Getting to Dry:
Management of Acute Decompensated Heart Failure with Volume Overload

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Disclosure

All planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Learning Objectives

1. Given a patient presenting with acute decompensated heart failure and volume overload, design an individualized strategy for relieving congestive symptoms.

2. Given a patient failing to meet volume goals, determine potential etiologies of diuretic resistance and design a modified strategy for relieving congestive symptoms.

3. Given a patient preparing for discharge following an episode of acute decompensated heart failure, design a strategy for reducing the risk of hospital readmission.
Growing prevalence of ADHF$^{1-3}$

Increased risk of mortality$^4$

Lack of evidence to guide clinicians$^5$

ADHF acute decompensated heart failure

DW is a 54 year-old white man with ischemic cardiomyopathy (EF 20%), hyperlipidemia, diabetes mellitus, and obstructive sleep apnea who presents with fatigue, shortness of breath, and abdominal discomfort of several weeks duration. He had a similar presentation 3 months ago. Today his breathing effort is labored and he has bilateral crackles over two-thirds the height of the lungs. Other pertinent findings include 2+ lower extremity edema and 10-kg weight gain. He is warm and well-perfused.

Current Medications:
- Aspirin 81 mg daily
- Atorvastatin 40 mg daily
- Lisinopril 10 mg daily
- Metoprolol succinate 100 mg daily
- Spironolactone 25 mg once daily
- Furosemide 40 mg twice daily
- Metformin 1000 mg twice daily
- Insulin glargine 25 units subq at night

Vitals: BP 118/78 mmHg, HR 71 bpm

<table>
<thead>
<tr>
<th>Value</th>
<th>134</th>
<th>98</th>
<th>28</th>
<th>182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate (bpm)</td>
<td>71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>134</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse Oximetry</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hemoglobin A1c: 8.9%
NT-proBNP 12,800 pg/mL
Chest x-ray: cardiomegaly, bilateral interstitial/alveolar edema; no effusions
Questions

1. What may have precipitated this heart failure exacerbation?
2. How should his congestive symptoms be managed? Provide recommendations regarding drug, dose, and frequency.
3. What should be done with his other guideline-directed medical therapy?
Questions

1. What may have precipitated this heart failure exacerbation?
Medication reconciliation to identify drug-related causes or contributors

- Most patients with heart failure have $\geq 5$ comorbidities and take $\geq 6$ chronic medications\(^1\)
- Use of nonprescription medications may be as high as 93%\(^2\)
- Nonadherence remains a major contributor to decompensation

COPD chronic obstructive pulmonary disease.
Diuretic Response

Diuretic Concentration

Normal

Heart Failure

Diminished maximal response

Higher doses required for effect

Lower peak due to delayed absorption

Questions

1. What may have precipitated this heart failure exacerbation?
2. How should his congestive symptoms be managed? Provide recommendations regarding drug, dose, and frequency.
**ASCEND**<sup>1</sup> Dyspnea at 6 hours

(p = NS)

**TRUE-AHF**<sup>2</sup> Persistent Heart Failure

(p = 0.63)

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Effects of Furosemide Over Time

- **Preload**: mmHg
- **Urine Output**: mL

Door-to-Furosemide Time

> 1 hour associated with 3-fold increase in mortality (6.0 vs. 2.3%, p=0.002)

References:
308 patients with ADHF randomized

- **High Dose Infusion**
  - 2.5x oral dose
  - infused over 24 hours

- **High Dose Bolus**
  - 2.5x oral dose
  - divided twice daily

- **Low Dose Infusion**
  - 1x oral dose
  - infused over 24 hours

- **Low Dose Bolus**
  - 1x oral dose
  - divided twice daily

Adjustment at 48 hours per clinician discretion

- **Change to oral therapy**
- **Continue current IV dose**
- **Increase IV dose by 50%**

Final evaluation of symptoms and renal function at 72 hours

ADHF acute decompensated heart failure

High Dose
• Greater net fluid loss
• Greater weight loss
• More symptomatic relief

Low Dose
• Less transient worsening of renal function

• Low-dose less likely to be transitioned to oral diuretics and more likely to require a dose increase at 48 hours\(^1\)
• *Transient* worsening of renal function in ADHF no worse than no change\(^2\)

ADHF acute decompensated heart failure
Bolus arm 2x as likely to require a dose increase (21% vs. 11%, p=0.01) and receive thiazide-type diuretics (16% vs. 7%, p=0.02)¹

Prior trials have shown greater fluid and weight loss with continuous infusions²

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Patients who may derive benefit from a continuous infusion?

• High bolus doses (toxicity risk)
• Delayed transcapillary refill rate (e.g., hypoalbuminemia)
• Hypotension with bolus administration
• Preload-dependent conditions (e.g., aortic stenosis, right ventricular failure)
Questions

1. What may have precipitated this heart failure exacerbation?

2. How should his congestive symptoms be managed? Provide recommendations regarding drug, dose, and frequency.

3. What should be done with his other guideline-directed medical therapy?
Renin-Angiotensin-Aldosterone System (RAAS)

- Increased vasoconstriction
- Increased volume retention
- Increased hypertrophy
- Increased fibrosis

Holding ACE inhibitor may increase length of stay (5.5 vs. 3.0 days, p=0.009)?
• In OPTIMIZE-HF, beta blocker continuation was associated with lower risk of death (HR 0.60, 95% CI 0.37-0.99, p=0.044)¹
• Confirmed in B-CONVINCED, which showed no worsening with continuation during hospitalization²

¹OPTIMIZE-HF
ATHENA-HF

- Patients with ADHF receiving spironolactone 12.5-25 mg randomized to continuation vs. increasing dose to 100 mg
- No differences in congestive endpoints (NT-proBNP or dyspnea scores), urine output, or weight change

ADHF acute decompensated heart failure, NT-proBNP n-terminal pro-brain natriuretic peptide

*JAMA Cardiol.* 2017 Sep 1;2(9):950–8.
• What about metformin?
Questions

4. Would your recommendations for the management of congestion change if DW had HFpEF rather than HFrEF? Why or why not?
# Ejection Fraction Breakdown in Recent ADHF Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Agent</th>
<th>Patients</th>
<th>Mean EF (%)</th>
<th>Patients with Preserved EF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCEND-HF</td>
<td>2011</td>
<td>Nesiritide</td>
<td>7147</td>
<td>NR</td>
<td>19.9%</td>
</tr>
<tr>
<td>DOSE</td>
<td>2011</td>
<td>Loop diuretics</td>
<td>308</td>
<td>34.8%</td>
<td>27.0%</td>
</tr>
<tr>
<td>RELAX-AHF</td>
<td>2012</td>
<td>Serelaxin</td>
<td>1161</td>
<td>38.7%</td>
<td>45.0%</td>
</tr>
<tr>
<td>ROSE-AHF</td>
<td>2013</td>
<td>Dopamine/nesiritide</td>
<td>360</td>
<td>31.6%</td>
<td>24.4%</td>
</tr>
<tr>
<td>TACTICS-HF</td>
<td>2017</td>
<td>Tolvaptan</td>
<td>257</td>
<td>33.0%</td>
<td>25.0%</td>
</tr>
<tr>
<td>TRUE-AHF</td>
<td>2017</td>
<td>Ularitide</td>
<td>2157</td>
<td>NR</td>
<td>34.8%</td>
</tr>
</tbody>
</table>

EF: ejection fraction, NR: not reported

Changes in Pressure-Volume Relationships with Reduced EF

A

Changes in Pressure-Volume Relationships with Preserved EF

B

EF ejection fraction, EDPVR end-diastolic pressure-volume relationship, ESPVR end-systolic pressure-volume relationship, Ees end-systolic elastance, SV stroke volume

Adapted from data provided in J Am Coll Cardiol. 2012 Jan 31;59(5):442–51.
## ROPA-DOP Preliminary Results

Patients (n=90) with ADHF and HFpEF randomized to bolus vs. continuous infusion

<table>
<thead>
<tr>
<th>Outcome at 72 hours</th>
<th>Intermittent Bolus</th>
<th>Continuous Infusion</th>
<th>p (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased serum creatinine</td>
<td>4.6%</td>
<td>16.0%</td>
<td>0.03</td>
</tr>
<tr>
<td>Worsening renal function</td>
<td>11.6%</td>
<td>36.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>Volume output</td>
<td>10.3 L</td>
<td>10.7 L</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Presented at 2017 Heart Failure Society of America Meeting.
DW experiences some minor improvement in dyspnea but his urine output is not robust and he fails to meet goal diuresis for two consecutive days (goal 2-3 L negative per day, but less than 2 L negative total for past 48 hours). He reports worsening abdominal discomfort and nausea/vomiting over the past 24 hours which is only partially relieved by antiemetics.

New medications:
- Furosemide 120 mg IV BID
- Insulin aspart sliding scale ACHS

Vitals: BP 112/72 mmHg, HR 74 bpm

\[
\begin{array}{ccc}
130 & 94 & 24 \\
3.8 & 28 & 1.4 \\
\end{array}
\]
Questions

5. What mechanisms might explain diuretic resistance in this patient?

6. What should be done to augment diuresis at this time? Provide recommendations regarding drug, dose, and frequency for at least two pharmacologic options.
Questions

5. What mechanisms might explain diuretic resistance in this patient?
Common Mechanisms of Diuretic Resistance

- Decreased gut absorption and/or renal perfusion
- Remodeling of the nephron
- Compensatory sodium reabsorption
- Neurohormonal activation
- Pharmacokinetic Mechanisms
- Pharmacodynamic Mechanisms
- Arginine vasopressin
- Renin-angiotensin-aldosterone system
- Loop of Henle
- Proximal convoluted tubule
- Distal convoluted tubule
- Collecting duct
- Glomerulus
Questions

5. What mechanisms might explain diuretic resistance in this patient?

6. What should be done to augment diuresis at this time? Provide recommendations regarding drug, dose, and frequency for at least two pharmacologic options.
Diuretic threshold

Diuretic Concentration

Time

Increase bolus dose

± Initiate continuous infusion

Diuretic threshold
Disadvantages to continuous infusion diuretics

• May encourage a “set it and forget it” mentality
• Overnight urination (i.e., fall risk, decreased sleep quality)
• Unknown safety of high-dose infusions
• Drug mismanagement (omitting boluses, “titrate” orders)
## Thiazide-Type Diuretics

<table>
<thead>
<tr>
<th>Agent</th>
<th>Metolazone</th>
<th>Chlorothiazide</th>
<th>Hydrochlorothiazide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral bioavailability</td>
<td>40-65%</td>
<td>N/A</td>
<td>65-75%</td>
</tr>
<tr>
<td>Usual dose (maximum/day)</td>
<td>2.5–5 mg once daily (20 mg)</td>
<td>500–1000 mg once to twice daily (2000 mg)</td>
<td>25–50 mg once to twice daily (100 mg)</td>
</tr>
<tr>
<td>Onset (peak)</td>
<td>2–3 h (6-8 h)</td>
<td>2 h (3–6 h)</td>
<td>2 h (3–6 h)</td>
</tr>
<tr>
<td>Duration of action</td>
<td>12–24 h</td>
<td>6–12 h</td>
<td>6–12 h</td>
</tr>
</tbody>
</table>
Metolazone vs. Chlorothiazide\(^1\)
\(p=0.026\) for noninferiority

From the available studies in ADHF\(^1-3\):
HCTZ < CTZ = MTZ

ADHF acute decompensated heart failure, CTZ chlorothiazide, HCTZ hydrochlorothiazide, MTZ metolazone

- Improvements in weight and fluid loss but not symptoms\(^1\)
- Confirmed the results of EVEREST\(^2\)
- 48 hours of therapy: $1200
- Have less expensive options for hyponatremia (furosemide plus hypertonic saline)\(^3-5\)

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Venous Vasodilation

- Mobilizes fluid in periphery
- Decongests kidneys

Nitroglycerin*  
Nitroprusside  
Nesiritide

Arterial Vasodilation

- Improved renal blood flow due to reduced impedance

Nitroprusside  
Nesiritide

- Nitroglycerin and nesiritide improve hemodynamics and some congestive symptoms but follow-up trials of nesiritide have been equivocal\textsuperscript{1-2}

*At high-doses (> 100 mcg/min), nitroglycerin exerts venous and arterial dilating effects.  
# Intravenous Vasodilators

<table>
<thead>
<tr>
<th>Agent</th>
<th>Nesiritide</th>
<th>Nitroglycerin</th>
<th>Nitroprusside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilation</td>
<td>Arterial, venous</td>
<td>Venous (mostly)</td>
<td>Arterial, venous</td>
</tr>
<tr>
<td>Onset</td>
<td>15 minutes</td>
<td>Immediate</td>
<td>Immediate</td>
</tr>
<tr>
<td>Half-life</td>
<td>20 minutes</td>
<td>4 minutes</td>
<td>2 minutes</td>
</tr>
<tr>
<td>Dosing</td>
<td>0.01–0.03 mcg/kg/min (± 2 mcg/kg bolus)</td>
<td>5–200 mcg/kg/min</td>
<td>0.3–3 mcg/kg/min</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• Longer half-life</td>
<td>• High doses required for arterial vasodilation</td>
<td>• Toxic metabolites in severe renal or hepatic impairment</td>
</tr>
<tr>
<td></td>
<td>• Cost</td>
<td>• Tachyphylaxis with extended duration</td>
<td>• Cost</td>
</tr>
</tbody>
</table>
Weight Loss and Dyspnea Scores

- Excluded patients on inotropes or vasodilators and those who required initiation were deemed treatment failures
- Average removal rate 250 mL/h to target 80% of excess body weight
- Ultrafiltration was also associated with fewer rehospitalizations (18 vs. 32%, p=0.037)

Ultrafiltration (UNLOAD)¹

<table>
<thead>
<tr>
<th>Weight Loss (kg)</th>
<th>Ultrafiltration</th>
<th>Standard care</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>5.0 vs. 3.1 kg (p=0.001)</td>
<td>6.4 vs. 6.1 (p=0.35)</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dyspnea Score

- 7
- 6
- 5
- 4
- 3
- 2
- 1

Despite the changes you made to DW’s therapy, his urine output does not improve and he is less than 1 L negative overnight. His latest vital signs include a blood pressure of 104/62 mmHg and heart rate of 82 bpm. Morning labs are significant for a serum creatinine of 1.9 (up from 1.4 mg/dL at admission). The team decides to place a pulmonary artery catheter which reveals the following information:

- Right atrium: 22 mmHg
- Right ventricle: 42/20 mmHg
- Pulmonary artery: 40/22 (28) mmHg
- Wedge pressure: 26 mmHg
- Cardiac output: 4.2 L/min
- Cardiac index: 2.0 L/min/m$^2$
- Systemic vascular resistance: 910 dynes·sec/cm$^5$

The patient is subsequently placed on dobutamine at 3 mcg/kg/min.
Questions

7. Would your recommendations for volume management change at this time? Why or why not?
PCWP or LVEDP (Preload) (mmHg)

Cardiac Index (Stroke Volume)

Heart failure

DW will likely need more diuretic rather than less

LVEDP left ventricular end-diastolic pressure
PCWP pulmonary capillary wedge pressure
ROSE-AHF Study Design

360 patients with ADHF and renal impairment

Randomized 1:1

Nesiritide Arm

Dopamine Arm

Randomized 2:1

Low-Dose Nesiritide (0.005 mcg/kg/min)

Placebo

Low-Dose Dopamine (2 mcg/kg/min)

72 hours

Final evaluation of urine output and renal function at 72 hours

ADHF acute decompensated heart failure
JAMA. 2013 Dec 18;310(23):2533-43.
## ROSE Study Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo</th>
<th>Dopamine</th>
<th>( \text{P} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative urine output</td>
<td>8296</td>
<td>8524</td>
<td>0.59</td>
</tr>
<tr>
<td>Change in cystatin C</td>
<td>0.11</td>
<td>0.12</td>
<td>0.72</td>
</tr>
<tr>
<td>Patient-reported symptoms (AUC)</td>
<td>4704</td>
<td>4553</td>
<td>0.43</td>
</tr>
<tr>
<td>Drug discontinued due to tachycardia</td>
<td>0.9%</td>
<td>7.2%</td>
<td>(&lt; 0.001)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo</th>
<th>Nesiritide</th>
<th>( \text{P} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative urine output</td>
<td>8296</td>
<td>8574</td>
<td>0.49</td>
</tr>
<tr>
<td>Change in cystatin C</td>
<td>0.11</td>
<td>0.07</td>
<td>0.36</td>
</tr>
<tr>
<td>Patient-reported symptoms (AUC)</td>
<td>4704</td>
<td>4498</td>
<td>0.62</td>
</tr>
<tr>
<td>Drug discontinued due to hypotension</td>
<td>10.4%</td>
<td>18.8%</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*JAMA.* 2013 Dec 18;310(23):2533-43.
Patients with ADHF and renal impairment randomized

Ultrafiltration 200 mL/h for 96 hours

<table>
<thead>
<tr>
<th>Home Dose</th>
<th>Furosemide Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 80 mg</td>
<td>40 mg IVB, then 5 mg/h</td>
</tr>
<tr>
<td>81-160 mg</td>
<td>80 mg IVB, then 10 mg/h + MTZ 5 mg</td>
</tr>
<tr>
<td>161-240 mg</td>
<td>80 mg IVB, then 20 mg/h + MTZ 5 mg BID</td>
</tr>
<tr>
<td>&gt; 240 mg</td>
<td>80 mg IVB, then 30 mg/h + MTZ 5 mg BID</td>
</tr>
</tbody>
</table>

If patient fails to meet urine output goals:
1. At 24 hours, advance diuretics
2. At 48 hours, Step 1 and consider vasodilators/inotropes
3. At 72-96 hours, Step 1-2 and consider hemodynamic guided-therapy ± MCS

ADHF acute decompensated heart failure, IVB intravenous bolus, MCS mechanical circulatory support, MTZ metolazone
JAMA. 2013 Dec 18;310(23):2533-43.
CARRESS-HF¹
Changes in Serum Creatinine

- More adverse effects also seen with ultrafiltration (72% vs. 57%, p=0.03)
- Disrupted renal counter-regulatory response?
- Masked low output?

**Mean Change from Baseline (mg/dL)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Pharmacologic</th>
<th>Ultrafiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h</td>
<td>-0.04</td>
<td>0.2</td>
</tr>
<tr>
<td>48 h</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>72 h</td>
<td>-0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>96 h</td>
<td>-0.3</td>
<td>0.23</td>
</tr>
<tr>
<td>7 d</td>
<td>-0.1</td>
<td>0.23</td>
</tr>
<tr>
<td>30 d</td>
<td>-0.4</td>
<td>0.23</td>
</tr>
<tr>
<td>60 d</td>
<td>-0.5</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Change at 96 hours
-0.04 vs. +0.23 (p=0.003)

(1) JAMA. 2013 Dec 18;310(23):2533-43.
After a week of inotropic support and aggressive diuresis, DW’s symptoms have significantly improved. He has been successfully weaned from dobutamine and is approaching his baseline weight. The team plans to send him home in the next several days and is preparing a discharge plan. Numerous changes have been made to his medication regimen during the hospitalization.

Current Medications:
• Aspirin 81 mg daily
• Atorvastatin 40 mg daily
• Isosorbide dinitrate 20 mg TID
• Hydralazine 50 mg TID
• Spironolactone 25 mg once daily
• Furosemide 80 mg IV once daily
• Insulin glargine 40 units subq at night
• Insulin aspart sliding scale ACHS

Vitals: BP 114/80 mmHg, HR 70 bpm

<table>
<thead>
<tr>
<th>Value</th>
<th>136</th>
<th>96</th>
<th>26</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>124</td>
<td>4.3</td>
<td>1.3</td>
</tr>
<tr>
<td>BP</td>
<td>4.3</td>
<td>24</td>
<td>1.3</td>
</tr>
</tbody>
</table>
Questions

8. What changes to this patient’s medication regimen should be considered as he approaches discharge?

9. What non-pharmacologic strategies might also reduce his risk of readmission?
Questions

8. What changes to this patient’s medication regimen should be considered as he approaches discharge?
Should the patient be changed to sacubitril/valsartan?

<table>
<thead>
<tr>
<th>Inclusions</th>
<th>Exclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NYHA Class II-IV symptoms</td>
<td>• Symptomatic hypotension</td>
</tr>
<tr>
<td>• Ejection fraction ≤ 35%</td>
<td>• Blood pressure &lt; 100/95 mmHg</td>
</tr>
<tr>
<td>• NT-proBNP ≥ 600 pg/mL or ≥ 400 if hospitalized in the last 12 months</td>
<td>• GFR &lt; 30 mL/min</td>
</tr>
<tr>
<td>• Enalapril equivalent ≥ 10 mg/day</td>
<td>• Serum potassium ≥ 5.4</td>
</tr>
<tr>
<td>• Unacceptable side effects</td>
<td>• Unacceptable side effects</td>
</tr>
</tbody>
</table>

- Compared to enalapril, sacubitril/valsartan reduced the composite of death or first hospitalization for heart failure (21.8 vs. 26.5%, p<0.001)

NYHA New York Heart Association, GFR glomerular filtration rate, NT-proBNP n-terminal pro-brain natriuretic peptide
## Diuretic Observation Prior to Discharge

Patients (n=123) observed on discharge diuretic < 24 or ≥ 24 hours prior to discharge

<table>
<thead>
<tr>
<th>Outcome</th>
<th>&lt; 24 hour (n=61)</th>
<th>≥ 24 hour (n=62)</th>
<th>p (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day heart failure readmission</td>
<td>11 (18%)</td>
<td>2 (3.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>60-day heart failure readmission</td>
<td>18 (29.5%)</td>
<td>6 (9.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-day heart failure readmission</td>
<td>23 (37.7%)</td>
<td>12 (19.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any heart failure readmission</td>
<td>34 (55.7%)</td>
<td>23 (37.1%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

J Card Fail. 2017 Jul 5. pii: S1071-9164(17)30201-4
Other Medication Adjustments

• Beta blocker?
• Ivabradine or digoxin?
• Non-heart failure medications?
EMPA-REG OUTCOME¹
Hospitalization for Heart Failure

- Hazard ratio 0.65 (95% CI 0.50-0.85) p=0.002

- Empagliflozin also associated with reduction in cardiovascular death (3.7% vs. 5.9%, p<0.001)
- Patients may require reduction in diuretic dose

Questions

8. What changes to this patient’s medication regimen should be considered as he approaches discharge?

9. What non-pharmacologic strategies might also reduce his risk of readmission?
• Pharmacist-provided patient education associated with > 40% reduction in readmissions across several trials\textsuperscript{1,2}

• Largest trial (PILL-CVD) did not impact readmissions but compared individualized to standardized education\textsuperscript{3}

• A single session at discharge unlikely to reduce readmissions significantly

• Medication adherence remains a major contributor to readmissions
• Pharmacists improve adherence rates, which have been associated with reductions in readmission of 19-43%\textsuperscript{1-3}
• Benefits greatest with longitudinal programs vs. single intervention

Example Adherence-Improvement Strategies

- Simplifying complex regimens (e.g., less frequently dosed medications, reducing unnecessary polypharmacy)
- Individualized education (e.g., adjusting diuretic based on weight)
- Improving medication-taking behavior (e.g., pillboxes, alerts, integrating medications into daily routines)
- Referral to pharmacist-managed bridge clinic\(^1\)
- Improving access by identifying lower cost alternatives

• Financial limitations are a major barrier
• Even within the same geographic area, 75-fold variability in cost observed
• Made more challenging by the fragmented health payment system
• Efforts to improve access requires a committed outpatient/community pharmacy team

The price for 30 days of generic digoxin ranged from $4 to $306 across the St. Louis area

Pulmonary Artery Pressure Monitoring

Sensor

Hospital System

Patient System

Images used with permission from St. Jude Medical.
# Patient Management in CHAMPION

**Adults with NYHA Class III heart failure and hospitalization within prior 12 months (n=550)**

<table>
<thead>
<tr>
<th></th>
<th>Hypovolemic</th>
<th>“Optivolemic”</th>
<th>Hypervolemic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Poor perfusion without congestive symptoms PA pressures below goal</td>
<td>No congestive symptoms PA systolic 15-35 mmHg PA diastolic 8-12 mmHg PA mean 10-25 mmHg</td>
<td>Congestive symptoms PA pressures above goal</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Decrease intensity of diuretics or vasodilators Liberalize fluid/salt intake Hold ACEi/ARB if renal function worsened Consider admission</td>
<td>Continue diuretic regimen Optimize GDMT</td>
<td>Increase intensity of diuretics or vasodilators Re-educate on fluid/salt intake</td>
</tr>
<tr>
<td><strong>Follow-Up</strong></td>
<td>≥ 2-3 days/week</td>
<td>Weekly (2-3 days/week if GDMT adjusted)</td>
<td>≥ 2-3 days/week</td>
</tr>
</tbody>
</table>

ACEi angiotensin-converting enzyme inhibitor, ARB angiotensin receptor blocker, GDMT guideline-directed medical therapy, PA pulmonary artery  
### CHAMPION Results

#### Primary endpoint (6 months)
- Hazard ratio 0.72
- (95% CI 0.60-0.85) \(p = 0.0002\)
- NNT = 9

#### Supplementary endpoint (mean 15 months of follow-up)
- Hazard ratio 0.63
- (95% CI 0.52-0.77) \(p < 0.0001\)
- NNT = 4

Also improved with W-IHM \(p < 0.05\):
- Mean PA pressures
- Days alive
- Quality of life

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**Number at risk**

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Treatment group</th>
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<tbody>
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<td>Time from implant (days)</td>
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<tr>
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</tbody>
</table>

PA: pulmonary artery, W-IHM: wireless implantable hemodynamic monitor

DW has a pulmonary artery (PA) pressure monitor placed during his admission and you are assigned to follow his PA pressures. Approximately 6 weeks after discharge, he calls the clinic with complaints of “feeling funny” and wants to know if it is related to his new medication (i.e., sacubitril/valsartan). You ask him to transmit readings from his PA pressure monitor, which reveals:

PA systolic 12 mmHg, PA diastolic 6 mmHg, and PA mean 8 mmHg

Heart failure medications:
• Sacubitril/valsartan 49/51 mg BID
• Metoprolol succinate 25 mg once daily
• Spironolactone 25 mg once daily
• Torsemide 60 mg once daily
Questions

10. What changes would you like to make to his heart failure regimen?
Changes driven largely by diuretics ($p < 0.0001$) → Diuretic adjustments were different among patients with preserved EF but not reduced EF ($p = 0.0045$ vs. $p = 0.91$)²

PA pressure monitoring permitted up-titration of GDMT ($p < 0.01$)

Getting to Dry: Management of Acute Decompensated Heart Failure with Volume Overload

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