Definitions and Indicators of Advanced HF

European Society of Cardiology (ESC)

- 1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA
- functional class III or IV)
 Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or of reduced cardiac output at rest (peripheral hypoperfusion)
- Objective evidence of severe cardiac dysfunction, shown by ≥1 of the following:
 - Low LVEF (<30%)
 - Severe abnormality of cardiac function on Doppler-echocardiography with a pseudonormal or b. restrictive mitral inflow pattern
 - High cardiac filling pressures (mean PCWP >16 mm Hg and/or mean RAP >12 mm Hg by c. pulmonary artery catheterization)
 - d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes Severe impairment of functional capacity shown by ≥1 of the following:
- - Inability to exercise a.
 - 6-MWT distance ≤300 m in women and/or patients aged ≥75 years b.
 - Peak VO2 <12 mL/kg/min
- History of ≥1 HF hospitalization in the past 6 months
- Presence of all the previous features despite "attempts to optimize" therapy, including diuretics, RAAS inhibitors, and beta-blockers unless these are poorly tolerated or contraindicated, and CRT

American College of Cardiology Foundation (ACCF)/ American Heart Association (AHA)

- Repeated (≥2) hospitalizations or ED visits for HF in the past year
- Progressive deterioration in renal function (eg, rise in BUN and creatinine)
- Weight loss without other cause (eg, cardiac cachexia)
- Intolerance of ACE inhibitors because of hypotension and/or worsening renal function
- Intolerance of beta-blockers because of worsening HF or hypotension
- Frequent systolic blood pressure <90 mm Hg 6.
- Persistent dyspnea with dressing or bathing requiring rest
- 8. Inability to walk 1 block on level ground because of dyspnea or fatigue
- Recent need to escalate diuretics to maintain volume status, often reaching a daily furosemide equivalent dose of >160 mg and/or the use of supplemental metolazone therapy
- 10. Progressive decline in serum sodium, usually to <133 mEq/L
- Frequent ICD shocks

Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)

- Profile 1 (critical cardiogenic shock): Patient with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and/or lactate levels.
- Profile 2 (progressive decline): Patient with declining function despite IV inotropic support, may be manifested by worsening renal function, nutritional depletion, or inability to restore volume balance. Also describes declining status in patients unable to tolerate inotropic therapy.
- Profile 3 (stable but inotrope dependent): Patient with stable blood pressure, organ function, nutrition, and symptoms on continuous IV inotropic support (or a temporary circulatory support device, or both), but demonstrating repeated failure to wean from support because of recurrent symptomatic hypotension or renal dysfunction.
- 4. Profile 4 (resting symptoms): Patient can be stabilized close to normal volume status but experiences daily symptoms of congestion at rest or during ADL. Doses of diuretics generally fluctuate at very high levels. More intensive management and surveillance strategies should be considered, which may in some cases reveal poor compliance that would compromise outcomes with any therapy. Some patients may shuttle between profiles 4 and 5.
- 5. Profile 5 (exertion intolerant): Comfortable at rest and with ADL but unable to engage in any other activity, living predominantly within the house. Patients are comfortable at rest without congestive symptoms but may have underlying refractory elevated volume status, often with renal dysfunction. If underlying nutritional status and organ function are marginal, patient may be more at risk than in profile 4 and require definitive intervention.
- 6. Profile 6 (exertion limited): Patient without evidence of fluid overload is comfortable at rest and with ADL and minor activities outside the home, but fatigues after first few minutes of any meaningful activity. Attribution to cardiac limitation requires careful measurement of peak VO2, in some cases with hemodynamic monitoring to confirm severity of cardiac impairment.
- Profile 7 (advanced NYHA functional class III): A placeholder for a more precise specification in future, this level includes patients who are without current or recent episodes of unstable fluid balance, living comfortably, with meaningful activity limited to mild physical exertion.

ACE, angiotensin-converting enzyme; ADL, activities of daily living; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CRT, cardiac resynchronization therapy; ED, emergency department; HF, heart failure; ICD, implantable cardioverter-defibrillator; IV, intravenous; LVEF, left ventricular ejection fraction; NT, N-terminal; NYHA, New York Heart Association; PCWP, pulmonary capillary wedge pressure; pro-BNP, pro-brain (B-type) natriuretic peptide; RAAS, renin-angiotensin-aldosterone system; RAP, right atrial pressure; 6-MWT, 6-minute walk test; VO2, oxygen consumption.

- Metra M, Ponikowski P, Dickstein K, et al. Advanced chronic heart failure: a position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2007;9:684-694.

 Fang JC, Ewald GA, Allen LA, et al. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. *J Card Fail*. 2015;21:519-534.
- Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of
- America. Circulation. 2017;136:e137-e161.
 Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the International Society for Heart and Lung Transplantation. J Am Coll Cardiol. 2009;53(15):e1-e90. Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant. 2009;28:535-541.