Management Strategies for Advanced Heart Failure

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Heart Failure Presentations

- Gradual onset of effort intolerance: dyspnea, CP, fatigue (+/- volume overload: abd distension, edema)
- Worsening chronic HF with either reduced or preserved LV systolic function
- Advanced HF with severe LV systolic dysfunction
- Acute HF: sudden increase in BP, MI/ischemia, arrhythmias, myocarditis
Heart Failure Presentations

• Gradual onset of effort intolerance: dyspnea, CP, fatigue (+/- volume overload: abd distension, edema)
• Worsening chronic HF with either reduced or preserved LV systolic function
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• Acute HF: sudden increase in BP, MI/ischemia, arrhythmias, myocarditis
Three-phase terrain of lifetime readmission risk after heart failure hospitalization.

- **Initial discharge**
- **“Transition Phase”**
- **“Plateau Phase”**
- **“Palliation and Priorities”**

*Akshay S. Desai, and Lynne W. Stevenson
Circulation. 2012;126:501-506*
Table 23. ESC Definition of Advanced HF

1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV)

2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion)

3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following:
   a. LVEF <30%
   b. Pseudonormal or restrictive mitral inflow pattern
   c. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterization
   d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes

4. Severe impairment of functional capacity shown by 1 of the following:
   a. Inability to exercise
   b. 6-Minute walk distance ≤300 m
   c. Peak $\dot{V}O_2$ <12 to 14 mL/kg/min

5. History of ≥1 HF hospitalization in past 6 mo

6. Presence of all the previous features despite “attempts to optimize” therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated

BNP indicates B-type natriuretic peptide; CRT, cardiac resynchronization therapy; ESC, European Society of Cardiology; GDMT, guideline-directed medical therapy; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PA, pulmonary artery; PWCP, pulmonary capillary wedge pressure; and RAP, right atrial pressure.
Table 24. Clinical Events and Findings Useful for Identifying Patients With Advanced HF

<table>
<thead>
<tr>
<th>Event</th>
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<tbody>
<tr>
<td>Repeated (≥2) hospitalizations or ED visits for HF in the past year</td>
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<tr>
<td>Progressive deterioration in renal function (e.g., rise in BUN and creatinine)</td>
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<tr>
<td>Weight loss without other cause (e.g., cardiac cachexia)</td>
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<tr>
<td>Intolerance to ACE inhibitors due to hypotension and/or worsening renal function</td>
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<tr>
<td>Intolerance to beta blockers due to worsening HF or hypotension</td>
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<tr>
<td>Frequent systolic blood pressure &lt;90 mm Hg</td>
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<tr>
<td>Persistent dyspnea with dressing or bathing requiring rest</td>
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<tr>
<td>Inability to walk 1 block on the level ground due to dyspnea or fatigue</td>
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<tr>
<td>Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose &gt;160 mg/d and/or use of supplemental metolazone therapy</td>
</tr>
<tr>
<td>Progressive decline in serum sodium, usually to &lt;133 mEq/L</td>
</tr>
<tr>
<td>Frequent ICD shocks</td>
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</table>

ACE indicates angiotensin-converting enzyme; BUN, blood urea nitrogen; ED, emergency department; HF, heart failure; and ICD, implantable cardioverter-defibrillator.
<table>
<thead>
<tr>
<th>Profiles</th>
<th>Brief Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS 1</td>
<td>Critical cardiogenic shock (Crash and burn)</td>
<td>Life-threatening hypotension despite rapidly escalating inotropic support.</td>
</tr>
<tr>
<td>INTERMACS 2</td>
<td>Progressive decline (Sliding fast on inotropes)</td>
<td>Declining function despite intravenous inotropic support.</td>
</tr>
<tr>
<td>INTERMACS 3</td>
<td>Stable but inotrope dependent (Dependent stability)</td>
<td>Stable on continuous intravenous inotropic support.</td>
</tr>
<tr>
<td>INTERMACS 4</td>
<td>Resting symptoms on oral therapy at home</td>
<td>Patient experiences daily symptoms of congestion at rest or during activities of daily living.</td>
</tr>
<tr>
<td>INTERMACS 5</td>
<td>Exertion intolerant</td>
<td>Patient is comfortable at rest and with activities of daily living but unable to engage in any other activity.</td>
</tr>
<tr>
<td>INTERMACS 6</td>
<td>Exertion limited (Walking wounded)</td>
<td>Patient has fatigue after the first few minutes of any meaningful activity.</td>
</tr>
<tr>
<td>INTERMACS 7</td>
<td>Advanced NYHA class III (Placeholder)</td>
<td>Patients living comfortably with meaningful activity limited to mild physical exertion.</td>
</tr>
</tbody>
</table>

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; NYHA = New York Heart Association. Adapted from: Stevenson LW, et al.²⁵
Remember acronym to assist in decision making for referral to advanced heart failure specialist:

I-NEED-HELP (also see Table 6)

I: IV inotropes
N: NYHA IIIB/IV or persistently elevated natriuretic peptides
E: End-organ dysfunction
E: Ejection fraction ≤35%
D: Defibrillator shocks
H: Hospitalizations >1
E: Edema despite escalating diuretics
L: Low blood pressure, high heart rate
P: Prognostic medication – progressive intolerance or down-titration of GDMT
Definition of Advanced HF

• **2009 ACCF/AHA HF guideline**, stage D was defined as:

  “patients with truly refractory HF who might be eligible for specialized, advanced treatment strategies, such as MCS, procedures to facilitate fluid removal, continuous inotropic infusions, or cardiac transplantation or other innovative or experimental surgical procedures, or for end-of-life care, such as hospice”
Treatment of HFrEF Stage C and D

†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.
‡See 2013 HF guideline.
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy-device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD,isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.
Step 1: Establish Dx of HFpEF; assess volume; initiate GDMT

HFpEF NYHA class I–IV (Stage C)

ACEI or ARB AND GDMT beta blocker; diuretics as needed (COR I)

Step 2: Consider the following patient scenarios

- NYHA class II–IV, provided est. CrCl >30 mL/min & K+<5.0 mEq/L
- NYHA class II–III HF Adequate BP on ACEI or ARB*: No C/I to ARB or sacubitril
- NYHA class III–IV, in black patients
- NYHA class II–III, LVEF ≥35%; (caveat: >1 y survival, >40 d post MI)
- NYHA class II–IV, LVEF ≤35%, NSR & QRS ≥150 ms with LBBB pattern
- NYHA class II–III, NSR, heart rate ≥70 bpm on maximally tolerated dose beta blocker

Step 3: Implement indicated GDMT. Choices are not mutually exclusive, and no order is inferred

- Aldosterone antagonist (COR I)
- Discontinue ACEI or ARB; initiate ARNI* (COR I)
- Hydral. Nitrates†‡ (COR I)
- ICD‡ (COR I)
- CRT or CRT-D‡ (COR I)
- Ivabradine (COR IIa)
Patient A.C.

• 30 y.o. man admitted to the ED at his local hospital in April 2017 with 3 week history of fatigue, weakness, orthopnea, PND, dyspnea, cough
• BP 138/106, RR 20, afebrile, HR 110 – sinus tachycardia, O2sat 100% on room air
• Initially treated with labetalol, dypnea worsened
• Chest CT: “patchy consolidation”
Patient A.C.

• PMH: depression, remote smoking - quit 5 years ago, smokeless tobacco – quit 2 years ago
• PSH: appendectomy, umbilical hernia repair
• FH: father with dilated cardiomyopathy, diagnosed at age 31, hx of LVAD and cardiac transplantation
Patient A.C.

• WBC 10.4, Hgb 16.1, platelets 362
• BUN 6, Cr 0.96, Na 142, K 4.0, LFTs normal
• CK 457, CK-MB 3.7, troponin I <0.04, d dimer 0.41
Echocardiogram

- Severely dilated left ventricle, 7.7 cm, LVEF 10-15%, stage 3 diastolic dysfunction, moderate mitral regurgitation
## Table 11. Recommendations for Invasive Evaluation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring with a pulmonary artery catheter should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms and/or when hemodynamics are uncertain</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>When ischemia may be contributing to HF, coronary arteriography is reasonable</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Endomyocardial biopsy can be useful in patients with HF when a specific diagnosis is suspected that would influence therapy</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute HF</td>
<td>III: No Benefit</td>
<td>B (305)</td>
</tr>
<tr>
<td>Endomyocardial biopsy should not be performed in the routine evaluation of HF</td>
<td>III: Harm</td>
<td>C</td>
</tr>
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COR indicates Class of Recommendation; HF, heart failure; and LOE, Level of Evidence.
Treatment of HFrEF Stage C and D

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Helping Cardiovascular Professionals
Patient A.C.

• Diuresed 2.5 kg with resolution of symptoms, carvedilol 3.125 mg bid and enalapril 2.5 mg daily begun
Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
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<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
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<tbody>
<tr>
<td>I</td>
<td>ACE-I: A</td>
<td>The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (Level of Evidence: A), OR ARBs (Level of Evidence: A), OR ARNI (Level of Evidence: B-R) in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HFrEF to reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data prompted clarification and important updates.</td>
</tr>
<tr>
<td></td>
<td>ARB: A</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>ARNI: B-R</td>
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2017 ACC/AHA/HFSA Guideline for the Management of Heart Failure - Focused Update of the 2013 ACCF/AHA Guideline
Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

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<tr>
<td>I</td>
<td>ARNI: B-R</td>
<td>In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data necessitated this recommendation.</td>
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2017 ACC/AHA/HFSA Guideline for the Management of Heart Failure -Focused Update of the 2013 ACCF/AHA Guideline
Patient A.C.

- ACEI was switched to ARNI
- ARNI and BB uptitrated to maximally tolerated doses
- He then had an episode of orthostatic syncope for which he was evaluated in the ED
- One month later he was hospitalized with a TIA. TEE demonstrated no cardiac source of embolus. Anticoagulation was begun.
Patient A.C.

- Echocardiogram 7 months after diagnosis showed no change in LV function
- Patient had progressive symptoms, now with orthopnea and DOE
Step 4
Reassess symptoms

Step 5
Consider additional therapy

- Palliative care
  (COR I)

- Transplant
  (COR I)

- Refractory NYHA class III-IV
  (Stage D)

- Symptoms improved

- LVAD
  (COR IIa)

- Investigational studies