Ed Diagnosis, Risk Stratification and Treatment of Acute Decompensated Heart Failure
“ED Diagnosis and Risk Stratification ADHF”

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Presenter Disclosure Information

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ED Diagnosis and Risk Stratification ADHF

FINANCIAL DISCLOSURE:
Research Grants (>\$10,000) Abbott, Alere, Baxter, Brahms, Novartis, The Medicine’s Company;
Consultant (<\$10,000) Abbott, Alere, Lily, The Medicine’s Company;
Speaker’s Bureau (<\$10,000) Abbott, Alere;
Ownership Interest (<\$10,000) Comprehensive Research Associates LLC, Vital Sensors, Emergencies in Medicine LLC.

UNLABELED/UNAPPROVED USES DISCLOSURE:
I will discuss unlabeled uses of Copeptin and Adrenomedullin (outstanding predictors of short term mortality in heart failure, but are not yet FDA approved)
Diagnosis
Most HF Comes Through the ED

October 2001 to December 2004; N=150,000

ED 78%
Inpatient Unit 20%
Inpatient Unit on Observation 1%
### Economic Impact of a Missed HF Diagnosis at Admission

<table>
<thead>
<tr>
<th>Length of Stay</th>
<th>Lost Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Missed Dx patients had 0.9 longer LOS</td>
<td>• 20% coded DRG 088</td>
</tr>
<tr>
<td>• $900 to 1200 higher cost/patient</td>
<td>– COPD</td>
</tr>
<tr>
<td></td>
<td>– ~ $1200 loss per patient</td>
</tr>
<tr>
<td></td>
<td>• 18% coded DRG 099</td>
</tr>
<tr>
<td></td>
<td>– Respiratory Signs &amp; Symp</td>
</tr>
<tr>
<td></td>
<td>– ~ $2100 less per patient</td>
</tr>
</tbody>
</table>

Based on study at UCMC, Christ Hospital, Jewish Hospital, Cleveland Clinic. Generalized to HF population of 1,000.
Prehospital Effects

- 8,315 EMS runs
  - 499 HF
  - Overall Mortality = 10.9%

- Excluded BP < 100
- Tx = ntg, ms, Lasix
- Linear relationship between high BP & Tx

- Treated n=241
- Untx’d n=252

- If EMS Tx: 36 min sooner
- Scene time: 1.9 mins longer

If treated, OR of survival 2.51 (1.37-4.55) p<0.01

Early treatment works

The Scary Part

106 non-HF final dx.....
BUT tx’d for HF by EMS

- Asthma, COPD, pneumonia, bronchitis
- Represented 15% of dyspneic patients

Mortality (p<0.05)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-HF treated for HF</td>
<td>13.6%</td>
</tr>
<tr>
<td>No treatment</td>
<td>8.2%</td>
</tr>
<tr>
<td>Treated with bronchodilators</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

Heart Failure

Pneumonia

Pneumothorax

Anemia

Pulmonary Embolus

Mondor's Syndrome

Tietze's disease

COPD exacerbation

Cyanide poisoning

Musculoskeletal Pain

MetHgb

IVDA Pulm Infarction

MethHgb

DKA

COPD exacerbation

Breast Cancer

IVDA Pulm Infarction

Subdiaphragm Abcess

Breast Cancer

Amniotic Fluid Embolus

Lung Cancer

Anxiety

Pneumomediastinum

Pneumomediastinum

Mediastinitis

Panic Attack

Pneumonia

Mondor's Syndrome

Metabolic acidosis

Anaphylaxis

Chemical Exposure

FB Aspiration

Chemical Exposure

Anemia

Lung Cancer

Empyema

Amniotic Fluid Embolus

Empyema

Pernicious Anemia

Heart Failure
How good is the H&P?

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hx of HF</td>
<td>62</td>
<td>94</td>
<td>80</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>56</td>
<td>53</td>
<td>54</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>47</td>
<td>88</td>
<td>72</td>
</tr>
<tr>
<td>Rales</td>
<td>56</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>S3 (auscultation)</td>
<td>20</td>
<td>99</td>
<td>66</td>
</tr>
<tr>
<td>JVD</td>
<td>39</td>
<td>94</td>
<td>72</td>
</tr>
<tr>
<td>Edema</td>
<td>67</td>
<td>68</td>
<td>68</td>
</tr>
</tbody>
</table>

• Excessive rapid filling of a stiff ventricle is suddenly halted; vibrations are audible as S3.  
  – Joshi, 1999

• CHF patients w/ an S3 at greater risk for:
  – HF hospitalization
  – death from pump failure
  – composite of death or hospitalization.  

• S3 has 99% specificity for CHF diagnosis.  
• **Internal Medicine residents recognized 20%**

• **Even trained clinicians cannot agree reliably on whether or not an S3 is present.**

• **Ability to detect an S3 by auscultation is poor and is not a function of the level or the experience of the examiner.**
  – Lok, et al. The accuracy and interobserver agreement in detecting the gallop sounds by cardiac auscultation. Chest 1998, 114(5), 1283-8
Genesis

ProANP

Stored Longer in Granules

1 98 99 126

ProBNP

Made Constitutively Briefly Stored in Granules

1 77 78 107

Mechanical and Neurohumeral Signals

Wall Stress

N-ANP

Corin

ANP

3 min

High Variability
Inferior Dx/Prognostic Test

Roche NT-pro-BNP

N-BNP

120 min

Small quantities in blood

Corin

BNP

20 min

Biosite
Beckman
Abbott
Bayer

ProBNP

120 min

Pharmacologic Actions of Endogenous hBNP

Hemodynamic (Balanced vasodilation)
- Veins\(^1\)
- Arteries\(^1\)
- Coronary arteries\(^2\)

Neurohumoral
- Aldosterone\(^3\)
- Endothelin\(^2\)
- Norepinephrine\(^3\)

Renal\(^1\)
- Diuresis
- Natriuresis

Cardiac
- Lusitropic\(^4\)
- Antifibrotic\(^5\)
- Antiremodeling\(^5\)

Natriuretic Peptide Teleology

Fish ANP
~ 800 pg/mL

Human BNP
< 100 pg/mL
NP’s vs. NYHA Class

Figure 3. Relationship between B-type natriuretic peptide (BNP) and N-terminal (NT)-proBNP and New York Heart Association (NYHA) functional classification. Data from Roche Diagnostics\textsuperscript{23} and Biosite Inc.\textsuperscript{24}

BNP and BMI

- 634 w/ HF
- Negative correlation between BMI & BNP

JACC 2003:138A
BNP & Renal F(n)

- BNP & CrCl w/ & w/o HF
- Excluded CrCl<15 & dialysis patients

Impact of BNP Assay on Accuracy

p < 0.0001 for BNP or Both vs Clinical Judgment

26 % wrong

### Univariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP Level (pg/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>98 (93-100)</td>
<td>92 (86-96)</td>
<td>90 (82-94)</td>
<td>98 (94-100)</td>
<td>95</td>
</tr>
<tr>
<td>100</td>
<td>94 (89-97)</td>
<td>94 (89-97)</td>
<td>92 (85-96)</td>
<td>96 (91-98)</td>
<td>94</td>
</tr>
<tr>
<td>115</td>
<td>90 (83-95)</td>
<td>96 (91-98)</td>
<td>94 (87-97)</td>
<td>94 (88-97)</td>
<td>94</td>
</tr>
<tr>
<td>120</td>
<td>90 (82-95)</td>
<td>96 (92-99)</td>
<td>95 (88-98)</td>
<td>93 (88-96)</td>
<td>94</td>
</tr>
<tr>
<td>150</td>
<td>87 (78-92)</td>
<td>97 (93-99)</td>
<td>95 (89-98)</td>
<td>91 (85-95)</td>
<td>93</td>
</tr>
</tbody>
</table>

BNP Levels in Clinical Use

- **Low BNP** (< 50-100 pg/mL)
  - The symptoms are NOT due to HF, unless….
    - Think of a different diagnosis (COPD, etc)

- **Medium BNP** (between 100 and 500 pg/mL)
  - Consider the differential (PE, Pulm HTN, etc)
  - Compare to prior BNP levels

- **High BNP** (>500 pg/mL)
  - HF likely, but you’d better think about it

- **Trending**
  - post-therapy: may help identify higher risk patients
## NT-proBNP Decision Statistics

Optimal NT-proBNP cut-points for the diagnosis or exclusion of acute HF among dyspnoeic patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Optimal cut-point</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmatory (‘rule in’) cut-points</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50 years (n = 184)</td>
<td>450 pg/mL</td>
<td>97</td>
<td>93</td>
<td>76</td>
<td>99</td>
<td>94</td>
</tr>
<tr>
<td>50 – 75 years (n = 537)</td>
<td>900 pg/mL</td>
<td>90</td>
<td>82</td>
<td>83</td>
<td>88</td>
<td>85</td>
</tr>
<tr>
<td>&gt;75 years (n = 535)</td>
<td>1800 pg/mL</td>
<td>85</td>
<td>73</td>
<td>92</td>
<td>55</td>
<td>83</td>
</tr>
<tr>
<td>Rule in, overall</td>
<td></td>
<td>90</td>
<td>84</td>
<td>88</td>
<td>66</td>
<td>85</td>
</tr>
<tr>
<td>Exclusionary (‘rule out’) cut-point</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients (n = 1256)</td>
<td>300 pg/mL</td>
<td>99</td>
<td>60</td>
<td>77</td>
<td>98</td>
<td>83</td>
</tr>
</tbody>
</table>

Adapted from Januzzi et al. ICON STUDY Eur Heart J. 2006 Feb;27(3):330-7
REDHOT Baseline BNP Values & Mortality

Median BNP values:

<table>
<thead>
<tr>
<th></th>
<th>30-Day</th>
<th>90-Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>764</td>
<td>727</td>
</tr>
<tr>
<td>Deceased</td>
<td>2,096</td>
<td>1,224</td>
</tr>
</tbody>
</table>

***P < 0.001

REDHOT: BNP & Patient Disposition

- Previous data link high BNP to morbidity & mortality
- Actual BNP values blinded to ED physician
- BNP median values ~22% higher in patients discharged home from ED

### Perceived NYHA Class in Patients Ultimately Admitted to the ED

<table>
<thead>
<tr>
<th>BNP</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200 pg/mL</td>
<td>1</td>
<td>14</td>
<td>18</td>
<td>11</td>
<td>44</td>
</tr>
<tr>
<td>≥200 pg/mL</td>
<td>10</td>
<td>103</td>
<td>168</td>
<td>93</td>
<td>374</td>
</tr>
</tbody>
</table>

- 11% of all patients admitted with BNP <200 pg/mL
- 66% of patients admitted with BNP <200pg/mL perceived to be NYHA III, IV
452 pts with acute dyspnea

randomized

Clinical Group

BNP Group

History, physical exam, ECG, chest X-ray, blood tests, SaO2

Rapid BNP Test (15 min)

Start of Specific Treatment

Further evaluation recommended: Echo & spirometry

Hospital Discharge

30-day Outcome
BASEL

Mortality through 30 days

No difference

Time to appropriate treatment

↓ 27 minutes (90 min vs. 63 min)  \( P=0.03 \)

Admission rate

↓ by 10% (85% vs. 75%)  \( P=0.008 \)

ICU admissions

↓ by 9% (24% vs. 15%)  \( P=0.014 \)

Results: Primary Endpoints

- **Time to Discharge (days):**
  - Clinical Group: 11.0
  - BNP Group: 8.0
  - *P* = 0.009
  - Decrease by 23%

- **Total Treatment Cost ($):**
  - Clinical Group: $7,264
  - BNP Group: $5,410
  - *P* = 0.006
  - Decrease by 26%

US savings $1,854

Risk Stratification
46,599
ED ADHF

Vasoactive by location

4,096 in ED 1.1 hr
3,499 inpatient 22 hr

Mortality Rate (%) % ICU Transfer Hospital LOS (days) ICU LOS (days) % Invasive Procedures

↑253% ↑500% ↑150% ↑155% ↑142%

*P = 0.0001

Mortality vs. Quartiles of Diuretic Time & BNP Level

Mortality

Time to Diuretic

<1.05 1.05-2.22 2.23-4.98 >4.98

<449 450-864 865-1738 >1738

BNP pg/mL
<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Add age</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>Add rate (min 20, max 45)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>Subtract points</td>
</tr>
<tr>
<td></td>
<td>&lt;90 = -30, 90-99 = -35, 100-119 = -40,</td>
</tr>
<tr>
<td></td>
<td>120-139 = -45, 140-159= -50,</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>160-179= -55, &gt; 180 = -60 Add level</td>
</tr>
<tr>
<td></td>
<td>(max = 60 mg/dL)</td>
</tr>
<tr>
<td>Sodium (meq/L)</td>
<td>Add 10 if &lt;136 meq/L</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>Add 10</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary</td>
<td>Add 10</td>
</tr>
<tr>
<td>Disease</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>Add 15</td>
</tr>
<tr>
<td>Dementia</td>
<td>Add 20</td>
</tr>
<tr>
<td>Hepatic Cirrhosis</td>
<td>Add 25</td>
</tr>
</tbody>
</table>

**Prediction Tool**

30-day mortality
N ~ 4,000 patients

If < 70 total points, 30 day mortality is <1%.
BNP vs. Outcomes

Cumulative probability of CHD visit, admission or death, %

- BNP >480 pg/ml
- BNP 230-480 pg/ml
- BNP <230 pg/ml

ADHERE CART: Predictors of Mortality

Highest to Lowest Risk Cohort
OR 12.9 (95% CI 10.4-15.9)

In-hospital Mortality According to Troponin T Quartile

<table>
<thead>
<tr>
<th>Troponin T Quartile</th>
<th>In-Hospital Mortality (%)</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.01</td>
<td>1.7</td>
<td>1773</td>
</tr>
<tr>
<td>&gt; 0.01-0.02</td>
<td>2.8</td>
<td>502</td>
</tr>
<tr>
<td>&gt; 0.02-0.06</td>
<td>3.3</td>
<td>1138</td>
</tr>
<tr>
<td>&gt; 0.06</td>
<td>6.3</td>
<td>1119</td>
</tr>
</tbody>
</table>

P <0.001

Mortality According to Time in Hospital and Troponin Status at Presentation

<table>
<thead>
<tr>
<th>Days in Hospital</th>
<th>Cumulative Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Troponin-negative</td>
</tr>
<tr>
<td>5</td>
<td>Troponin-positive</td>
</tr>
</tbody>
</table>

P <0.001*

*Dashed lines show 95% CI

### AHF Acute Outcomes vs. Troponin

<table>
<thead>
<tr>
<th>Event</th>
<th>Troponin (-)</th>
<th>Troponin (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 65,590</td>
<td>N = 4,410</td>
</tr>
<tr>
<td>CABG, IABCP, intubation</td>
<td>6%</td>
<td>18%</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>4.1 days</td>
<td>5.1 days</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>2.3 days</td>
<td>2.9 days</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.7%</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

*P < 0.0001*
48,629 (63%) out of 77,467 pt episodes had BNP assessment at initial evaluation.
42,636 (87.6%) with troponin I or T along with BNP levels.

Q2 2003 to Q4 2004.
OU Risk Stratification

Analysis of the following variables:
- Gender
- Age > 70 years
- Insurance status
- Diabetes
- HTN
- CHF
- Renal insufficiency
- CAD
- Ejection fraction <40%
- Systolic BP >160 (SBP)
- No ischemic or infarction ECG change (iECG)
- Cr< 2.5 mg/dl
- BUN<60 mg/dl
- Normal initial troponin
- Hct>30 mg/dl
- Sodium > 136 mEq/dl
- No pulmonary edema on CXR
- Initial pulse oximetry >90%

Results: N=499

27% of ADHF patients defined as “low risk” by the following independent variables:

- Significant variables from univariate analysis:
  - SBP > 160
  - No iECG
  - Normal initial Troponin I

- Significant variables after multivariate analysis:
  - SBP >160 and
  - Normal initial Troponin I

Diercks et al. J Cardiac Failure 2004;10(No 4 suppl):S118
OU Risk Stratification

Analysis of the following variables:

- Gender
- Age
- Details of medical Hx
- Clinical course
- Initial ED Systolic BP
- Treatment
- Disposition
- Laboratory data:
  - B-type natriuretic peptide
  - Cr
  - BUN
  - Hg
  - Sodium level

Results: N=385

Univariate analysis showed the following had statistically significant association with admissions:

- Elevated Cr
- Elevated BUN

Multivariate analysis showed only the following had a significant relation to admissions:

- BUN > 30mg/dL

Burkhardt Annals Emerg Med 2004;44:S99-S100
ED Dyspnea

**Age > 40y, not clearly asthma**

**Possible HF?:** Consider BNP [creatinine & BMI]

- **BNP < 100:** Low
- **100-500:** Gestault
- **> 500:** High

**Disposition/Risk Stratification**

- **Low**
  - BUN < 30<sup>a</sup>
  - BP > 160 mmHg<sup>b</sup>
  - Tn (-)<sup>b</sup>

- **Gestault**
  - S<sub>3</sub>

- **High**
  - BUN > 43 mg/dL<sup>c</sup>
  - BP < 115 mmHg
  - Cr > 2.75 mg/dL

---

Bach Trial
- Prospective ED trial of shortness of breath
- N=1641

- 568 with HF (34.6 %)
  - 52% were male
  - 36% had a prior history of HF
  - 20 (3.5%) died by 14 days
  - 65 (11.4%) were dead by 90 days
Copeptin (ADH-AVP)

- Nonapeptide with endocrine, hemodynamic, and osmoregulatory effects
- Produced in hypothalamus; secreted upon hemodynamic and osmotic stimuli
- Peripheral effects by V1a, V1b, and V2 receptors.
- Inadequate AVP = DI; Excess AVP = SIADH
- Increased AVP; is part of the endocrine response to cardiac arrest, shock, and circulatory stress
AHF Time Dependent Mortality
Presented as C statistic

<table>
<thead>
<tr>
<th>Marker</th>
<th>14 day Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP</td>
<td>0.512*</td>
</tr>
<tr>
<td>NTproBNP</td>
<td>0.585*</td>
</tr>
<tr>
<td>A type natriuretic peptide</td>
<td>0.589*</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>0.625</td>
</tr>
<tr>
<td>Endothelin</td>
<td>0.682</td>
</tr>
<tr>
<td>Adrenomedullin (ADM)</td>
<td>0.720</td>
</tr>
<tr>
<td>Arginine vasopressin (AVP)</td>
<td>0.773</td>
</tr>
<tr>
<td>AVP + ADM</td>
<td>0.784</td>
</tr>
</tbody>
</table>

* p > 0.05

Peacock WF. Acad EM 2011;18(9):947-958.
Procalcitonin

- **PCT**
  - Prohormone of calcitonin
  - Selectively responds to systemic and septic infections.
  - PCT increases in 2 to 3 hours after septic infection.

- **In BACH**
  - Elevated PCT assoc with 90 day mortality ($p=0.025$)
    - Patients with pneumonia + HF do worse than those with HF alone
PCT in HF

• If increased PCT, twice as likely to receive antibiotics (p=0.0008)

• Top quintile of PCT (0>.205 ng/ml) had worse outcome if did not receive antibiotics (p=0.046)
  – Treat them all??
If very low PCT (<0.051 ng/ml), 1st quintile, have higher mortality if treated with antibiotics (p=0.049)
Summary: ED Dyspnea Rules

1) There are penalties for being wrong

2) There are penalties for being slow
   • You’ve got 4 hours...period.

3) All patients must go somewhere
   • Rules 1 & 2 still apply

4) Don’t bankrupt the house
   • Rules 1, 2 and 3 still apply
Please Submit Your Questions?

You can ask questions at any time during the presentation via the web by clicking your “Ask a Question” button, typing your question in the open area & clicking the “Ask Question” button to submit.
ED Treatment of Acute Decompensated Heart Failure

Phillip D. Levy, MD, MPH, FACEP
Associate Professor
Associate Director of Clinical Research
Wayne State University Department of Emergency Medicine
Presenter Disclosure Information

• Phillip D. Levy, MD, MPH
  – Treatment of Acute Decompensated Heart Failure

• FINANCIAL DISCLOSURE
  – Grant/Research Support: Corthera, Inc., The Medicines Company, Bayer Schering AG
  – Stock Interest: Emergencies in Medicine
  – Speakers Bureau: Society of Chest Pain Centers
Purpose of This Lecture

• To summarize current guideline-based recommendations for the treatment of acute decompensated heart failure

• To discuss emerging concepts in targeted management of acute heart failure
Overview of Acute Therapy

- Ultrafiltration: Aqual natriuresis
- Bilevel or continuous positive airway pressure: Preload reduction
- Nitrates, nitroprusside, dobutamine: Arterial vasodilation
- Dobutamine, dopamine, milrinone: Increased inotropy
- Nitrates, morphine: Venodilation
- Furosemide: Natriuresis
Therapeutic Goals

• Stabilization phase (first 24-48 hours)
  – Improve symptoms
  – Balance hemodynamics
  – Achieve euvolemia
  – Avoid harm!
    • Myocyte injury
    • Renal damage

• Implementation phase (> 48 hours)
  – Initiate life-saving interventions
    • ACE inhibitors, β-blockers, etc

Summary of recommendations for acute HF

- 18 class I
  - Only 1 (NP testing) based on level A evidence
- 4 class IIa
- 1 class IIb
- 1 class III
Patients admitted with HF and with evidence of significant fluid overload should be treated with intravenous loop diuretics. Therapy should begin in the emergency department or outpatient clinic without delay, as early intervention may be associated with better outcomes for patients hospitalized with decompensated HF (32,567,568). (Level of Evidence: B) If patients are already receiving loop diuretic therapy, the initial intravenous dose should equal or exceed their chronic oral daily dose. Urine output and signs and symptoms of congestion should be serially assessed, and diuretic dose should be titrated accordingly to relieve symptoms and to reduce extracellular fluid volume excess. (Level of Evidence: C)
When diuresis is inadequate to relieve congestion, as evidenced by clinical evaluation, the diuretic regimen should be intensified using either:

a. higher doses of loop diuretics;

b. addition of a second diuretic (such as metolazone, spironolactone, or intravenous chlorothiazide); or

c. continuous infusion of a loop diuretic. *(Level of Evidence: C)*

Ultrafiltration is reasonable for patients with refractory congestion not responding to medical therapy *(Level of Evidence: B)*.
In patients with evidence of severely symptomatic fluid overload in the absence of systemic hypotension, vasodilators such as intravenous nitroglycerin, nitroprusside or nesiritide can be beneficial when added to diuretics and/or in those who do not respond to diuretics alone. *(Level of Evidence: C)*
Executive Summary: HFSA 2010 Comprehensive Heart Failure Practice Guideline

HEART FAILURE SOCIETY OF AMERICA

Summary of recommendations for acute HF
– 26 total
• 3 based on level A evidence
• 9 specifically related to acute therapeutic intervention
In the absence of symptomatic hypotension, intravenous nitroglycerin, nitroprusside or nesiritide may be considered as an addition to diuretic therapy for rapid improvement of congestive symptoms in patients admitted with ADHF. (Strength of Evidence = B)

Intravenous vasodilators (nitroglycerin or nitroprusside) and diuretics are recommended for rapid symptom relief in patients with acute pulmonary edema or severe hypertension. (Strength of Evidence = C)
Use of non-invasive positive pressure ventilation may be considered for severely dyspneic patients with clinical evidence of pulmonary edema. (Strength of Evidence = A)
Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

Alasdair Gray, M.D., Steve Goodacre, Ph.D., David E. Newby, M.D., Moyra Masson, M.Sc., Fiona Sampson, M.Sc., and Jon Nicholl, M.Sc., for the 3CPO Trialists*

---

Graph showing the probability of survival over days for patients receiving noninvasive ventilation (CPAP or NIPPV) compared to standard oxygen therapy. The table below shows the number of patients at risk at each time point:

<table>
<thead>
<tr>
<th>Days</th>
<th>CPAP or NIPPV</th>
<th>Standard therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>667</td>
<td>348</td>
</tr>
<tr>
<td>5</td>
<td>609</td>
<td>318</td>
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<tr>
<td>10</td>
<td>591</td>
<td>307</td>
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<td>15</td>
<td>583</td>
<td>301</td>
</tr>
<tr>
<td>20</td>
<td>577</td>
<td>296</td>
</tr>
<tr>
<td>25</td>
<td>570</td>
<td>292</td>
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<td>30</td>
<td>567</td>
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<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard Oxygen Treatment (N = 367)</th>
<th>CPAP (N = 346)</th>
<th>NIPPV (N = 356)</th>
<th>All Patients (N = 1069)</th>
<th>P Value†</th>
</tr>
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<tbody>
<tr>
<td>Initial treatment — % of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>93</td>
<td>88</td>
<td>91</td>
<td>90</td>
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</tr>
<tr>
<td>Diuretics</td>
<td>90</td>
<td>89</td>
<td>89</td>
<td>89</td>
<td>0.89</td>
</tr>
<tr>
<td>Opioids</td>
<td>55</td>
<td>50</td>
<td>49</td>
<td>51</td>
<td>0.31</td>
</tr>
<tr>
<td>Inspired oxygen — liters/min</td>
<td>12±4</td>
<td>12±4</td>
<td>12±4</td>
<td>12±4</td>
<td>0.44</td>
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<tr>
<td>Ventilation pressure — cm of water</td>
<td>—</td>
<td>10±4</td>
<td>Inspiratory 14±5, expiratory 7±3</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Started assigned treatment — no./total no. (%)‡</td>
<td>365/366 (99.7)</td>
<td>337/343 (98.3)</td>
<td>344/354 (97.2)</td>
<td>1046/1063 (98.4)</td>
<td>0.02</td>
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<tr>
<td>Completed assigned treatment — no./total no. (%)¶</td>
<td>298/363 (82.1)</td>
<td>285/340 (83.8)</td>
<td>267/352 (75.9)</td>
<td>850/1055 (80.6)</td>
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<tr>
<td>Changed to new treatment — no.</td>
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<tr>
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<tr>
<td>CPAP</td>
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<td>12</td>
<td></td>
<td></td>
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<tr>
<td>NIPPV</td>
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<td>Standard treatment</td>
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<tr>
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<td>26 (7.1)</td>
<td>10 (2.9)</td>
<td>15 (4.2)</td>
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<tr>
<td>Respiratory distress</td>
<td>31 (8.4)</td>
<td>5 (1.4)</td>
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<td>Other</td>
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<td>24 (6.9)</td>
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</tr>
</tbody>
</table>
# Acute Heart Failure Syndromes: Emergency Department Presentation, Treatment, and Disposition: Current Approaches and Future Aims

A Scientific Statement From the American Heart Association

Neal L. Weintraub, MD, Chair; Sean P. Collins, MD, MSc, Co-Chair; Peter S. Pang, MD; Phillip D. Levy, MD, MPH; Allen S. Anderson, MD; Cynthia Arslanian-Engoren, PhD, RN, FAHA; W. Brian Gibler, MD, FAHA; James K. McCord, MD; Mark B. Parshall, PhD, RN; Gary S. Francis, MD, FAHA; Mihai Gheorghiade, MD; on behalf of the American Heart Association Council on Clinical Cardiology and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation

<table>
<thead>
<tr>
<th></th>
<th>ACS</th>
<th>AHFS</th>
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<tbody>
<tr>
<td>Incidence</td>
<td>1 million/y</td>
<td>1 million/y</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehospital</td>
<td>High</td>
<td>?</td>
</tr>
<tr>
<td>In-hospital</td>
<td>3%–4%</td>
<td>3%–4%</td>
</tr>
<tr>
<td>60–90 d</td>
<td>2%</td>
<td>10%</td>
</tr>
<tr>
<td>Targets of therapy</td>
<td>Clearly defined-thrombosis</td>
<td>Unclear</td>
</tr>
<tr>
<td>Clinical trial results</td>
<td>Beneficial</td>
<td>Minimal, no benefit, harmful</td>
</tr>
<tr>
<td>ACC/AHA Guidelines</td>
<td>Level A</td>
<td>Minimal level A/B, mostly C</td>
</tr>
</tbody>
</table>
Effect of Nesiritide in Patients with Acute Decompensated Heart Failure

Self-Assessed Change in Dyspnea at 6 and 24 Hours

6 Hours
P = 0.03

Placebo (N=3444) Nesiritide (N=3416)

42.1 44.5

28.7 29.5

34.1 32.8

21.7 20.3

27.5 27.5

38.6 37.8

22.1 21.2

Markedly better
Moderately better
Minimally better
No change
Minimally worse
Moderately worse
Markedly worse

P = 0.007

Placebo (N=3398) Nesiritide (N=3371)

66.1 68.2

0 0

9.5 8.6

Effect of Nesiritide in Patients with Acute Decompensated Heart Failure

Death from Any Cause or Rehospitalization for Heart Failure at 30 Days

- Placebo:
  - Death: 10.1%
  - Rehospitalization: 6.1%

- Nesiritide:
  - Death: 9.4%
  - Rehospitalization: 6.0%

P = 0.31
Hazard ratio, 0.93 (95% CI, 0.8–1.08)
# Effect of Nesiritide in Patients with Acute Decompensated Heart Failure

<table>
<thead>
<tr>
<th>Safety end points</th>
<th>Nesiritide (N=3496)</th>
<th>Placebo (N=3511)</th>
<th>Percentage-Point Difference or Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from cardiovascular causes — no./total no. (%)</td>
<td>112/3498 (3.2)</td>
<td>124/3509 (3.5)</td>
<td>-0.3 (-1.2 to 0.5)</td>
<td>0.44</td>
</tr>
<tr>
<td>Sudden death from cardiac causes — no./total no. (%)</td>
<td>19/3324 (0.6)</td>
<td>16/3327 (0.5)</td>
<td>0.1 (-0.3 to 0.4)</td>
<td>0.61</td>
</tr>
<tr>
<td>Hypotension — no./total no. (%)</td>
<td>930/3498 (26.6)</td>
<td>538/3509 (15.3)</td>
<td>11.3 (9.4 to 13.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>748/3498 (21.4)</td>
<td>436/3509 (12.4)</td>
<td>9.0 (7.2 to 10.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>250/3496 (7.2)</td>
<td>141/3509 (4.0)</td>
<td>3.2 (2.1 to 4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;25% decrease in estimated GFR from study-drug initiation — no./total no. (%)</td>
<td>1032/3289 (31.4)</td>
<td>968/3278 (29.5)</td>
<td>1.09 (0.98 to 1.21)</td>
<td>0.11</td>
</tr>
<tr>
<td>Baseline estimated GFR &lt; 60 ml/min/1.73 m²</td>
<td>484/1714 (28.2)</td>
<td>449/1717 (26.2)</td>
<td>1.11 (0.96 to 1.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>Baseline estimated GFR ≥ 60 ml/min/1.73 m²</td>
<td>548/1575 (34.8)</td>
<td>519/1561 (33.2)</td>
<td>1.07 (0.92 to 1.24)</td>
<td>0.38</td>
</tr>
</tbody>
</table>
Other Major Acute HF Trials to Date

(Grouped By Main Inclusion Criteria)

- **Non-hypotensive requiring IV therapy**
  - VMAC \(^1\)
  - PROTECT \(^2\)

- **Inotrope dependent**
  - SURVIVE \(^3\)
  - REVIVE \(^4,5\)

- **Respiratory distress**
  - 3CPO \(^6\)

- **Non-hypotensive with reduced EF**
  - OPTIME-HF \(^7\)
  - EVEREST \(^8,9\)

- **All comers**
  - VERITAS \(^10\)

---

\(^1\) The VMAC Investigators JAMA 2002;287:1531-40.
\(^3\) Mebazza et al. JAMA. 2007;297:1883-91.
\(^5\) Packer M. Presented at the AHA 2005 Scientific Sessions.
\(^6\) Gray et al. NEJM 2008;359:142-51.
Perpetuates the Long-Standing Reliance on Diuresis

<table>
<thead>
<tr>
<th></th>
<th>Q1</th>
<th>Q12</th>
</tr>
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<tbody>
<tr>
<td>Oral medications before hospitalization in patients with LVSD* and history of HF, n (%)</td>
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<td></td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>1737 (66.5)</td>
<td>1739 (62.0)</td>
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<tr>
<td>β-blockers</td>
<td>1421 (51.3)</td>
<td>2206 (68.8)</td>
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<tr>
<td>Aldosterone receptor antagonists</td>
<td>433 (16.8)</td>
<td>502 (20.7)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>2487 (82.0)</td>
<td>2743 (80.7)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>1332 (43.9)</td>
<td>1165 (34.3)</td>
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<tr>
<td>IV medications during hospitalization, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inotrope</td>
<td>1208 (14.7)</td>
<td>763 (7.9)</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>626 (7.6)</td>
<td>350 (3.6)</td>
</tr>
<tr>
<td>Milrinone</td>
<td>340 (4.1)</td>
<td>151 (1.6)</td>
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<tr>
<td>Dopamine</td>
<td>545 (6.6)</td>
<td>404 (4.2)</td>
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<tr>
<td>Nitroglycerin</td>
<td>751 (9.1)</td>
<td>840 (8.7)</td>
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<tr>
<td>Nesiritide</td>
<td>418 (5.1)</td>
<td>2054 (21.4)</td>
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<tr>
<td>Diuretics</td>
<td>7237 (88.0)</td>
<td>8393 (87.3)</td>
</tr>
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</table>
MEDICAL INTELLIGENCE

CURRENT CONCEPTS

Cardiac Decompensation

ALBERTO RAMÍREZ, M.D., AND
WALTER H. ABELMANN, M.D.
The impact of early standard therapy on dyspnoea in patients with acute heart failure: the URGENT-dyspnoea study

Does Everyone Really Need Diuresis?

Diuretics for acute HF can depend on specialty of treating physician

<table>
<thead>
<tr>
<th>Evaluation or management</th>
<th>EM</th>
<th>IM</th>
<th>p</th>
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<tr>
<td>Items included in history taking (n, mean)</td>
<td>4.01</td>
<td>4.64</td>
<td>&lt;0.001</td>
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<td>Items included at physical exam (n, mean)</td>
<td>4.26</td>
<td>4.22</td>
<td>0.65</td>
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<tr>
<td>Use of diuretics (% of cohort)</td>
<td>10.7</td>
<td>80.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Use of nitroglycerin (% of cohort)</td>
<td>17.3</td>
<td>9.5</td>
<td>&lt;0.05</td>
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<tr>
<td>Oxygen (% of cohort)</td>
<td>33.3</td>
<td>36.9</td>
<td>0.284</td>
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<td>BiPAP/intubation (% of cohort)</td>
<td>13.1</td>
<td>10.7</td>
<td>0.306</td>
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Wrong Treatment to the Wrong Patient at the Wrong Time?

Median survival (50% mortality) and 95% confidence limits in patients with HF after each HF hospitalization.

What is Acute Heart Failure?

- **Syndrome** defined by:
  - Inadequate cardiac performance
    - Diminished inotropy
    - Impaired compliance and relaxation
  - Hemodynamic derangements
    - Intrinsic
    - Extrinsic
  - Neurohormonal imbalance
  - Alterations in volume status
The current and future management of acute heart failure syndromes

Peter S. Pang¹,³, Michel Komajda², and Mihai Gheorghiade³*

¹Department of Emergency Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; ²Department of Cardiology, Hopital Pitie-Salpetriere and University Pierre et Marie Curie, Paris, France; and ³Center for Cardiovascular Quality and Outcomes, Department of Medicine, Northwestern University, Feinberg School of Medicine, 645 N Michigan Ave, Suite 1006, Chicago, IL 60611, USA

# EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population

Markku S. Nieminen\(^1\*)\), Dirk Brutsaert\(^2\), Kenneth Dickstein\(^3\), Helmut Drexler\(^4\), Ferenc Follath\(^5\), Veli-Pekka Harjola\(^1\), Matthias Hochadel\(^6\), Michel Komajda\(^7\), Johan Lassus\(^1\), Jose Luis Lopez-Sendon\(^8\), Piotr Ponikowski\(^9\), and Luigi Tavazzi\(^10\) on behalf of the EuroHeart Survey Investigators

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Decomp. HF</th>
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<th>Cardiogenic shock</th>
<th>Hypert. HF</th>
<th>Right HF</th>
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<td>ACS (%)</td>
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<td>71.9</td>
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<td>STEMI</td>
<td>11.1</td>
<td>8.4</td>
<td>17.0</td>
<td>55.4</td>
<td>4.7</td>
<td>6.2</td>
</tr>
<tr>
<td>Non-STEMI</td>
<td>10.0</td>
<td>7.7</td>
<td>22.4</td>
<td>12.9</td>
<td>5.4</td>
<td>5.3</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>9.1</td>
<td>8.6</td>
<td>10.0</td>
<td>3.6</td>
<td>14.3</td>
<td>2.7</td>
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<tr>
<td>Arrhythmia (%)</td>
<td>32.4</td>
<td>32.9</td>
<td>29.3</td>
<td>29.7</td>
<td>34.5</td>
<td>33.9</td>
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<tr>
<td>Atrial</td>
<td>29.4</td>
<td>30.1</td>
<td>25.7</td>
<td>18.8</td>
<td>34.0</td>
<td>33.0</td>
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<tr>
<td>Ventricular</td>
<td>4.1</td>
<td>3.7</td>
<td>5.2</td>
<td>13.0</td>
<td>2.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Valvular cause (%)</td>
<td>26.8</td>
<td>30.2</td>
<td>24.1</td>
<td>17.4</td>
<td>12.6</td>
<td>32.7</td>
</tr>
<tr>
<td>Infection (%)</td>
<td>17.6</td>
<td>18.5</td>
<td>17.1</td>
<td>11.8</td>
<td>15.6</td>
<td>17.1</td>
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<tr>
<td>Non-compliance with therapy</td>
<td>22.2</td>
<td>24.6</td>
<td>16.9</td>
<td>7.9</td>
<td>21.9</td>
<td>18.1</td>
</tr>
</tbody>
</table>

Dyspnea 1,2,3,4

• Primary symptom
  – Common denominator = ↑ LVEDP

• 2 predominant pathways
  – Hypertensive ("vascular failure")
    • Acute fluid shift
  – Normotensive ("congestive failure")
    • Gradual fluid accumulation

• Associated with hypotension in ~ 5%
  – Hypoperfusion

Society of Chest Pain Centers Recommendations for the Evaluation and Management of the Observation Stay Acute Heart Failure Patient

A Report From the Society of Chest Pain Centers Acute Heart Failure Committee

AHF patient with SBP > 160 mm Hg
Immediate sublingual NTG
Topical/IV vasodilator (NTG, NES)
Add IV loop diuretic if volume overloaded

- Good response
- Good urine output
- SBP normalized
- Troponin negative

Admit to ED observation unit
Continued improvement
Consider discharge

No improvement
Consider additional therapy

Worsens

Reassess for clinical improvement
- Poor response
- Poor urine output
- SBP < 90 or > 210 mm Hg
- Troponin elevated
- Respiratory embarrassment

Admit to hospital
Repeat 2 mg boluses of IV NTG

- Non-randomized, open-label
  - 29 intervention and 45 historical controls
  - Mean dose = 6.5 mg (± 3.4) mg
- Primary end-points
  - Intubation in 13.8% (vs. 26.7%)
  - BiPAP in 6.9% (vs. 20.0%)
  - ICU admission in 37.9% (vs. 80.0%)
  - AMI in 17.2% (vs. 28.9%)
  - Hypotension in 1 patient (vs. none)
What About ACE Inhibitors?

- Limited data in acute setting
- Sublingual captopril (25 mg) \(^1,2\)
  - Diminished rate of intubation (?)
  - Improved dyspnea scores at 30 min
  - Early improvements in SVI and CI
- IV enalaprilat \(^3\)
  - Improved hemodynamics with 1 mg infusion
  - No data on bolus dosing

Coming Soon To a Pharmacy Near You?

Clevidipine for Severe Hypertension in Acute Heart Failure: A VELOCITY Trial Analysis

- Trial in acute HF underway
  - PRONTO study

Relaxin for the treatment of patients with acute heart failure (Pre-RELAX-AHF): a multicentre, randomised, placebo-controlled, parallel-group, dose-finding phase IIb study

John R Teerlink, Marco Metra, G Michael Felker, Piotr Ponikowski, Adriaan A Voors, Beth Davison Weatherly, Alon Marmor, Amos Katz, Jacek Grzybowski, Elaine Unermori, Sam L Teichman, Gad Cotter

- Targeted patients SBP $\geq 125$ mmHg and eGFR 30–75 mL/min/1.73 m$^2$

Self Reported Dyspnea Improvement

![Graph showing change in systolic blood pressure and self-reported dyspnea improvement over time.](image)

A Cautionary Word About Morphine!

<table>
<thead>
<tr>
<th>Model</th>
<th>Morphine use vs no morphine OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality rate (%)</td>
<td>13.0 vs 2.4</td>
</tr>
<tr>
<td>Unadjusted (n = 20 782 vs 126 580)</td>
<td>6.08 (5.76 to 6.41)</td>
</tr>
<tr>
<td>Adjusted* (n = 20 251 vs 123 055)</td>
<td>5.27 (4.96 to 5.60)</td>
</tr>
<tr>
<td>Adjusted† (n = 17 637 vs 100 662)</td>
<td>4.84 (4.52 to 5.18)</td>
</tr>
</tbody>
</table>

All p values <0.001.
*Blood urea nitrogen (BUN), systolic BP, age, creatinine, dyspnoea at rest, chronic dialysis, heart rate, inotrope use, vasodilator use.
†Blood urea nitrogen (BUN), systolic BP, age, creatinine, dyspnoea at rest, chronic dialysis, heart rate, inotrope use, vasodilator use, raised troponin.

Society of Chest Pain Centers Recommendations for the Evaluation and Management of the Observation Stay Acute Heart Failure Patient

A Report From the Society of Chest Pain Centers Acute Heart Failure Committee

**AHF patient with SBP 120-160 mm Hg**

- Partial response
- Elevated SBP

- **IV loop diuretic**

- **Reassess for clinical improvement**

- Good response
- Good urine output
- Good renal function
- Normal SBP
- Troponin negative

- Poor response
- Poor urine output
- Poor renal function
- Diuretic resistant
- Low SBP (< 90 mm Hg)
- Troponin elevated

**Add IV vasodilator (NTG, NES)**

- Good response
- Continue to observation unit
  - **Admit to ED observation unit**
  - Consider discharge

- No improvement
  - **Consider additional therapy**
    - Worsens
      - **Admit to hospital**
    - Continued improvement
      - **Consider discharge**
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*

<table>
<thead>
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<th>Bolus Every 12 Hr (N=156)</th>
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<tr>
<td>Age — yr</td>
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</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>115 (74)</td>
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<td>116 (74)</td>
</tr>
<tr>
<td>White race — no. (%)</td>
<td>114 (73)</td>
<td>108 (71)</td>
<td>106 (70)</td>
<td>116 (74)</td>
</tr>
<tr>
<td>Dose of oral furosemide or furosemide equivalent — mg/day</td>
<td>134±53</td>
<td>127±50</td>
<td>131±52</td>
<td>131±51</td>
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<tr>
<td>Ejection fraction (%)</td>
<td>35±18</td>
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<tr>
<td>Hospitalization for heart failure within previous 12 mo — no./total no. (%)</td>
<td>114/155 (74)</td>
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<td>Ischemia as cause of heart failure — no. (%)</td>
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<tr>
<td>Oxygen saturation — %</td>
<td>96±3</td>
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<tr>
<td>Sodium — mg/dl</td>
<td>138±4</td>
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<tr>
<td>BUN — mg/dl</td>
<td>37±21</td>
<td>38±24</td>
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<td>37±22</td>
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<tr>
<td>Creatinine — mg/dl</td>
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<td>6758±6961</td>
</tr>
</tbody>
</table>
Global Assessment
Bolus vs. Continuous

AUC with bolus infusions, 4236±1440
AUC with continuous infusion, 4373±1404
P=0.47

Global Assessment
High vs. Low Dose

AUC with low-dose strategy, 4171±1436
AUC with high-dose strategy, 4430±1401
P=0.06

Death, Rehospitalization, or ED Visit

Hazard ratio with continuous infusion, 1.15 (95% CI, 0.83–1.60)
P=0.41

Hazard ratio with high-dose strategy, 0.83 (95% CI, 0.60–1.16)
P=0.28

## Secondary Endpoints

<table>
<thead>
<tr>
<th>End Point</th>
<th>Bolus Every 12 Hr (N=156)</th>
<th>Continuous Infusion (N=152)</th>
<th>P Value</th>
<th>Low Dose (N=151)</th>
<th>High Dose (N=157)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC for dyspnea at 72 hr</td>
<td>4456±1468</td>
<td>4699±1573</td>
<td>0.36</td>
<td>4478±1550</td>
<td>4668±1496</td>
<td>0.04</td>
</tr>
<tr>
<td>Freedom from congestion at 72 hr — no./total no. (%)</td>
<td>22/153 (14)</td>
<td>22/144 (15)</td>
<td>0.78</td>
<td>16/143 (11)</td>
<td>28/154 (18)</td>
<td>0.09</td>
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<tr>
<td>Change in weight at 72 hr — lb</td>
<td>−6.8±7.8</td>
<td>−8.1±10.3</td>
<td>0.20</td>
<td>−6.1±9.5</td>
<td>−8.7±8.5</td>
<td>0.01</td>
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<tr>
<td>Net fluid loss at 72 hr — ml</td>
<td>4237±3208</td>
<td>4249±3104</td>
<td>0.89</td>
<td>3575±2635</td>
<td>4899±3479</td>
<td>0.001</td>
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<tr>
<td>Change in NT-proBNP at 72 hr — pg/ml</td>
<td>−1316±4364</td>
<td>−1773±3828</td>
<td>0.44</td>
<td>−1194±4094</td>
<td>−1882±4105</td>
<td>0.06</td>
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<tr>
<td>Worsening or persistent heart failure — no./total no. (%)</td>
<td>38/154 (25)</td>
<td>34/145 (23)</td>
<td>0.78</td>
<td>38/145 (26)</td>
<td>34/154 (22)</td>
<td>0.40</td>
</tr>
<tr>
<td>Treatment failure — no./total no. (%) †</td>
<td>59/155 (38)</td>
<td>57/147 (39)</td>
<td>0.88</td>
<td>54/147 (37)</td>
<td>62/155 (40)</td>
<td>0.56</td>
</tr>
<tr>
<td>Increase in creatinine of &gt;0.3 mg/dl within 72 hr — no./total no. (%)</td>
<td>27/155 (17)</td>
<td>28/146 (19)</td>
<td>0.64</td>
<td>20/147 (14)</td>
<td>35/154 (23)</td>
<td>0.04</td>
</tr>
<tr>
<td>Length of stay in hospital — days</td>
<td></td>
<td></td>
<td>0.97</td>
<td></td>
<td></td>
<td>0.55</td>
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<tr>
<td>Median</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>3–9</td>
<td>3–8</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Alive and out of hospital — days</td>
<td></td>
<td></td>
<td>0.36</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Median</td>
<td>51</td>
<td>51</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Interquartile range</td>
<td>42–55</td>
<td>38–55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Worsening Renal Function Persistent in Both Groups

Relation of Worsened Renal Function During Hospitalization for Heart Failure to Long-Term Outcomes and Rehospitalization

David E. Lanfear, MD, MS\textsuperscript{a,b,*}, Edward L. Peterson, PhD\textsuperscript{c}, Janis Campbell, RN\textsuperscript{b}, Hemant Phatak, PhD\textsuperscript{d}, David Wu, PhD\textsuperscript{d}, Karen Wells, BS\textsuperscript{c}, John A. Spertus, MD, MPH\textsuperscript{e}, and L. Keoki Williams, MD, MPH\textsuperscript{b}

\[ p = 0.025 \]
Alternatives to Diuresis?

- Vasopressin antagonists
  - Conivaptan
    - Dual V1/V2 receptor antagonist
  - Tolvaptan
    - V2 receptor antagonist >> V1
  - Lixivaptan
    - V2 receptor antagonist >>> V1

- Adenosine receptor antagonists

- Ultrafiltration
Ultrafiltration

- Veno-venous hemoconcentration
  - Extract up to 500 cc/hr
- Maintains hemodynamic stability and electrolyte balance
- Possible in ED observation unit
- Exact indications not clear

Ultrafiltration vs IV Diuretics for Pts Hospitalized with ADHF

Hypotensive Pathway

Low cardiac output/cardiacogenic shock
Evidence of decreased perfusion
Altered mental status
Cool extremities
SBP < 90 mm Hg

Consider fluid bolus

IV inotrope
(milrinone, dobutamine, dopamine)
- consider invasive hemodynamic monitoring

Admit ICU

Assess for response to therapy

IV vasodilator*
(NTG, NES, NTP)
IV diuretic

Pulmonary congestion
Poor urine output

If good response after inotrope and IV vasodilator

Consider transfer to in-hospital telemetry floor

A Search for Novel Inotropes

A Search for Novel Inotropes

Bottom Line: Acute HF is a Heterogeneous Condition

<table>
<thead>
<tr>
<th></th>
<th>ADHERE (N = 107,920)</th>
<th>EHFS (N = 11,327)</th>
<th>OPTIMIZE-HF (N = 34,059)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, (yr)</td>
<td>75</td>
<td>71</td>
<td>73</td>
</tr>
<tr>
<td>Women (%)</td>
<td>52</td>
<td>47</td>
<td>52</td>
</tr>
<tr>
<td>Prior HF (%)</td>
<td>75</td>
<td>65</td>
<td>87</td>
</tr>
<tr>
<td>LVEF 0.40 (%)</td>
<td>59</td>
<td>46</td>
<td>52</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>57</td>
<td>68</td>
<td>50</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>72</td>
<td>53</td>
<td>71</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>44</td>
<td>27</td>
<td>42</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>31</td>
<td>43</td>
<td>31</td>
</tr>
<tr>
<td>Renal insufficiency (%)</td>
<td>30</td>
<td>18</td>
<td>NA</td>
</tr>
</tbody>
</table>

Gheorghiade et al. Am J Cardiol 2005;96(suppl):11G-17G.
A Proposed Model for Initial Assessment and Management of Acute Heart Failure Syndromes

Mihai Gheorghiade, MD
Eugene Braunwald, MD

Clinical severity

De novo or chronic heart failure

Comorbidities

Precipitants

Blood pressure

Heart rate and rhythm
AHFS phenotype defined (approximate incidence)

- Profoundly hypertensive (~25%)
  - Primary: afterload reduction with vasodilator therapy
  - Secondary: diuresis if associated volume overload

- Normal to moderately hypertensive (~50%)
  - Primary: volume reduction with diuretic therapy with possible ultrafiltration
  - Secondary: blood pressure reduction

- Hypotensive (5-10%)
  - Primary: output and perfusion increase with inotropes and vasopressors; fluids if overdiuresed
  - Secondary: mechanical ventricular assist devices

- Cardiogenic Shock (~1%)
  - Primary: improve cardiac function with inotropes and possibly mechanical ventricular assist devices
  - Secondary: vasopressors or vasodilators (if increased vascular resistance) to enhance perfusion

- Acute coronary syndrome* (?)
  - Primary: coronary artery reperfusion
  - Secondary: anti-platelet and anti-coagulation medications; nitrates

- Arrhythmogenic* (?)
  - Primary: rate or rhythm control with medications as per ACLS guidelines; cardioversion or pacing if unstable
  - Secondary: diuresis and blood pressure reduction as needed

- Right heart failure* (?)
  - Primary: reperfusion if RV infarct; anticoagulation (and possibly lytics) if pulmonary embolism; pulmonary artery pressure reduction; diuresis
  - Secondary: albuterol and ipratropium nebulizers; surgical intervention
Take Home Message

- ED management of acute HF suffers from a lack of substantive evidence
- Diuresis remains the mainstay of existing treatment guidelines and is appropriate first-line therapy for most
- Afterload reduction, often seen as an adjunct, is especially beneficial for patients with “vascular failure”