

Heart Failure Council of Thailand (HFCT) 2019 Heart Failure Guideline: Advanced Heart Failure

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Definition

In some cases of heart failure (HF), the clinical syndrome is progressive. Despite appropriate treatments, these patients have severe symptoms, recurrent HF hospitalization, and various irreversible end-organ dysfunctions. During this stage of disease, hospitalization due to acute decompensated heart failure is usually prolonged and may relate to hemodynamic instabilities that result in low blood pressure and/or systemic hypoperfusion.

This stage of HF is referred to differently in the literature, with terms that include advanced HF, stage D HF, end-stage HF, and refractory HF. Similarly, a variety of guideline-based definitions have been proposed to characterize advanced HF⁽¹⁻³⁾ (Table 1). Clinical findings suggestive of advanced HF are outlined in Table 2. Types of end-organ dysfunction that may develop due to chronic advanced HF include cachexia, chronic kidney disease, cardiac cirrhosis, hypoalbuminemia, and pulmonary hypertension due to left heart disease.

Occasionally, patients with severe cardiac dysfunction and high mortality rate may present with relatively mild symptoms; therefore, a thorough

prognosis assessment is necessary in each individual patient to identify patients with advanced HF.

Treatment

In advanced HF, the patient's goal of care is an important determinant of the treatment strategy that is developed from an assortment of complex and advanced treatments. The patient's goal of care and the treatment alternatives should be discussed with the patient, the patient's family, and the patient's caregiver(s). All advanced HF treatments are relatively invasive, and these treatments are considered "life changing" for patients and their families; therefore, the process of shared decision-making is needed. The discussion should focus on the outcomes that are relevant to the patient. Patients should be made aware of the natural course of the disease, and the nature of each treatment option prior to proceeding with treatment.

Regarding medications, digoxin may be considered in patients with advanced HF in addition to neurohormonal modulators, such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEI/ARB), angiotensin receptor-neprilysin inhibitor (ARNI), beta blockers (BB), and mineralocorticoid receptor antagonist (MRA), to alleviate symptoms and decrease HF hospitalization⁽⁴⁾. There is limited evidence to support the continuous long-term use of intravenous inotrope, but it may allow patients to gain functional capacity and improve so-called "quality of death", especially in patients who depend on inotropic medications^(5,6).

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Table 1. Definitions of advanced HF from various guidelines

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|--|--|
| ACC/AHA 2009 (stage D HF) ⁽¹⁾ | “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.” |
| ACC/AHA 2013 (stage D HF) ⁽²⁾ | “A subset of patients with chronic HF will continue to progress and develop persistently severe symptoms despite maximum GDMT. Patients with marked HF symptoms at rest or recurrent hospitalizations despite GDMT.” |
| ESC 2007 ⁽³⁾ | <ol style="list-style-type: none"> 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 as demonstrated by the presence of at least 1 of the following: <ol style="list-style-type: none"> a. LVEF <30% b. Pseudonormal or restrictive mitral inflow pattern c. Mean PCWP >16 mmHg and/or RAP >12 mmHg by PA catheterization d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes 4. Severe impairment of functional capacity as demonstrated by the presence of 1 of the following: <ol style="list-style-type: none"> a. Inability to exercise b. 6-minute walk test distance ≤300 m c. Peak VO₂ <12 to 14 mL/kg/minute 5. History of ≥1 HF hospitalization in past 6 months 6. Presence of all of the previous features despite “attempts to optimize” therapy, including diuretics and GDMT (unless they are poorly tolerated or contraindicated) and CRT when indicated. |

ACC=American College of Cardiology; AHA=American Heart Association; BNP=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; MCS=mechanical circulatory support; NT-proBNP=N-terminal pro b-type natriuretic peptide; NYHA=New York Heart Association; PA=pulmonary artery; PCWP=pulmonary capillary wedge pressure; RAP=right atrial pressure; VO₂=Oxygen uptake

The 1-year mortality rate in patients with advanced HF is approximately 20% to 50%⁽⁷⁾. Heart transplant is a gold standard treatment with a 1-, 3-, and 5-year post-transplant survival rate of 88%, 79%, and 72%, respectively⁽⁸⁾. Half of patients who underwent transplants lived more than 13 years after their operation. Transplant success depends upon a large multidisciplinary team that is responsible for processes that include pre-transplant care, donor selection, the transplant operation itself, and post-transplant management. Contraindication for heart transplant may limit candidacy in many patients due to the scarcity of donors and the complications associated with post-transplant care (Table 3).

More recently, mechanical circulatory support systems (MCS) have been developed to unload the ventricle in patients with advanced HF. There are multiple devices available with various indications. Device selection depends upon patient severity,

prognosis, and transplant candidacy. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) classification may help physicians identify patients with advanced HF who would benefit from MCS, and guide the appropriate timing for implantation⁽⁹⁾ (Table 4).

Palliative care is a patient and family centered type of care that optimizes quality of life (QoL) by anticipating, preventing/minimizing, and treating suffering. Since HF is a serious illness that is treatable, but not curable in most cases, palliative care is appropriate in most patients with HF, especially during the advanced phase. After thorough discussions with both the patient and the family, palliative interventions, such as home inotropes, turning off the implantable cardioverter defibrillator (ICD), discussion about advanced directive, and symptomatic measures with opioids and benzodiazepines, may be initiated.

All treatment options for advanced HF (Table 5)

Table 2. Clinical findings suggestive of advanced HF*

Persistent severe symptoms

- NYHA Functional Class III, IV
- Dyspnea while taking a shower, eating, talking, or at rest
- Homebound

Two or more HF hospitalizations within 6 months*

Can no longer tolerate the same doses of ACEI/ARB, ARNI, or BB that were previously tolerable

Requires high-dose diuretics (daily furosemide equivalent dose >240 mg) and/or supplementation with secondary diuretics

End-organ failure

- Cachexia (BMI <19)
- CKD stage >3, progressive worsening in BUN and/or Cr levels, hyponatremia
- Cardiac cirrhosis, hypoalbuminemia
- Pulmonary hypertension due to left heart disease

Multiple ICD shocks

Unresponsive to CRT treatment

Dependence on intravenous inotropic medications

ACEI=angiotensin converting enzyme inhibitors; ARB= angiotensin II receptor blockers; ARNI=angiotensin receptor-neprilysin inhibitor; BB=beta blockers; BMI=body mass index; BUN=blood urea nitrogen; CKD=chronic kidney disease; Cr=creatinine; CRT=cardiac resynchronization therapy; HF= heart failure; ICD=implantable cardioverter defibrillator; NYHA=New York Heart Association

* After exclusion of any reversible causes, and after providing optimal treatment, including HF self-care (e.g., fluid and salt limitation, medication adherence), medical therapy, and CRT/ICD therapy

Table 3. Suggested contraindications for heart transplantation

- Other serious non-reversible comorbidities with poor prognosis
 - Active infection
 - Active or recent cancer
 - Pharmacologically irreversible pulmonary hypertension (PVR >3 to 6 wood unit, TPG >15 mmHg)
 - Irreversible renal dysfunction (e.g., creatinine clearance <30 mL/minute)
 - Chronic liver disease and cirrhosis
 - Poorly controlled diabetes
 - Severe peripheral arterial or cerebrovascular diseases
 - Systemic disease with multiple organ involvement
 - Pre-transplant BMI >35 kg/m²
 - Current alcohol or drug abuse
 - Any patients for whom social supports are deemed insufficient
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BMI=body mass index; PVR=pulmonary vascular resistance; TPG=transpulmonary gradient

should be considered in concert with all stakeholders to achieve the patient's goal of living, whether it is survival, QoL, or both. The decision regarding the most suitable treatment can be a dynamic process that can rapidly change over time with changes in the patient's condition.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Jessup M, Abraham WT, Casey DE, Feldman AM, Francis GS, Ganiats TG, et al. 2009 focused update:

Table 4. Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) level and profiles for patients with advanced heart failure

| Level | Description | NYHA Class | Suggested implant timing |
|-------|---|---------------|--------------------------|
| 1 | Critical cardiogenic shock | IV | Hours |
| 2 | Progressive decline despite inotropic support | IV | Hours to days |
| 3 | Stable but inotrope dependent; can be in hospital or at home | IV | Week to months |
| 4 | Resting symptoms; recurrent decompensated HF | IV ambulatory | Variable |
| 5 | Exertion intolerant; comfort at rest; symptoms with minimal ADL | IV ambulatory | Variable |
| 6 | Exertion limited; possible ADL, but meaningful activity limitations | III | Variable |
| 7 | Advanced NYHA Functional Class III | III | Variable |

ADL=activities of daily living; NYHA=New York Heart Association

Table 5. Summary of recommendations regarding the diagnosis and management of advanced HF

| Recommendations | COR | LOE |
|--|-----|-----|
| Diagnosis | | |
| A thorough prognosis assessment is recommended in patients with persistent symptomatic HF to identify patients with advanced HF. | I | C |
| It is recommended to investigate the etiology of heart failure, patient treatment compliance, and alternative explanations for symptoms in patients with advanced HF. | I | C |
| Management | | |
| Treatment selection in patients with advanced HF depends upon patient's goal of care, prognosis, and transplant candidacy. | I | C |
| Patients considered for heart transplant or MCS should be managed in conjunction with a referral center for advanced HF. | I | C |
| Medication | | |
| Digoxin may be considered in patients with advanced HF to improve symptoms and reduce HF hospitalization. | IIb | B |
| Continuous long-term use of intravenous inotropes, such as dobutamine, milrinone, levosimendan, and dopamine, may be considered in patients with advanced HF _{rEF} to maintain end-organ performance, and to facilitate evaluation for an appropriate treatment, such as heart transplant, MCS, palliative care, or other treatments. | IIb | B |
| Continuous long-term use of intravenous inotropes is not recommended in patients with life-threatening arrhythmia, in patients who demonstrate no hemodynamic response to these medications, or in patients with HF _{pEF} . | III | C |
| Heart transplant | | |
| In patients carefully determined to be transplant candidates, heart transplantation is recommended to improve survival, symptoms, and quality of life. | I | C |
| Mechanical circulatory support (MCS), including LVAD and VA-ECMO | | |
| In carefully selected patients, short-term MCS should be considered in patients with severe cardiogenic shock to improve hemodynamic status during the patient evaluation process ("bridge to decision"). | IIa | B |
| In carefully selected patients, short-term or long-term MCS should be considered in patients with advanced HF that are transplant candidates to improve survival, symptoms, and quality of life while they wait for a suitable donor ("bridge to transplant"). | IIa | B |
| In carefully selected patients, long-term MCS should be considered in patients with advanced HF that are not transplant candidates to improve survival, symptoms, and quality of life ("destination therapy"). | IIa | B |
| Palliative care | | |
| Integration of palliative care as an adjunctive treatment in combination with other curative treatments is recommended for patients with advanced HF to improve quality of life. | I | B |
| In patients with a prognosis of weeks to months, an end-of-life or specialized hospice care service should be considered. | IIa | B |

COR=class of recommendation; EF=ejection fraction; HF=heart failure; HF_{pEF}=heart failure with preserved ejection fraction; LOE=Level of evidence; LVAD=left ventricular assist devices; MCS=mechanical circulatory support; VA-ECMO=veno-arterial extracorporeal membrane oxygenation

- ACCF/AHA 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. *Circulation* 2009;119:1977-2016.
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;62:e147-239.
 3. Metra M, Ponikowski P, Dickstein K, McMurray JJ, Gavazzi A, Bergh CH, 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;9:684-94.
 4. Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med* 1997;336:525-33.
 5. Ginwalla M. Home inotropes and other palliative care. *Heart Fail Clin* 2016;12:437-48.
 6. Hershberger RE, Nauman D, Walker TL, Dutton D, Burgess D. Care processes and clinical outcomes of continuous outpatient support with inotropes (COSI) in patients with refractory endstage heart failure. *J Card Fail* 2003;9:180-7.
 7. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;345:1435-43.
 8. International Society for Heart & Lung Transplantation. International thoracic organ transplant (TTX) registry data slides [Internet]. 2017 [cited 2019 Jan 14]. Available from: <https://ishltregistries.org/registries/slides.asp>.
 9. Stevenson LW, Pagani FD, Young JB, Jessup M, Miller L, Kormos RL, et al. INTERMACS profiles of advanced heart failure: the current picture. *J Heart Lung Transplant* 2009;28:535-41.