Advanced (Stage D) Heart Failure: A Statement From the Heart Failure Society of America Guidelines Committee

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ABSTRACT

We propose that stage D advanced heart failure be defined as the presence of progressive and/or persistent severe signs and symptoms of heart failure despite optimized medical, surgical, and device therapy. Importantly, the progressive decline should be primarily driven by the heart failure syndrome. Formally defining advanced heart failure and specifying when medical and device therapies have failed is challenging, but signs and symptoms, hemodynamics, exercise testing, biomarkers, and risk prediction models are useful in this process. Identification of patients in stage D is a clinically important task because treatments are inherently limited, morbidity is typically progressive, and survival is often short. Age, frailty, and psychosocial issues affect both outcomes and selection of therapy for stage D patients. Heart transplant and mechanical circulatory support devices are potential treatment options in select patients. In addition to considering indications, contraindications, clinical status, and comorbidities, treatment selection for stage D patients involves incorporating the patient's wishes for survival versus quality of life, and palliative and hospice care should be integrated into care plans. More research is needed to determine optimal strategies for patient selection and medical decision making, with the ultimate goal of improving clinical and patient centered outcomes in patients with stage D heart failure. (*J Cardiac Fail 2015;21:519–534*)

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The contemporary perspective of heart failure emphasizes the progressive nature of the disease through clinically identifiable stages.[1] Stage D heart failure describes advanced progression of the heart failure syndrome characterized by structural abnormalities of the heart and severe resting symptoms despite optimal medical, surgical, and device therapy. The terms "stage D" and "advanced" are used interchangeably in the present document. Although a discussion of advanced heart failure in this context has traditionally been limited to those suffering from severe myocardial systolic dysfunction, or heart failure with reduced ejection fraction (HFrEF), our understanding of heart failure with preserved ejection fraction (HFpEF) has recently evolved. Although the latter is likely a compendium of disorders for which even the natural history remains unclear and the optimal treatment strategy unresolved, there are clearly patients with HFpEF who meet the definition of stage D.

Identification of patients in stage D is a clinically relevant undertaking because treatments are limited, morbidity is progressive, and survival is short. Recognition or acknowledgement of advanced heart failure may be elusive for patients, families, and even providers, because the signs and symptoms are often chronic, insidious, and nonspecific. Late recognition, and therefore late referral, of stage D patients limits therapeutic options, because the ability to survive advanced therapies, such as heart transplantation or mechanical circulatory support (MCS) implantation, is predicated on the overall physiologic, nutritional, and psychosocial status of the patient. Patients can also present acutely with stage D heart failure (eg, acute myocardial infarction with cardiogenic shock or fulminant myocarditis). Such patients are quite different from chronic heart failure patients that gradually progress to stage D, but they are equally if not more clinically challenging owing to limited data to guide clinical decision making.

With the advent of specialty training in advanced heart failure and recognition of this expertise,[2] there is a clear need to reassess the current state of the field. In the present statement, we review the current status and understanding of stage D heart failure, with particular emphasis on patient assessment, triggers for timely referral, treatment options, and research priorities.

Epidemiology and Survival

Data are scarce regarding the epidemiology of stage D heart failure. Data from Olmstead County, Minnesota, suggests that <1% of patients with heart failure are in stage D.[3] Worldwide data are not available. When HFrEF reaches stage D, patients are subject to exceptionally high mortality. In the landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, stage D patients who were treated medically experienced 75% mortality at 1 year and virtually no survival at 2 years.[4] Optimally treated patients in the Investigation of Non–Transplant-Eligible Patients Who Are Inotrope Dependent (INTREPID) trial had survival rates of 22% at 6 months and 11% at 1 year.[5] In a random population-based sample from Olmstead County, stage D heart failure was associated with only 20% 5-year survival.[3] Patients bridging to end of life on continuous inotropes have the poorest survival: 6% at 1 year.[6]

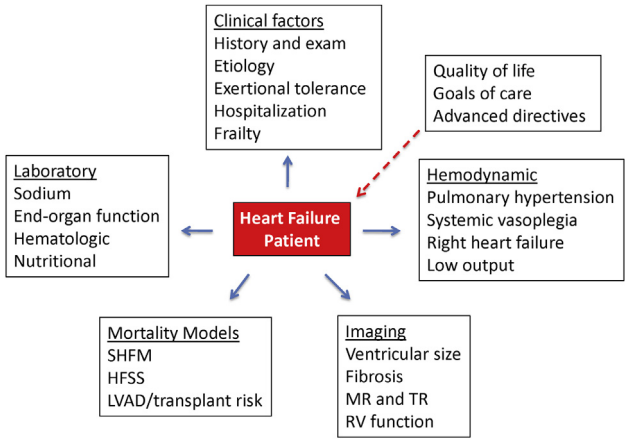

Fig. 1. Assessment domains in advanced (stage D) heart failure. SHFM, Seattle Heart Failure Model; HFSS, Heart Failure Survival Score; LVAD, left ventricular assist device; MR, mitral regurgitation; TR, tricuspid regurgitation; RV, right ventricular.

Defining Advanced Heart Failure

A precise definition of advanced heart failure is important, but it has proven to be difficult because heart failure progression is highly variable and the exact course is uncertain.[7] One can debate whether advanced heart failure should be primarily defined by subjective signs and symptoms, mortality risk, or other more objective variables, such as imaging assessments, biomarkers, and hemodynamics (Fig. 1). Symptoms can be nonspecific and do not necessarily correlate with mortality risk. Attempts to characterize heart failure progression are relevant for describing populations, but they remain too imprecise for assessment of individual patients.[8–10] Current prognostic models are limited by the interpatient variability of heart failure progression, which impairs the applicability of derivation samples and validation in specific patient cohorts. Defining advanced heart failure based on mortality risk is also difficult because there is no consensus on the expected survival that defines advanced.

Various definitions and indicators have been proposed for advanced heart failure (Table 1).[1,11–13] There is usually no single event that defines a patient as having advanced or stage D heart failure. Rather, a pattern of clinical characteristics should suggest that a patient has become refractory to traditional therapies. These characteristics include repeated hospitalizations for heart failure, intolerance or reduction of doses of neurohormonal antagonists, escalation of diuretics, development of end-organ dysfunction, malnutrition (or cardiac cachexia), and refractory arrhythmias with or without device shocks.[1] These "triggers" can identify the