Management of Acute Heart Failure

Teerapat Yingchoncharoen MD, FASE

Ramathibodi hospital
Powervote Setting

b.socrative.com

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TEERAPAT

กรอกชื่อ

Mahidol University

Acute heart failure for cardiologists
Typical proportions of HF hospitalization in ADHERE registry

- **HF with HTN**
- **Acute Pulmonary Edema**

- **LVEF ≥ 55%**
- **LVEF 40-55%**
- **LVEF < 40**

- **Cardiogenic shock <2%**
- **SBP <90mmHg <10%**

- Symptoms not due to HF
- Other suspected hypotension

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Case #1

64-year-old female

NICM EF 25%, returned from vacation 2 days ago

DOE, walking distance ↓ from 1 km to 150 m

4-pillow orthopnea, 4 kgs weight gain

PE: alert and oriented, BP 105/75 mmHg, P=82

JVP 15 cmH$_2$O, bibasilar rales, 2+ edema, warm extremities

Cr 1.6 (baseline 1.2)

On Carvedilol, Lisinopril, Spironolactone, Furosemide
What is the best initial therapy

A. Stop beta blocker and ACE I

B. Start IV furosemide at 1-2.5 times of the home oral equivalent dose

C. Start Dobutamine drip

D. Start Milrinone drip

E. Instruct the patient not to take anymore vacation
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC
Initial Management of AHF

Patient with suspected AHF

Urgent phase after first medical contact

1. Cardiogenic shock?

Circulatory support
- pharmacological
- mechanical

Immediate stabilization and transfer to ICU/CCU

2016 ESC Guidelines for management of Heart Failure
Initial Management of AHF

Patient with suspected AHF

1. Cardiogenic shock?
   - Yes
     - Circulatory support
       - Pharmacological
       - Mechanical
   - No

2. Respiratory failure?
   - Yes
     - Ventilatory support
       - Oxygen
       - Non-invasive positive pressure ventilation (CPAP, BiPAP)
       - Mechanical ventilation

Immediate stabilization and transfer to ICU/CCU
### Oxygen and ventilation Rx

<table>
<thead>
<tr>
<th>Level</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Monitoring of transcutaneous arterial oxygen saturation (SpO₂) is recommended</td>
</tr>
<tr>
<td>IIa</td>
<td>Oxygen therapy is recommended in patients with AHF and SpO₂ &lt;90% or PaO₂ &lt; 60 mmHg to correct hypoxemia</td>
</tr>
<tr>
<td>IIb</td>
<td>Intubation is recommended, if respiratory failure, leading to hypoxemia (PaO₂ &lt; 60), hypercapnia (PaCO₂ &gt; 50 mmHg) and acidosis (pH &lt; 7.35), cannot be managed non-invasively</td>
</tr>
</tbody>
</table>

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2016 ESC Guidelines for management of Heart Failure
Non-invasive positive pressure ventilation (CPAP, BiPAP) should be considered in patients with respiratory distress (RR>25/min, SpO2 <90%) and started as soon as possible in order to decrease respiratory distress and reduce the rate of mechanical endotracheal intubation.

Non-invasive positive pressure ventilation can reduce blood pressure and should be used with caution in hypotensive patients. Blood pressure should be monitored regularly when this treatment is used.
Initial Management of AHF

Patient with suspected AHF

- **Urgent phase after first medical contact**

  - 1. Cardiogenic shock?
    - Yes
      - Circulatory support
        - pharmacological
        - mechanical
    - No

  - 2. Respiratory failure?
    - Yes
      - Ventilatory support
        - oxygen
        - non-invasive positive pressure ventilation (CPAP, BiPAP)
        - mechanical ventilation
    - No

Immediate stabilization and transfer to ICU/CCU
Criteria for ICU/CCU admission

- High risk patients (persistent significant dyspnea, hemodynamic instability, severe arrhythmias, AHF due to ACS)
- Need for intubation (or already intubated)
- Signs/symptoms of hypotension
- SpO2 < 90% despite supplemental oxygen
- Use of accessory muscles for breathing, RR > 25/min
- Heart rate < 40 or > 130 bpm, SBP < 90 mmHg

2016 ESC Guidelines for management of Heart Failure
Immediate phase (initial 60–120 minutes)

Identification of acute aetiology:
- C: acute Coronary syndrome
- H: Hypertension emergency
- A: Arrhythmia
- M: acute Mechanical cause
- P: Pulmonary embolism

Immediate initiation of specific treatment

Follow detailed recommendations in the specific ESC Guidelines

Diagnostic work-up to confirm AHF
Clinical evaluation to select optimal management

Immediate stabilization and transfer to ICU/CCU
Acute Etiology of AHF

ACS
- Coronary reperfusion
- Antithrombotic therapy

Hypertensive Emergency
- IV Anti-HTN

Life-threatening arrhythmia/bradycardia
- Follow ACLS (DCCV or Pacing)

Acute mechanical cause/severe valvular disease
- Echo
- Surgical/percutaneous intervention

PE
- Lytics
- Sx
Immediate phase (initial 60–120 minutes)

Identification of acute aetiology:
- C acute Coronary syndrome
- H Hypertension emergency
- A Arrhythmia
- M acute Mechanical cause
- P Pulmonary embolism

No

Diagnostic work-up to confirm AHF
Clinical evaluation to select optimal management

Yes

Immediate initiation of specific treatment

Follow detailed recommendations in the specific ESC Guidelines

Immediate stabilization and transfer to ICU/CCU
Diagnosis and initial prognostic evaluation

Lab test at presentation

Natriuretic peptides

Acute heart failure is unlikely if:
- BNP < 100 pg/mL (vs 35 pg/mL in chronic setting)
- NT-proBNP < 300 pg/mL (vs 125 pg/mL in chronic )
- MR-proANP < 120 pg/mL

Other labs
- cTn, BUN, Cr, Electrolytes, LFT, TSH
Diagnosis and initial prognostic evaluation

Additional investigations

ECG
- Underlying cardiac diseases (AF, ischemia)
- Rarely normal in AHF

CXR
Normal in up to 20% of AHF

Echo
Preferably within 48 hours from admission
Immediate: Cardiogenic shock or life threatening structural CV diseases
Diagnosis and initial prognostic evaluation

Lung ultrasounds

B Lines
- Vertical, hyper echoic rays projection from pleural line (ring down artifact)
- Reflects fluid in the interlobular septum
Congestion at rest?

NO

Warm&Dry

Cold&Dry

Outpatient Rx

Evidence for low perfusion
- Cold sweated extremities
- Oliguria
- Mental confusion
- Dizziness
- Narrow pulse pressure

Evidence for congestion
- Orthopnea/PND
- Jugular venous distention
- Peripheral (bilateral edema)
- Congested hepatomegaly
- Gut congestion, ascites
- Hepatojugular reflux
- Valsalva square wave

YES

Warm&Wet

Cold&Wet

Diuresis

Outpatient Rx

Diuresis

?Fluid challenge
Inotropes
(CCU)

Inotropes or Vasodil
(CCU)
'Wet and Warm' patient (typically elevated or normal systolic blood pressure)

Vascular type – fluid redistribution
- Hypertension predominates
  - Vasodilator
  - Diuretic

Cardiac type – fluid accumulation
- Congestion predominates
  - Diuretic
  - Vasodilator
  - Ultrafiltration (consider if diuretic resistance)
Decongestion Strategy

IV loop diuretics
- Institute EARLY in the ER
- Dose should equal or exceed PO dose
- Furosemide PO to IV conversion 2:1
- Furosemide 40 mg = Torsemide 10 mg

To enhance diuretic effectiveness
- AC PO dose
- Limit sodium intake (?)
HFSA 2010 Practice Guideline
Acute HF—Sodium

Recommendation 12.12

A low sodium diet (2 g daily) is recommended for most hospitalized patients.

Strength of Evidence = C

In patients with recurrent or refractory volume overload, stricter sodium restriction may be considered.

Strength of Evidence = C
HFSA 2010 Practice Guideline
Acute HF—Fluid Restriction

Recommendation 12.13

Fluid restriction (<2 liters/day):

- **Is recommended** in patients with moderate hyponatremia (serum sodium < 130 mEq/L)
- **Should be considered** to assist in treatment of fluid overload in other patients.

Strength of Evidence = C

In patients with severe (serum sodium < 125 mEq/L) or worsening hyponatremia, stricter fluid restriction may be considered.

Strength of Evidence = C
Order for one day

**IV furosemide**
- If on furosemide as an outpatient
  - Total daily dose as IV ____mg; max 180 mg
- No po furosemide at home
- Cr < 2.0: Start with 40 mg IVP
- Cr > 2.0: Start with 80 mg IVP

Goal:
- UOP > 250-500 mL in 2 hours

Inadequate response:
- Double previous IV dose (max = 360 mg)

Order for continuation

- Low salt diet (Na < 2 g/day)
- Fluid restriction (2000 cc/24h)
  - if Na < 125 mg/dL restrict fluid to 1500 cc/24hr
In administration of loop diuretics which statement is correct?

A. Bolus dosing results in less diuresis and less clinical improvement than continuous infusion

B. Continuous infusion results in worsened renal function compared to bolus dosing

C. Higher dose of diuretic results in faster weight loss and a shorter hospital stay than a lower dose diuretics

D. None of the above
Diuretic Strategies in Patients with Acute Decompensated Heart Failure

G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Elizabeth O. Ofili, M.D., M.P.H., Kevin J. Anstrom, Ph.D., Adrian F. Hernandez, M.D., Steven E. McNulty, M.S., Eric J. Velazquez, M.D., Abdallah G. Kfoury, M.D., Horng H. Chen, M.B., B.Ch., Michael M. Givertz, M.D., Marc J. Semigran, M.D., Bradley A. Bart, M.D., Alice M. Mascette, M.D., Eugene Braunwald, M.D., and Christopher M. O’Connor, M.D., for the NHLBI Heart Failure Clinical Research Network*

*Acknowledgment of support from the National Heart, Lung, and Blood Institute, National Institutes of Health (grant nos.: HL069285, HL068413, HL086351, HL054161, HL054168, HL054172, HL054173, HL054174, HL054194, HL054208, HL065613, HL070975)
DOSE Trial: Study Design

Acute Heart Failure (1 symptom AND 1 sign) <24 hours after admission

2x2 factorial randomization

Low Dose (1 x oral) Q12 IV bolus
Low Dose (1 x oral) Continuous infusion
High Dose (2.5 x oral) Q12 IV bolus
High Dose (2.5 x oral) Continuous infusion

48 hours

1) Change to oral diuretics
2) continue current strategy
3) 50% increase in dose

72 hours

Co-primary endpoints

60 days

Clinical endpoints

Felker et al. NEJM 2011;364:797
DOSE Study
Symptoms Relief (VAS)

A Bolus vs. Continuous Infusion
AUC with bolus infusions, 4236±1440
AUC with continuous infusion, 4373±1404
P=0.47

B Low-Dose vs. High-Dose Strategy
AUC with low-dose strategy, 4171±1436
AUC with high-dose strategy, 4430±1401
P=0.06

Mahidol University
Felker et al. NEJM 2011;364:797
DOSE Study

Change in serum Cr at 72 hours

![Graph showing change in creatinine with different doses.](image)
DOSE Study
Change in serum Cr

High dose
Low dose

p=0.28
p=0.07
p=0.85
p=0.34
p=0.59
p=0.81

Cr (mg/dL)

Days

0 1 2 3 4 7 60
DOSE Study
Take Home Messages

No substantial outcome difference between equal doses of continuous infusion vs twice daily bolus injection of furosemide.

Higher doses may be somewhat more efficacious (2.5 x previous daily oral dose).

Average furosemide dose used in DOSE was 100 mg q 12 hrs up to 300 mg BID x 3 days.
Intravenous Diuretic Therapy for the Management of Heart Failure and Volume Overload in a Multidisciplinary Outpatient Unit

Leo F. Buckley, PharmD,* Danielle M. Carter, PharmD,* Lina Matta, PharmD, MPH,* Judy W. Cheng, PharmD, MPH,† Craig Stevens, PharmD,* Roman M. Belenkiy, PharmD,* Laura J. Burpee, NP,† Michelle A. Young, NP,† Cynthia S. Weiffenbach, RN,† Jennifer A. Smallwood, MPH,† Lynne W. Stevenson, MD,† Akshay S. Desai, MD, MPH†

JACC Heart Failure 2016 Jan;4(1);1-8
**FIGURE 1  Standardized IV Diuretic Administration Protocol**

<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>
FIGURE 4  Efficacy Outcomes in Notable Subgroups

Weight loss was expressed in kilograms and urine output in liters. Outcomes were similar between patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). Successful decongestion was achieved in the majority of patients.
Regarding low dose dopamine in ADHF, which statement is correct?

A. Low dose dopamine results in more diuresis at 72 hours when compared to placebo

B. Low dose dopamine results in more cystatin-C change when compared to placebo

C. Low dose nesiritide is better than low dose dopamine for renal outcome

D. Neither low dose nesiritide nor low dose dopamine results in more diuresis at 72 hours when compared to placebo
Low Dose Dopamine Vs Low Dose Nesiritide

ROSE Study Design

AHF + Renal Dysfunction N = 360
Open; 1 to 1 randomization

Nesiritide Strategy N = 177
Double-blind; 2 to 1 randomization
Low Dose Nesiritide (72 hours) N = 119
Placebo N = 58
Pooled Placebo (N=119)

Dopamine Strategy N= 183
Double-blind; 2 to 1 randomization
Low Dose Dopamine (72 hours) N = 122
Placebo N = 61

Standardized Diuretic Dosing For 1st 24 hours
2.5 x Outpt Furosemide Equivalent in Divided (BID) IV Doses
Low Dose Dopamine: Co-primary End-points

**72 Hour Urine Volume**
- Placebo: 8.3 L
- Dopamine: 8.5 L
- P = 0.58

**Change in Cystatin-C**
- Placebo: 0.11 mg/L
- Dopamine: 0.12 mg/L
- P = 0.72

Mahidol University
Chen HH et al. JAMA 2013
Low Dose Nesiritide

**Co-primary End-points**

**72 Hour Urine Volume**

- Placebo: 8.3 L
- Nesiritide: 8.6 L
- P = 0.25

**Change in Cystatin-C**

- Placebo: 0.11 mg/L
- Nesiritide: 0.07 mg/L
- P = 0.35

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Chen HH et al. JAMA 2013
## Safety Endpoints

<table>
<thead>
<tr>
<th>Study Drug Tolerance</th>
<th>Dopamine (n=122)</th>
<th>Placebo (N = 119)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study drug d/c - Hypotension</td>
<td>0.9%</td>
<td>10.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Study drug d/c - Tachycardia</td>
<td>7.2%</td>
<td>0.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Study drug d/c – Any Cause</td>
<td>23%</td>
<td>25%</td>
<td>0.72</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Drug Tolerance</th>
<th>Nesiritide (n=119)</th>
<th>Placebo (N = 119)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study drug d/c - Hypotension</td>
<td>18.8%</td>
<td>10.4%</td>
<td>0.07</td>
</tr>
<tr>
<td>Study drug d/c - Tachycardia</td>
<td>0%</td>
<td>0.9%</td>
<td>0.50</td>
</tr>
<tr>
<td>Study drug d/c – Any Cause</td>
<td>25%</td>
<td>25%</td>
<td>0.94</td>
</tr>
</tbody>
</table>
Arginine Vasopressin Antagonists
Tolvaptan: Site of action

V2 Receptor: Free water absorption

Acute heart failure for cardiologists
Effects of Oral Tolvaptan in Patients Hospitalized for Worsening Heart Failure
The EVEREST Outcome Trial

Marvin A. Konstam, MD
Mihai Gheorghiade, MD
John C. Burnett, Jr, MD
Liliana Grinfeld, MD
Aldo P. Maggioni, MD
Karl Swedberg, MD
James E. Udelson, MD
Faiez Zannad, MD
Thomas Cook, PhD
John Ouyang, PhD
Christopher Zimmer, MD
Cesare Orlandi, MD
for the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST) Investigators

Context  Vasopressin mediates fluid retention in heart failure. Tolvaptan, a vasopressin V₂ receptor blocker, shows promise for management of heart failure.

Objective  To investigate the effects of tolvaptan initiated in patients hospitalized with heart failure.

Design, Setting, and Participants  The Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST), an event-driven, randomized, double-blind, placebo-controlled study. The outcome trial comprised 4133 patients within 2 short-term clinical status studies, who were hospitalized with heart failure, randomized at 359 North American, South American, and European sites between October 7, 2003, and February 3, 2006, and followed up during long-term treatment.

Intervention  Within 48 hours of admission, patients were randomly assigned to receive oral tolvaptan, 30 mg once per day (n=2072), or placebo (n=2061) for a minimum of 60 days, in addition to standard therapy.

Main Outcome Measures  Dual primary end points were all-cause mortality (superiority and noninferiority) and cardiovascular death or hospitalization for heart failure (superiority only). Secondary end points included changes in dyspnea, body weight, and edema.

Results  During a median follow-up of 9.9 months, 537 patients (25.9%) in the tolvaptan group and 543 (26.3%) in the placebo group died (hazard ratio, 0.98; 95% confidence interval [CI], 0.87-1.11; P=.68). The upper confidence limit for the mortality difference was within the prespecified noninferiority margin of 1.25 (P<.001). The composite
Cardiovascular Mortality or Heart Failure Hospitalization

Log-Rank Test: $P = .42$
Peto-Peto-Wilcoxon Test: $P = .55$
Stratified Peto-Peto-Wilcoxon Test: $P = .56$

JAMA. 2007;297:1319-1331
EVEREST: Key Entry Criteria

**Inclusions**
- Hospitalized for decompensated HF <48 hours
- LVEF ≤ 40%
- Fluid overload; >2 of the following:
  - Jugular venous distention
  - Pitting edema (>1+)
  - Dyspnea

**Exclusion**
- Recent of planned revascularization or device implant
- STEMI during hospitalization
- SBP < 90 mmHg
- Cr > 3.5 mg%, K > 5.5 mEq/L; Hb <9%

EVEREST : Conclusions

- In pts hospitalized with HF, oral tolvaptan 30 mg OD, facilitates management of volume overload with
  - Early and sustained weight reduction
  - Improvement in dyspnea (d1) and edema (d7)
  - Normalization of serum Na in hyponatremic pts
  - No worsening renal function
- Long-term treatment had no effect on long-term mortality or HF morbidity
Clinical Course of Patients With Hyponatremia and Decompensated Systolic Heart Failure and the Effect of Vasopressin Receptor Antagonism With Tolvaptan

PAUL J. HAUPTMAN, MD,1 JOHN BURNETT, MD,2 MIHAI GHEORGHIADE, MD,3 LILIANA GRINFELD, MD,4 MARVIN A. KONSTAM, MD,5 DUSAN KOSTIC, MD,6 HOLLY B. KRASA, MS,6 ALDO MAGGIONI, MD,7 JOHN OU-YANG, PhD,6 KARL SWEDBERG, MD,8 FAIEZ ZANNAD, MD, PhD,9 CHRIS ZIMMER, MD,6 AND JAMES E. UDELSON, MD,5 ON BEHALF OF THE EVEREST INVESTIGATORS

St. Louis, Missouri; Rochester, Minnesota; Chicago, Illinois; Buenos Aires, Argentina; Boston, Massachusetts; Rockville, Maryland; Florence, Italy; Gothenburg, Sweden; Nancy, France

ABSTRACT

Background: Patients with decompensated heart failure, volume overload, and hyponatremia are challenging to manage. Relatively little has been documented regarding the clinical course of these patients during standard in-hospital management or with vasopressin antagonism.

Methods and Results: The Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan database was examined to assess the short-term clinical course of patients hospitalized with heart failure and hyponatremia and the effect of tolvaptan on outcomes. In the placebo group, patients...
### Time to All-cause Mortality

<table>
<thead>
<tr>
<th>Condition</th>
<th># Subjects</th>
<th># Events</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVEREST All Patients</td>
<td>TLV 2072, PLC 2061</td>
<td>537, 543</td>
<td>0.76</td>
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<tr>
<td>Na+ &lt; 135 mEq/L</td>
<td>TLV 243, PLC 232</td>
<td>116, 106</td>
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<td>Na+ &lt; 130 mEq/L</td>
<td>TLV 38, PLC 54</td>
<td>22, 36</td>
<td>0.30</td>
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</table>

### Time to First Occurrence of CV Mortality or HF Hospitalization

<table>
<thead>
<tr>
<th>Condition</th>
<th># Subjects</th>
<th># Events</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>EVEREST All Patients</td>
<td>TLV 2072, PLC 2061</td>
<td>871, 829</td>
<td>0.42</td>
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<tr>
<td>Na+ &lt; 135 mEq/L</td>
<td>TLV 243, PLC 232</td>
<td>137, 142</td>
<td>0.38</td>
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<td>Na+ &lt; 130 mEq/L</td>
<td>TLV 38, PLC 54</td>
<td>26, 43</td>
<td>0.12</td>
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### Time to First Occurrence of CV Mortality or CV Hospitalization

<table>
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</thead>
<tbody>
<tr>
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<td>TLV 2072, PLC 2061</td>
<td>1006, 958</td>
<td>0.37</td>
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<tr>
<td>Na+ &lt; 135 mEq/L</td>
<td>TLV 243, PLC 232</td>
<td>146, 158</td>
<td>0.16</td>
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<tr>
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<td>TLV 38, PLC 54</td>
<td>26, 46</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Patients with Heart Failure and Hyponatremia

Subjects With Baseline Sodium [Na\(^+\)] ≥130 mEq/L (ITT Population)

- **Samsca\(^\circledast\):** 2,034, 1,784, 1,424, 1,095, 844, 580, 398, 235, 95
- **Placebo:** 2,007, 1,748, 1,415, 1,090, 824, 569, 394, 228, 92

Hazard Ratio: 1.065
95% CI Limits: 0.973, 1.165

Subjects with Baseline Sodium [Na\(^+\)] <130 mEq/L (ITT Population)

- **Samsca\(^\circledast\):** 38, 23, 14, 12, 10, 7, 5, 3, 1
- **Placebo:** 54, 19, 13, 9, 8, 4, 2, 2, 2

Hazard Ratio: 0.603
95% CI Limits: 0.372, 0.979

Overall CV Mortality/Morbidity (ITT) HR 1.04; 95%CI (.95-1.14).

Overall CV Mortality/Morbidity (ITT) HR 1.04; 95%CI (.95-1.14).
Arginine Vasopressin Antagonists

In patients hospitalized with volume overload, including HF, who have persistent severe hyponatremia and are at risk for or having active cognitive symptoms despite water restriction and maximization of GDMT, vasopressin antagonists may be considered in the short term to improve serum sodium concentration in hypervolemic, hyponatremic states with either a V2 receptor selective or a nonselective vasopressin antagonist.
Practical Use of Tolvaptan

Start in-hospital, start dose 7.5/15 mg, maximum dose at 60 mg OD

Frequent monitoring of serum $[\text{Na}^+]$ (at least q 8 hr on D1 and daily onward)

Stop all fluid restriction (especially first 24 hours of therapy)
Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies

\[ \text{CARRESS-HF, UNLOAD} \]

Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury

\[ K > 6.5 \text{ mEq/L, pH} < 7.2, \text{BUN} > 125 \text{ mg/dL, Cr} > 3.4 \text{ mg/dL} \]
Summary
When congestion fails to improve in response to diuretics, consider

1. Reevaluate presence/absence of congestion
2. Sodium/fluid restriction
3. Increasing dose of loop diuretics
4. Continuous IV infusion diuretics
5. Sequential nephron blockade
6. Optimize hemodynamics (PAC-guided therapy)
7. Vasopressin antagonists
8. Ultrafiltration
Case #2

58-year-old male

Longstanding hypertensive heart disease, EF 60%

2 days of increasing dyspnea, orthopnea

BP 190/100, PR 64/min, warm extremities, rales halfway up both lung fields, JVP 14 cmH2O
hypertensive retinal change

Labs : Normal CBC, Cr 1.9 (baseline 1.4)

ECG : No ischemia
What is the best initial therapy

A. Milrinone drip

B. Start IV furosemide + IV NTG

C. Start IV furosemide and HCTZ

D. Add Hydrazine and ISDN

E. Add Lisinopril and amlodipine, follow BP’s
'Wet and Warm' patient (typically elevated or normal systolic blood pressure)

Vascular type – fluid redistribution
Hypertension predominates
- Vasodilator
- Diuretic

Cardiac type – fluid accumulation
Congestion predominates
- Diuretic
- Vasodilator
- Ultrafiltration (consider if diuretic resistance)
IV Vasodilators: Overview

In acute HF associated with
1. Acute mitral regurgitation
2. Acute aortic regurgitation
3. Severe hypertension

Beneficial effects:
- Decrease BP and improve the efficacy of cardiac work
- Speed symptoms relief
- Possibly decrease risk for CCU, mechanical ventilation
- No proven change in mortality

Nitroglycerin, Nitroprusside, Nesiritide
Nitroglycerin

For patients with SBP > 90 mmHg (and without symptomatic hypotension)

- Nitroglycerin 0.6 mg sublingually, repeated every 5-10 mins for 3-4 doses

- Nitroglycerin IV

  Starting dose: 10-20 mcg/min titrate 5-10 mcg/min every 5 minutes (maximal dose 200 mcg/min)
Nitroprusside

Primary arteriolar dilator

- Dose:
  - Start at 0.3 mcg/kg/min
  - Titrate upward by 0.2 mcg/kg/min at 3-5 mins interval
  - Maximum dose 5 mcg/kg/min

- Nitroprusside toxicities:
  - Cyanide intoxication: Metabolic acidosis
  - Thiocyanate toxicity: Hyperreflexia, seizures, altered mentation

Advantages:
- Potent
- Fine titration

Disadvantages:
- CCU and arterial line
- Thiocyanate toxicity esp in renal/hepatic insufficiency
- No randomized trials
‘Wet and Cold’ patient

Systolic blood pressure < 90 mm Hg

YES
- Inotropic agent
- Consider vasopressor in refractory cases
- Diuretic (when perfusion corrected)
- Consider mechanical circulatory support if no response to drugs

NO
- Vasodilators
- Diuretics
- Consider inotropic agent in refractory cases
### Properties of Beta-stimulants, Inotropic vasodilators (inodilators)

<table>
<thead>
<tr>
<th>Drug example</th>
<th>$\alpha &gt; \beta$</th>
<th>$\beta_1$ stimulation</th>
<th>Mixed $\beta_1$ &amp; $\beta_2$ effects</th>
<th>PDE inhibitors</th>
<th>Dopaminergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>NE</td>
<td>Dobutamine (also some $\beta_2$)</td>
<td>Epinephrine (also some alpha)</td>
<td>Milrinone</td>
<td>Dopamine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inotropic effects</th>
<th>++</th>
<th>++</th>
<th>+++</th>
<th>+</th>
<th>++</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arteriolar vasodilation</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Vasoconstriction</td>
<td>+++</td>
<td>0</td>
<td>++</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Chronotropic effect</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Increase in BP</td>
<td>+++</td>
<td>0/+ (by $\uparrow$ CO)</td>
<td>++</td>
<td>-</td>
<td>0/+ (vasocons)</td>
</tr>
<tr>
<td>Use in CHF</td>
<td>+</td>
<td>++</td>
<td>0</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

Mahidol University

Acute heart failure for cardiologists
Selecting the proper inotropes

Patients with acute heart failure requiring inotropic therapy

- Increased PA pressure: Milrinone
- Chronic βB Use: Milrinone
- Hypotension: Dobutamine, Dopamine, Norepinephrine
- Acute cardiorenal dysfunction: Dopamine, Dobutamine
- IHD: Dobutamine
## Positive Inotropes and Vasopressors in Acute Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>Bolus</th>
<th>Infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>No</td>
<td>2-20 mcg/kg/min (β+)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>No</td>
<td>&lt;3 mcg/kg/min : Renal effect (δ+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-5 mcg/kg/min : Inotropic (β+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 5 mcg/kg/min : (β+), vasopressor (α+)</td>
</tr>
<tr>
<td>Milrinone</td>
<td>25-75 mcg/kg over 10-20 mins</td>
<td>0.375-0.75 mcg/kg/min</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>No</td>
<td>0.2-1.0 mcg/kg/min</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Bolus 1 mg can be given IV during resuscitation repeated q 3-5 mins</td>
<td>0.05-0.5 mcg/kg/min</td>
</tr>
</tbody>
</table>
Venous thromboembolism prophylaxis with low dose unfractionated heparin, low molecular weight heparin, or fondaparinux to prevent proximal deep venous thrombosis and pulmonary embolism is recommended for patients who are admitted to the hospital with ADHF and who are not already anticoagulated and have no contraindication to anticoagulation.

Strength of Evidence = B
Summary

Underlying Heart Diseases (cardiomyopathies) → Precipitating Factors → ADHF → ? Hemodynamics

Acute heart failure for cardiologists
Common Precipitating factors of HF

1. Non-compliance to diet and medications
2. Myocardial ischemia
3. Poorly controlled hypertension
4. Cardiac arrhythmias (esp. AF)
5. Infections
6. Anemia
7. Worsening renal function
8. Thyroid abnormalities
9. Use of new medications (esp. NSAIDs)
Before discharging AHF patients

- Exacerbating factors addressed
- Near optimal volume status achieved
- Optimal pharmacologic therapy (ACE inhibitor/ARB and β-blocker) achieved or intolerance documented
- Comorbidities well managed
- Left ventricular ejection fraction documented
- Smoking cessation counseling initiated
- Patient and family education provided
- Follow-up visit scheduled within 7 to 10 days
Natural History of Heart Failure

**Goal:**
- Maintain QOL
- Advanced HF management
- Palliative care, End-of-life

**Goal:**
- Confirm the diagnosis of HF
- Establish the cause
- Treat cause and precipitating factors
- Decongestion, restoration of hemodynamics
- Define risk and prognosis
- Start GDMT pre-discharge

**Goal:**
- Treatment and prevention of precipitating factors (AF, OSA)
- Optimization of GDMT
- Disease modifying approach eg. CRT
- Prevention of readmission / mortality

Thank you for your attention

Feel free to ask questions at
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Ramathibodi hospital