Decongestion in heart failure with normal blood pressure

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Disclosures

• Scholarship from the Hellenic Society of Cardiology, Athens, Greece

• Scholarship from the Kaufman Center of Heart Failure, Cleveland Clinic, Cleveland, USA

• Scholarship from Medtronic (Advanced Heart Failure Fellows Program), USA
Case Presentation

• 68 year old African-American female
• Presented in the ED with NYHA IV symptomatology. Previously she could walk almost half a block before becoming too short of breath to continue, however now she becomes short of breath even at rest
• Increase in lower extremity edema, despite continuing to take her furosemide 40mg PO BID
• Increase in orthopnea from 2 pillow to 45 degree orthopnea
• Mental confusion over the last week
• No chest pain
• 3.5 kg weight gain over the last 1-2 weeks
Medical History

- Non Ischemic Cardiomyopathy (Recent coronary angiography: normal) - HFrEF (Ejection Fraction 15%)
- LBBB (left bundle branch block)
- CRT-D (non-responder-QRS 190 ms)
- Pulmonary sarcoidosis (lung biopsy in 1973-untreated)
- Diabetes mellitus type 2 (15-20 years)
- Paroxysmal atrial fibrillation (5 years)
- Peripheral artery disease (fusiform dilation of the innominate artery -1.9cm at the root- and right popliteal aneurysm -stent September 2016-)
- She reports 2 recent hospitalization for decompensated heart failure (<6 months)
- Social: lives alone (divorced, 3 children), non-smoker
Medications

• metoprolol 100 mg (1/4 x 2)
• sacubitril-valsartan (49-51) mg x2
• spironolactone 25 mg x 1
• furosemide 40 mg x 2
• hydralazine 10 mg x 2
• isosorbide dinitrate 5 mg x2
• apixaban 5 mg x 2
• aspirin 81 mg x 1
• amiodarone 200 mg x 1
• pantoprazole 40 mg x 1
• metformin 500 mg x 2
Clinical examination

- tachypnea and tachycardia
- jugular venous distention
- “cold and wet”
- lower limb edema
- S3
- Rales
- BP: 100/80 mmHg
- SPO2: 88%
Hypoperfusion is *not synonymous* with hypotension, but often hypoperfusion is accompanied by hypotension.
Systolic Blood Pressure at Admission, Clinical Characteristics, and Outcomes in Patients Hospitalized With Acute Heart Failure

Mihai Gheorghida, MD, William T. Abraham, MD; Nancy M. Albert, RN, PhD; et al

Abstract

Context The association between systolic blood pressure (SBP) at admission, clinical characteristics, and outcomes in patients hospitalized for heart failure who have reduced or relatively preserved systolic function has not been well studied.

Objective To evaluate the relationship between SBP at admission, clinical profile, and outcomes in patients hospitalized for acute heart failure.

Design, Setting, and Patients Cohort study using data from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry and performance improvement program for patients hospitalized with heart failure at 324 US hospitals between March 2003 and December 2004. Patients were divided into quartiles by SBP at hospital admission (<120, 120-139, 140-161, and >161 mm Hg). In-hospital outcomes were based on 48,502 patients aged 18 years or older with heart failure. Of the 41,267 patients with left ventricular function assessed, 21,146 (51%) had preserved (left ventricular fraction >0.50) ventricular function. Postdischarge outcomes were based on a prespecified subgroup (n = 3791, 10% of patients) with follow-up data assessed between 90 and 96 days.

Main Outcome Measures In-hospital and postdischarge mortality.

Results Patients with higher SBP were more likely to be female and black and to have preserved systolic function. Fifty percent of the patients had SBP higher than 140 mm Hg at admission. Patients with lower SBP at admission had higher in-hospital and postdischarge mortality rates. Higher SBP at admission was associated with lower in-hospital mortality rates (1.4%, 1.0%, 0.8%, 0.6%, and 0.4%, respectively, for SBP <120, 120-139, 140-161, and >161 mm Hg). Postdischarge mortality rates in the follow-up cohort of SBP at admission of 140-161, 161-179, and >180 mm Hg were 1.8%, 1.6%, and 1.4%, respectively, for SBP <120 mm Hg (P = .001 for all comparisons). Postdischarge mortality rates in the follow-up cohort of SBP at admission of 140-161, 161-179, and >180 mm Hg were 1.8%, 1.6%, and 1.4%, respectively, for SBP <120 mm Hg (P = .001 for all comparisons).

Conclusions Systolic hypertension is common in patients hospitalized for heart failure. Systolic blood pressure is an independent predictor of mortality and mortality in patients with heart failure with either reduced or relatively preserved systolic function. Low SBP (<120 mm Hg) at hospital admission identifies patients who have a poor prognosis despite medical therapy. These findings may have important implications because characteristics and outcomes differ greatly among patients with heart failure with varying SBP.
Laboratory values

- NT pro-BNP: 6,449
- Hb: 11.3 mg/dL
- Ht: 37.3%
- Glu: 117 mg/dL
- BUN: 42 mg/dL
- Crea: 1.48 mg/dL
- eGFR: 42 mL/min/1.73 m²
- ALT: 29 U/L
- AST: 30 U/L
- Na: 141 mEq/L
- K: 4.6 mEq/L
- Troponin T: <0.01
- TSH: 3.35
- Lactate: 1.4
Echocardiography
Echocardiography
Intensive Care Unit

- Drip Lasix (0.3 mg/kg/h)
- Nitroprusside (10-200mcg/min)
## Diuretics

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms. It is recommended to regularly monitor symptoms, urine output, renal function and electrolytes during use of i.v. diuretics.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics the initial recommended dose should be 20–40 mg i.v. furosemide (or equivalent); for those on chronic diuretic therapy, initial i.v. dose should be at least equivalent to oral dose.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>It is recommended to give diuretics either as intermittent boluses or as a continuous infusion, and the dose and duration should be adjusted according to patients’ symptoms and clinical status.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Combination of loop diuretic with either thiazide-type diuretic or spironolactone may be considered in patients with resistant oedema or insufficient symptomatic response.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

DOSE study

Time-to-Furosemide Treatment and Mortality in Patients Hospitalized With Acute Heart Failure

ABSTRACT

BACKGROUND Acute heart failure (AHF) is a life-threatening disease requiring urgent treatment, including a recommendation for immediate institution of loop diuretics.

OBJECTIVES The authors prospectively evaluated the association between time-to-diuretic treatment and clinical outcome.

METHODS REALITY-AHF (Registry Focused on Very Early Presentation and Treatment in Emergency Department of Acute Heart Failure) was a prospective, multicenter, observational cohort study that primarily aimed to assess the association between time to loop diuretic treatment and clinical outcome in patients with AHF admitted through the emergency department (ED). Door-to-furosemide (DOF) time was defined as the time from patient arrival at the ED to the first intravenous furosemide injection. Patients with a DOF time <60 min were pre-defined as the early treatment group. Primary outcome was all-cause in-hospital mortality.

RESULTS Among 1,291 AHF patients treated with intravenous furosemide within 24 h of ED arrival, the median DOF time was 90 min (IQR: 36 to 186 min), and 481 patients (37.3%) were categorized as the early treatment group. These patients were more likely to arrive by ambulance and had more signs of congestion compared with the nonearly treatment group. In-hospital mortality was significantly lower in the early treatment group (2.3% vs. 6.0% in the nonearly treatment group; p = 0.002). In multivariate analysis, earlier treatment remained significantly associated with lower in-hospital mortality (odds ratio: 0.39; 95% confidence interval: 0.20 to 0.76; p = 0.006).

CONCLUSIONS In this prospective multicenter, observational cohort study of patients presenting at the ED for AHF, early treatment with intravenous loop diuretics was associated with lower in-hospital mortality. (Registry focused on very early presentation and treatment in emergency department of acute heart failure syndrome; UMIN000014105) (J Am Coll Cardiol 2017;69:3042-51) © 2017 by the American College of Cardiology Foundation.
### Vasodilators - Inotropes

<table>
<thead>
<tr>
<th>Vasodilators</th>
<th>IIa</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.v. vasodilators should be considered for symptomatic relief in AHF with SBP &gt;90 mmHg (and without symptomatic hypotension).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms and blood pressure should be monitored frequently during administration of i.v. vasodilators.</td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inotropic agents - dobutamine, dopamine, levosimendan, phosphodiesterase III (PDE III) inhibitors</th>
<th>IIb</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term, i.v. infusion of inotropic agents may be considered in patients with hypotension (SBP &lt;90 mmHg) and/or signs/symptoms of hypoperfusion despite adequate filling status, to increase cardiac output, increase blood pressure, improve peripheral perfusion and maintain end-organ function.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| An intravenous infusion of levosimendan or a PDE III inhibitor may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypotension with subsequent hypoperfusion. | IIb | C   |

| Inotropic agents are not recommended unless the patient is symptomatically hypotensive or hypoperfused because of safety concern. | III  | A   |

# B-blockers/ACE-inhibitors/MRAs

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In case of worsening of chronic HFrEF, every attempt should be made to continue</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>evidence-based, disease-modifying therapies, in the absence of haemodynamic instability or contraindications.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the case of de novo HFrEF, every attempt should be made to initiate these therapies after haemodynamic stabilization.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>


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<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFrEF patients requiring HF hospitalization on GDMT should continue GDMT unless hemodynamic instability or contraindicated</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Initiation of beta-blocker therapy at a low dose is recommended after optimization of volume status and discontinuation of intravenous agents</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>
PARADIGM-HF trial

<table>
<thead>
<tr>
<th>NYHA Functional Class-no. (%)</th>
<th>LCZ-696 (N=4187)</th>
<th>Enalapril (N=4212)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>180 (4.3)</td>
<td>209 (5.0)</td>
</tr>
<tr>
<td>II</td>
<td>2998 (71.6)</td>
<td>2921 (69.3)</td>
</tr>
<tr>
<td>III</td>
<td>969 (23.1)</td>
<td>1049 (24.9)</td>
</tr>
<tr>
<td>IV</td>
<td>33 (0.8)</td>
<td>27 (0.6)</td>
</tr>
<tr>
<td>Missing data</td>
<td>7 (0.2)</td>
<td>6 (0.1)</td>
</tr>
</tbody>
</table>

Hydralazine/ Isosorbide dinitrate

Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure

**Hydralazine and isosorbide dinitrate**

Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated LV in NYHA Class III–IV despite treatment with an ACE-I a beta-blocker and an MRA to reduce the risk of HF hospitalization and death.

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>532</th>
<th>466</th>
<th>401</th>
<th>340</th>
<th>285</th>
<th>232</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isosorbide dinitrate plus hydralazine</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Hydralazine and isosorbide dinitrate**

The combination of hydralazine and isosorbide dinitrate is recommended for African Americans with NYHA class III–IV HFrEF on GDMT

I A
Right Heart Catheterization

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Nitroprusside / Furosemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>PA (mean)</td>
<td>62/35 (44)</td>
<td>49/25 (33)</td>
</tr>
<tr>
<td>PCWP</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>TPG (DPG)</td>
<td>26 (9)</td>
<td>16 (8)</td>
</tr>
<tr>
<td>PVR</td>
<td>7</td>
<td>2.76</td>
</tr>
<tr>
<td>PAPi</td>
<td>1.17</td>
<td>1.04</td>
</tr>
<tr>
<td>SVR</td>
<td>1761</td>
<td>943</td>
</tr>
<tr>
<td>CI</td>
<td>1.22</td>
<td>3.3</td>
</tr>
<tr>
<td>SvO2</td>
<td>32</td>
<td>58</td>
</tr>
</tbody>
</table>

Pulmonary artery catheter may be considered in patients who, despite pharmacological treatment present refractory symptoms (particularly with hypotension and hypoperfusion).
Metabolic stress test

• The test was terminated due to fatigue
• Inadequate heart rate response (77%) (CRT)
• Functional capacity 2.3 METS (high risk patient)
• Peak VO\textsubscript{2} (30 sec avg) = 9.0 ml/kg/min at RER = 0.84 (inadequate effort), which corresponds to 37% of predicted peak VO\textsubscript{2} (based on percent functional aerobic impairment)
• VE/VCO\textsubscript{2} = 47 (VE/VCO\textsubscript{2} greater than 45 is consistent with a prognostically significant increase of physiologic dead space)
• Oxygen saturation by pulse oximeter were 94% at rest and 91% at peak exercise.
• Weber Class D
Pharmaceutical treatment at discharge

- aspirin 81mg x 1
- apixaban 5mg x 2
- LCZ-696 (49/51)mg x 2 – switched to ramipril 5 mg x 1
- spironolactone 25mg x 1
- furosemide 40mg x 1
- hydralazine 10mg x 2 – increased to 50mg x 3
- isosorbide dinitrate 5mg x 2 – increased to 20mg x 3
- amiodarone 200 mg x 1
- pantoprazole 40 mg x 1
- metformin 500 mg x 2
### INTERMACS classification

<table>
<thead>
<tr>
<th>INTERMACS level</th>
<th>NYHA Class</th>
<th>Description</th>
<th>Device</th>
<th>1y survival with LVAD therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cardiogenic shock “Crash and burn”</td>
<td>IV</td>
<td>Haemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical hypoperfusion of target organs (severe cardiogenic shock).</td>
<td>ECLS, ECMO, percutaneous support devices</td>
<td>52.6±5.6%</td>
</tr>
<tr>
<td>2. Progressive decline despite inotropic support “Sliding on inotropes”</td>
<td>IV</td>
<td>Intravenous inotropic support with acceptable blood pressure but rapid deterioration of renal function, nutritional state, or signs of congestion.</td>
<td>ECLS, ECMO, LVAD</td>
<td>63.1±3.1%</td>
</tr>
<tr>
<td>3. Stable but inotrope dependent “Dependent stability”</td>
<td>IV</td>
<td>Haemodynamic stability with low or intermediate doses of inotropics, but necessary due to hypotension, worsening of symptoms, or progressive renal failure.</td>
<td>LVAD</td>
<td>78.4±2.5%</td>
</tr>
<tr>
<td>4. Resting symptoms “Frequent flyer”</td>
<td>IV ambulatory</td>
<td>Temporary cessation of inotropic treatment is possible, but patient presents with frequent symptom recurrences and typically with fluid overload.</td>
<td>LVAD</td>
<td>78.7±3.0%</td>
</tr>
<tr>
<td><strong>5. Exertion intolerant “Housebound”</strong></td>
<td>IV ambulatory</td>
<td>Complete cessation of physical activity, stable at rest, but frequently with moderate fluid retention and some level of renal dysfunction.</td>
<td>LVAD</td>
<td><strong>93.0±3.9%</strong></td>
</tr>
<tr>
<td>6. Exertion limited “Walking wounded”</td>
<td>III</td>
<td>Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity.</td>
<td>LVAD / Discuss LVAD as option</td>
<td>-</td>
</tr>
<tr>
<td>7. “Placeholder”</td>
<td>III</td>
<td>Patient in NYHA Class III with no current or recent unstable fluid balance.</td>
<td>Discuss LVAD as option</td>
<td>-</td>
</tr>
</tbody>
</table>
Evaluation for advanced therapies

• LHC 2017: normal

• PET 6/19/18: “Garland” sign
  • Cardiac: focal inflammation of inferior anterior RA myocardium / inflammation of LV

• CT abdo pelvis: atherosclerotic calcifications, chronic congestive hepatopathy

• Lung biopsy 1970s: sarcoidosis, no treatment
Evaluation for advanced therapies

- Blood Type A positive
- BMI: 29.9 kg/m²
- MELD: 15
- Panel-reactive antibody (PRA): class I 0, class II 50
- Prior Sternotomy: 0
  - CRT-D
Evaluation for advanced therapies

➢ Renal
BUN: 25, Crea: 1.28 (eGFR:50)

➢ Pulmonary
FVC: 1.46, FEV1: 1.78, ratio: 0.82
CT-chest (last 2016)

➢ Liver
AST: 27, ALT: 25, ALP: 78
Amylase: 124, GGT: 80
TBil: 0.9, Alb: 3.6, TP: 7.1
HIV, Hep B, Hep A, Hep C negative

➢ Vascular
Abdo US - normal
Renal US – veins patent, arterial 0-59% stenosis
Carotid US – RICA 20-39%, LICA 20-39%
Moderate bilateral disease;
Ankle Brachial Index: Rt 0.53, Lt 0.47

Hgb 12.2 (Hct 40.5)
TSH 4.8, T4 10.5, T3 92
Pap smear: **
Mammogram: **
Colonoscopy: **
Left Ventricular Assist Devices

Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:

LVEF <25% and, if measured, peak VO₂ < 12 mL/kg/min.

≥ 3 HF hospitalizations in previous 12 months without an obvious precipitating cause.

Dependence on i.v. inotropic therapy.

Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥ 20 mmHg and SBP ≤ 80–90 mmHg or CI ≤ 2 L/min/m²).

Absence of severe right ventricular dysfunction together with severe tricuspid regurgitation.

MCS

MCS is beneficial in carefully selected* patients with stage D HF in whom definitive management (e.g., cardiac transplantation) is anticipated or planned

IIa B

Nondurable MCS is reasonable as a “bridge to recovery” or “bridge to decision” for carefully selected* patients with HF and acute profound disease

IIa B

Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HF/EF

IIa B


56% of patients were able to tolerate ACE inhibitors
22% could tolerate β-blockers

MOMENTUM-3

Heart Transplantation

**Patients to consider**
End-stage HF with severe symptoms, a poor prognosis, and no remaining alternative treatment options. Motivated, well informed, and emotionally stable. Capable of complying with the intensive treatment required postoperatively.

**Contraindications**
- Active infection.
- Severe peripheral arterial or cerebrovascular disease.
- Pharmacologically irreversible pulmonary hypertension (LVAD should be considered with a subsequent re-evaluation to establish candidacy).
- Cancer (a collaboration with oncology specialists should occur to stratify each patient as to their risk of tumour recurrence).
- Irreversible renal dysfunction (e.g. creatinine clearance <30 mL/min).
- Systemic disease with multi-organ involvement.
- Other serious co-morbidity with poor prognosis.
- Pre-transplant BMI >35 kg/m² (weight loss is recommended to achieve a BMI <35 kg/m²).
- Current alcohol or drug abuse.
- Any patient for whom social supports are deemed insufficient to achieve compliant care in the outpatient setting.

**Cardiac transplantation**
Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management


Every life deserves the best care