Acute Heart Failure: Money, Myths, & ‘True’ Facts

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Disclosures

• **Consultant and/or honoraria** from: Cardioxyl, Janssen, Medtronic, Novartis, Relypsa, Roche Diagnostics, Trevena, scPharmaceuticals

• Will NOT discuss anything off-label

• **Research Support:** NIH/NCATS training grant
• The evidence...
• Why?
• An approach to management
• A contrarian view
• Admissions & Re-admissions
MEDICAL INTELLIGENCE

CURRENT CONCEPTS
Cardiac Decompensation

Alberto Ramírez, M.D., and Walter H. Abelmann, M.D.
## Current Early AHF Therapeutics

### 2015
- Sit the patient upright
- Oxygen
- Positive pressure ventilation
- Morphine
- Diuretics
- Nitrates
- Digoxin
- IABP
- Inotropes (？Levosimendan)
- **Nesiritide**

### 1974
- Sit the patient upright
- Oxygen
- Positive pressure ventilation
- Morphine
- Diuretics
- Nitrates
- Digoxin
- IABP
- **Phlebotomy**
- **Rotating Tourniquets**

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IABP=intra-aortic balloon pump

Ramirez, Abelmann NEJM 1974
AHF Epidemiology

• ~5.5 million persons currently diagnosed with HF, with 840,000 new diagnoses each year

• 1,000,000 admissions/year with primary diagnosis of HF

• 3.6 million primary or secondary diagnoses of HF

• > $20 billion USD/year in the US

• Most common cause of admission & re-admission for Medicare beneficiaries

Yancy et.al. J Am Coll Cardiol. 2013
Mozaffarian et.al. JACC. 2014
Jencks et.al. NEJM, 2009
Demographic and Clinical Characteristics of AHF Patients

<table>
<thead>
<tr>
<th>Median age (years)</th>
<th>75</th>
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<tbody>
<tr>
<td>Women</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Hx of CAD</td>
<td>60%</td>
</tr>
<tr>
<td>Hx of Hypertension</td>
<td>70%</td>
</tr>
<tr>
<td>Hx of Diabetes</td>
<td>40%</td>
</tr>
<tr>
<td>Hx of Atrial Fibrillation</td>
<td>30%</td>
</tr>
<tr>
<td>Renal abnormalities</td>
<td>30%</td>
</tr>
<tr>
<td>SBP &gt;140 mm Hg</td>
<td>50%</td>
</tr>
<tr>
<td>SBP 90-140 mm Hg</td>
<td>45%</td>
</tr>
<tr>
<td>SBP &lt;90 mm Hg</td>
<td>5%</td>
</tr>
</tbody>
</table>

Cleland JGF et al. *Eur Heart J.* 2003; 24: 442;
33%
All-Cause Mortality After Each Subsequent Hospitalization for HF

Heart Failure
- 1st admission (n = 14,374)
- 2nd admission (n = 3,358)
- 3rd admission (n = 1,123)
- 4th admission (n = 417)

1st hospitalization: 30-day mortality = 12%; 1-year mortality = 34%

Inpatient Unit / Obs Status: 20%
Observation Unit: <1%
Inpatient Unit / Obs Status: 1%

Emergency Department: 78%

n=187,565

The ADHERE Registry
Initial Approach

1. Treat the life-threat
2. Establish the diagnosis
3. Determine the clinical profile
4. Identify and manage the precipitant
5. Alleviate symptoms
6. Organ protection
7. Risk stratification/disposition

Gheorghiade & Pang, JACC 2009
Diagnosis

- BNP vs. NT-proBNP
  - < 300 ng/mL - HF unlikely
  - Age < 50 years, NT-proBNP >450 pg/mL - HF likely
  - Age 50-75 years, NT-proBNP >900 pg/mL – HF likely
  - Age >75 years, NT-proBNP >1800 – HF likely

- Comets...
Recently, lung ultrasound has emerged as a new sonographic technique to evaluate many pulmonary conditions.

B-lines
(Ultrasound Lung Comets)
CLINICAL PROFILE
IV Therapies

ADHERE, EHFS-II, EUROObservational

Yancy et.al. JACC 2006, Nieminen et.al. EHJ 2006, Maggioni et.al. EJHF 2010
Acute Heart Failure Profiles

- Systemic Volume Overload
- Low-Output Failure
- Hypertensive HF “re-distribution”
Figure 1 Initial Approach to AHF Management Algorithm

LOW SBP

Hypotensive AHF Pathway

Clinical suspicion of AHF?

Severe respiratory distress?

Cardiogenic shock or symptomatic hypotension?

Perform focused history and exam

Signs of hypoperfusion or altered mental status?

AHF likely?

Systolic Blood Pressure?

NORMAL SBP

Normotensive AHF Pathway (SBP 100-140mmHg)

HIGH SBP

Hypertensive AHF Pathway (SBP > 140mmHg)

Options:
- NIV
- ETT
- If hypertensive, consider vasodilation

Initial Work-up
- ECG
- CXR
- CBC, Chem-7
- Consider NP, Troponin, other biomarkers

Consider alternative diagnosis

no
Figure 2: Algorithm for the Initial Treatment of Hypertensive (SBP > 140mmHg) AHF

1. SBP > 140mmHg?
   - Immediate sublingual NTG
   - IV loop diuretic

2. RE-ASSESS:
   - Is patient improving?
   - SBP still high (SBP > 140mmHg)?
   - Good urine output?
   - Consider IV Vasodilator*

3. Consider NIV
   - if dyspneic, tachypneic, increased work of breathing

4. Consider transition of therapy:
   - from NIV to FM or NC
   - IV vasodilator to topical NTG

   Patient improved.

   yes

   no
Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema

Gad Cotter, Einat Metzkor, Edo Kaluski, Zwi Faigenberg, Rami Miller, Avi Simovitz, Ori Shaham, Doron Marghitay, Maya Koren, Alex Blatt, Yaron Moshkovitz, Ronit Zaidenstein, Ahuva Golik

• IV ISDN 3 mg q 5 min (n = 52) vs. IV furosemide (N = 52) 80 mg q 15 min
  – Mean dose ISDN = 11.4 (± 6.8) mg
  – Mean dose furosemide = 200 (± 65) mg

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Group A (n=52)</th>
<th>Group B (n=52)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Required mechanical ventilation</td>
<td>7 (13%)</td>
<td>21 (40%)</td>
<td>0.0041</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>9 (17%)</td>
<td>19 (37%)</td>
<td>0.047</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>13 (25%)</td>
<td>24 (46%)</td>
<td>0.041</td>
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</tbody>
</table>

Nitrates in AHF

Patients with AHF (LVEF = 42%-43%)

- Predominant Nitrate (n=52)
- Predominant Furosemide (n=52)

Event Rate, %

<table>
<thead>
<tr>
<th>Event</th>
<th>Predominant Nitrate</th>
<th>Predominant Furosemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death in Hospital</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(within 12 hours)</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(within 24 hours)</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Any AE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P<.05

Figure 3: Algorithm for the Initial Treatment of Normotensive AHF (SBP of 100 to 140mmHg)

SBP 100 to 140mmHg

- Start IV loop diuretics

Consider Vasodilators if SBP > 120mmHg (SL, Topical, IV)

REASSESS!
- Is patient improving?
- Improved vital signs?
- Good urine output?

Consider NIV if dyspneic, tachypneic, increased work of breathing

Were adequate doses of IV diuretics given?
Alternative diagnosis?
Untreated precipitant?

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*

Acute Heart Failure (1 symptom AND 1 sign)
Home diuretics dose ≥ 80 mg and ≤240 mg furosemide <24 hours after admission

2x2 factorial randomization

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

48 hours

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

Inclusion Criteria

• ≥18 years old
• Prior clinical diagnosis of heart failure with daily home use of oral loop diuretic for at least one month
• Daily oral dose of furosemide ≥ 80 mg and ≤240 mg (or equivalent)
• Identified within 24 hours of hospital admission
• Heart failure defined by at least 1 symptom (dyspnea, orthopnea, or edema) AND 1 sign (rales on auscultation, peripheral edema, ascites, pulmonary vascular congestion on chest radiography)
• Anticipated need for IV loop diuretics for at least 48 hours
• Willingness to provide informed consent
Global Assessment and Change in Cr at 72 hours

• NO difference between bolus or continuous
• NO difference between high or low dose

• BUT...significantly more diuresis, weight loss, and relief from dyspnea, and trend towards better symptom improvement (p=0.06)
• No differences in 60 day outcomes
Low BP
Real? Or Baseline?

Low cardiac output/Cardiogenic Shock
Evidence of decreased perfusion (i.e. altered mental status, cool extremities)
Low SBP (< 100mmHg)

Cautious fluid bolus

IV Inotrope (Dobutamine, Dopamine, Milrinone)
(Consider vasopressor)

RE-ASSESS!
- Is patient improving?
- Vital signs improving?
- Good urine output?

CONFIRM: is this really worsening HF vs. baseline severe advanced HF?

Still congested?
- Consider IV vasodilator
- Consider IV diuretic

If failure to improve, unable to add additional therapy, may need IABP
The 5 Things to Remember

1. Vasopressors
2. Inotropes
3. Ventilatory Support
4. Revascularization / Reperfusion
5. Repair of Mechanical complications
Dobutamine

• 2-20 ucg/kg/min
• (be wary of potential hypotension)
FIRST Trial

Dobutamine

No dobutamine

P <0.0001

O’Connor et.al., AHJ 1999
GRIM REAPER, INC.

Taking Care of Business
Since the Dawn of Man

motifake.com
Another Approach

1. Pump (weak or stiff)
2. Volume (overload or re-distribution)
3. Tone (vascular)
4. Electrical (rate & rhythm)
5. Plumbing (coronaries – primary ischemia)
6. Valvular
7. Extra-cardiac
Chief complaint of SOB or CP

Vital signs
HR, BP, RR, O₂ saturation, temperature

ABC’s
1. Airway
2. Breathing
3. Circulation

Immediate resuscitation (have team members begin IV, place on O₂ and telemonitor)
1. Control the airway (consider intubation if needed)
2. Ensure adequate oxygenation/ventilation (consider NIV)
3. Ensure adequate perfusion (i.e. pressors, volume, defibrillation)

Consider immediate life threats
1. Shock (cardiogenic, hemorrhagic, septic)
2. Significant hypoxia/hypercarbia (flash pulmonary edema, PE, COPD/asthma, pneumonia)
3. ACS
4. Unstable arrhythmias (bradycardia and tachycardia)
5. Aortic dissection/aneurysmal rupture
6. Cardiac tamponade
7. Massive/submassive PE
8. Tension PTX

Diagnostic work up begins in parallel (same time)
1. EKG/rhythm strip
2. CXR
3. Bedside ECHO/US (consider)
4. Lab work/POC testing

Clinically stable to pursue further diagnostic evaluation and therapeutic management? (ED management occurs in parallel, not in series as is traditionally taught in medical school)

AHF is first or high on differential?

Yes

Precipitants of AHF? (this may still include potential life threats)

Determine initial phenotype

Begin phenotype/precipitant driven care

Re-assess patient frequently and treat according to initial impression/diagnosis

Consider alternative diagnoses (perhaps initial diagnostic impression was incorrect?) and reassess

Other diagnosis more likely or confirmed (i.e. ACS, PE, pneumonia) Manage appropriately

Continue resuscitation and diagnostic evaluation

NOT controlled

Intact or stable

Intact or stable

History and physical exam

EKG (repeat when clinically indicated)

CXR

Consider bedside ECHO/US

Lab work/POC testing

ACS=acute coronary syndrome; AHF=acute heart failure; BP=blood pressure; COPD=chronic obstructive pulmonary disease; CP=cor-pulmonale; CXR=chest X-ray; ECHO=echocardiogram; ED=Emergency Department; EKG=electrocardiogram; HR=heart rate; IV=intravenous; NIV=non-invasive ventilation; PE=pulmonary embolism; POC=point-of-care; PTX=pneumothorax; RR=respiratory rate; SOB=shortness of breath; US=ultrasound

Template created by the AHF Academy
Novel Therapy:

• Corvilinex

• Given cautious Class IIb, LOE B in guidelines

• Based on multiple retrospective and small prospective studies (Total n = < 500)
Would you use the drug?
ACE I (n=92)

- RCT of 58 patients
  - Improvement in APEX score
  - 2 vs 5 intubations in treatment group (NS)
  - 6 vs 9 had MI in treatment group
  - 31% of patients had AMI
- Prospective cohort of 14 AHF patients (of 65 with HTN), 9 of whom ‘improve’
  - NO long term data
- RCT of 20 patients with APE
  - Reductions in PCWP, improvements in RBF, no adverse short term effects
  - NO long term data
Evidence Based Medicine?

Which Acute Heart Failure pharmacologic therapy has the best evidence?

(n= 7141 patients in prospective RCT)

- Hundreds more patients studied in hemodynamic trials
Show me the money
Disposition Reality: AHF

90%

80%
What would it take to discharge an ED patient with AHF?
Early Deaths in Patients With Heart Failure Discharged From the Emergency Department

A Population-Based Analysis

Douglas S. Lee, MD, PhD; Michael J. Schull, MD, MSc; David A. Alter, MD, PhD; Peter C. Austin, PhD; Andreas Laupacis, MD, MSc; Alice Chong, BSc.
Where’s the evidence?
Hospital Strategies to Reduce Heart Failure Readmissions

Where Is the Evidence?*

Javed Butler, MD, MPH, Andreas Kalogeropoulos, MD, PhD

Atlanta, Georgia
**Patients with significant comorbidities that would prevent discharge from ED or within 24 hours should be admitted (e.g. uncontrolled DM, superimposed pneumonia)

BNP in ED

- **BNP < 400 pg/ml**
  - Is it HF?
    - No
    - Treat other condition
      - Yes
      - BUN > 43, SBP < 115, Cr > 2.8, O2 Sat < 93%, Troponin release
        - No
          - Recent admission
          - Yes*
          - Observation Unit (OU)**
            - No
              - 7 days follow-up
              - Back to baseline?
                - Yes
                  - If yes -> Discharge**
                - No
                  - No
                    - Yes*
        - Yes
          - Regular Care Ward
  - Yes
    - BUN > 43, SBP < 115, Cr > 2.8, O2 Sat < 93%, Troponin release
      - No
        - Recent admission
        - Yes*
        - Observation Unit (OU)**
          - No
            - 7 days follow-up
            - Back to baseline?
              - Yes
                - If yes -> Discharge**
              - No
                - No
                  - No
                    - Yes
                      - Consider ICU
          - Yes*
        - Regular Care Ward
  - BNP > 1000 pg/ml
    - Admit*
      - BUN > 43, SBP < 115, Cr > 2.8, O2 Sat < 93%
        - No
          - Observatin Unit (OU)**
          - Yes
          - Observation Unit (OU)**
        - Yes
          - Observation Unit (OU)**

Reducing readmission starts in ED
1. Admission BNP to clarify Dx
2. Discharge of low risk patients
3. Risk Stratification for appropriate treatment
4. Appropriate utilization of OU
5. Targeted early visit post ED and OU discharge

*Consider discharge/OU pathway if minimal change (<25%) in BNP level from discharge
Observation Status
1. Flexibility
2. Efficient
3. Value
Observation: *Purpose*

- Simultaneously treat and risk-stratify
  - improve diagnostic accuracy
  - improve treatment outcomes
  - decrease costs
  - improve patient satisfaction

- *(Does the patient need to be admitted?)*
Keys to Success

• Patient selection (70% discharge proportion)
• Protocol and adherence
• Discharge criteria
• Patient education
• Interdisciplinary
• Data

Ross M et.al. Critical Pathways in Cardiology, 2012
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

Writing committee

Co-chairs: W. FRANK PEACOCK¹ & GREGG C. FONAROW²

Subcommittee chairs

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Risk stratification: SEAN P. COLLINS⁴ & MIHAI GHEORGHIADE⁵,  
Treatment: J. DOUGLAS KIRK⁶ & GERAΣIMOS FILIPPATOS⁷,  
Discharge criteria: DEBORAH B. DIERCKS⁶,  
Patient education: ROBIN J. TRUPP⁸, BRIAN HIESTAND⁹ & EZRA A. AMSTERDAM¹⁰

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Inclusion

1. Previous history of HF
2. Acceptable vital signs (SBP >100mmHg, RR < 32, HR < 130, O2 Sat > 90%)
3. High likelihood of improvement to baseline within 24 hours
4. No acute comorbidities

Discharge Criteria

1. Subjective improvement
2. Acceptable vital signs (O2sat >94%  RR < 20, HR < 100, SBP > 100mmHg)
3. Negative serial EKG, markers, good electrolyte pattern, acceptable ECHO if done
4. Adequate diuresis (> 1L, decrease in weight, decrease in JVD)
5. CHF discharge checklist (GDMT, HF education, follow up)
• 327 patients, 239 (73%) were discharged from OU

<table>
<thead>
<tr>
<th>(mean +/- SD) or median (IQR)</th>
<th>Discharged from OU</th>
<th>Admitted from OU</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.4 (+/-15)</td>
<td>60.2 (+/- 13)</td>
<td>0.661</td>
</tr>
<tr>
<td>BNP</td>
<td>708 (254-1683)</td>
<td>1063 (552-2067)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cr</td>
<td>1.2 (13-23)</td>
<td>1.3 (1.1-1.6)</td>
<td>0.056</td>
</tr>
<tr>
<td>EF</td>
<td>35 (20-55)</td>
<td>22.5 (15-43)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Schraeger et.al. AEM 2013
<table>
<thead>
<tr>
<th></th>
<th>Discharged from OU</th>
<th>Admitted from OU</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total 30 day Inpatient time (days)</td>
<td>1.7 (0.0-5.1)</td>
<td>3.5 (2.3-5.8)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>30 day Readmissions</td>
<td>24 (10.0%)</td>
<td>11 (12.5%)</td>
<td>0.5237</td>
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<tr>
<td>90 day Readmissions</td>
<td>52 (21.8%)</td>
<td>24 (27.3%)</td>
<td>0.2950</td>
</tr>
</tbody>
</table>

Schraeger et al. AEM 2013
Sent in for “Protocol”
"Insanity: Doing the same thing over and over again and expecting different results."

- Albert Einstein
The Future
Cardiac Troponin and Outcome in Acute Heart Failure

W. Frank Peacock IV, M.D., Teresa De Marco, M.D., Gregg C. Fonarow, M.D., Deborah Diercks, M.D., Janet Wynne, M.S., Fred S. Apple, Ph.D., and Alan H.B. Wu, for the ADHERE Investigators
AHF Contributes to the Progression of HF

**Goal:** prevent myocardial and renal damage and implement “life-saving therapies”

**Hypothesis:** with each hospitalization there is myocardial and/or renal damage
Day 60 Cardiovascular (CV)/Renal Hospitalization or Death

34% positive baseline troponin

21% develop positive troponin by day 7

n=288

Days from Randomization

Estimate Cumulative Risk (%)

All Negative
Converter
Positive Baseline

O'Connor C M et al. Circ Heart Fail 2011;4:724–32
Pre-specified Plasma Biomarkers

**Troponin T**
(Geometric mean change)

**NT-pro-BNP**
(Geometric mean change)

**Cystatin C**
(Geometric mean change)

- 93% of patients had an elevated hsTnT at baseline
- Prevention of cardiomyocyte loss
- Alleviation of cardiac wall stress and decongestion
- Prevention of renal function loss

These changes have shown to be predictive of outcome value in AHF

180 Day Cardiovascular Death

HR 0.63 (CI 0.41, 0.96); $P=0.028$

<table>
<thead>
<tr>
<th></th>
<th>ACS</th>
<th>AHF</th>
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<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>1 million/yr</td>
<td>1 million/yr</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pre-hospital</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 day</td>
<td>2%</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Targets of Therapy</strong></td>
<td>Clearly defined thrombosis</td>
<td>Unclear</td>
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<tr>
<td><strong>Clinical Trial Results</strong></td>
<td>Beneficial</td>
<td>Minimal, no benefit, harmful</td>
</tr>
<tr>
<td><strong>ACCF/AHA Guidelines</strong></td>
<td>Level A</td>
<td>Minimal level A/B, mostly C</td>
</tr>
</tbody>
</table>

Weintraub et.al. Circulation 2010