
</tr>
<tr>
<td>D</td>
<td>&gt; 240</td>
<td>±</td>
</tr>
</tbody>
</table>

Adjust it to the next step in Table upward if UO is < 3L/day

At 48-72 hours, Persistent Congestion (Wet&Warm)
Low dose Dopamine/Dobutamine (2 ug/kg/min)

NTG/Nesiritide

Advanced Cardiorenal Therapy

Decongestion Related WRF Does Not Alter Acute-HF Prognosis

Metra et al, Circ Heart Fail 2012;5:54-62

WRF/No Cong >> No WRF/Cong
Heart Failure Phenotype:
Predominantly related to **Congestive Renal Failure Phenotype**

How to identify **Congestive Renal Failure** Phenotype of HF?

**Clinical Findings:**
Venous Congestion (Elevated JVP), Acute CRS, Warm Response to Treatment

**Multimarker Biomarker Strategies**

**Identify phenotypic variables**
- History/Clinical findings
- Labs
- Biomarkers (clinical labs and omics)
- ECG
- Comprehensive Imaging

Intrarenal Venous Flow Pattern: A Window into Congestive Renal Failure

- **Normal Continuous Intrarenal venous flow (IRVF)**

- **HF with Congestive Renal Failure**
  - DisContinuous Biphasic IRVF
  - DisContinuous Monophasic IRVF

HF Treatment
one-size-fits-all approach

Hemodynamic Stable HF
60% with Diuretic Resistance
80% NYHA III-IV

<table>
<thead>
<tr>
<th>Category</th>
<th>Maintenance diuretic dose (mg)*</th>
<th>IV furosemide dose</th>
<th>Optional†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose</td>
<td>≤ 40</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Standard dose</td>
<td>41-160</td>
<td>Numeric equivalent of maintenance diuretic dose</td>
<td>20</td>
</tr>
<tr>
<td>High dose</td>
<td>161-300</td>
<td>200</td>
<td>20</td>
</tr>
<tr>
<td>Mega dose</td>
<td>≥ 301</td>
<td>200</td>
<td>20</td>
</tr>
</tbody>
</table>

*Bolus is given at the beginning, followed by infusion for maintenance.
†Optional diuretic dose.
‡Thiazide diuretic is an alternative to furosemide.
Conclusion

Congestion is the Main Causes of ADHF

**Venous Congestion** (JVP, Gut Congestion) rather than reduced CO, may be the primary hemodynamic factor driving **WRF in ADHF**

**Congestive Renal Failure**

**HypoTENSION ≠ HypoPERFUSION**

**Diuretic Resistance:**
Increasing Diuretic Dosage
Sequential Nephron Blockade with Different Diuretics

**Urine-output-guided diuretic adjustment**
“Stepwise Pharmacological Care Algorithm” (SPCA)
Thank You

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