Universal Definition and Classification of Heart Failure

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Editorial

Universal Definition and Classification of Heart Failure: Is It universal? Does It Define Heart Failure?

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A milestone event in heart failure (HF) has occurred. For the first time, a universal definition of HF has emerged via the aggregate efforts of representatives from the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, and Japanese Heart Failure Society with endorsement by Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and the Chinese Heart Failure Association.

The new definition first describes HF as a "clinical syndrome"; next, it obligates the definition to include either symptoms or signs attributable to structural and/or functional cardiac abnormality; and then requires corroboration with either elevated natriuretic peptides or hemodynamic (either measured directly or inferred noninvasively) evidence of congestion (Table 1). To appreciate this new definition, it is important to recognize what it supplants: the traditional pathophysiologic definition—"a condition in which the heart cannot pump enough blood to meet the body's needs." The pathophysiologic definition is difficult to apply clinically and frankly fails in patients who, for example, maintain cardiac output via tachycardia or left ventricular dilatation despite a reduced ejection fraction. The necessity to develop a new definition was self-evident.

The new definition embraces mechanistic heterogeneity and is importantly ejection fraction agnostic. It highlights the syndromic nature of the condition, and notably, infers biology. The explicit requirement for both structural or functional heart disorders and the detection of natriuretic peptides elaborated in response to changes in intraventricular pressure and subsequent increases in wall stress now establishes a biological premise as a necessity to diagnose HF. Natriuretic peptides play a central role in confirming or excluding a diagnosis of HF in many clinical settings, yet they have not been included in most definitions of HF. The specific mention of these biomarkers in the universal definition of HF is foundational and analogous to the universal definition of myocardial infarction, where elevations of a biomarker (troponin) are fundamental to the definition.

The progress this new definition represents is not trivial. This is not perfunctory academic musing, but a critical thesis that recalibrates both the clinical and the scientific approaches. As a new statement of primacy, patients who fail to meet the requirements of this definition may benefit from the freedom to explore different modes of therapy. For example, those with heart muscle disorders only, or cardiomyopathies, need not carry the hefty diagnosis of HF; rather, the focus can be on familial tendencies for dilated cardiomyopathies, arrhythmogenic cardiomyopathies, and/or inherited causes of sudden death.

This writing committee also addressed the stages of HF (Table 1). The additional texture addressing American College of Cardiology/American Heart Association stage A and stage B as "at risk for HF" and "pre-HF," respectively, greatly facilitates new discovery of pre-emptive therapies halting the progression from pre-HF stages to overt HF. Given the change in patient outcomes associated with advancing stages, this is a major step forward. Moreover, the delineation of these earlier stages as pre-HF and not HF itself (the latter now restricted to the symptomatic state) supports clearer clinical communication—risk factors for HF are just that; they are not part of the definition of HF,

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Table 1. Comparison of the New Universal Definition With Prior Definitions of HF

Prior Definitions (Examples)	Universal Definition	Comments
HF is the inability of the heart to pump blood to the body at a rate commensurate with its needs, or to do so only at the cost of high filling pressures.	HF is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.	The universal definition includes the core elements of identifying HF as a *clinical syndrome* (ie, a typical cluster of symptoms and signs) and evidence of structural/functional heart disease, while adding, for the first time, mention of raised natriuretic peptides—biomarkers with the highest class of recommendation to support or refute a diagnosis of HF.
Stages are • HF stage A, patients at high risk for HF but without structural heart disease or symptoms of HF; • HF stage B, structural heart disease but without signs or symptoms of HF; • HF stage C, structural heart disease with prior or current symptoms of HF; and • HF stage D, refractory HF requiring specialized interventions.	Stages are • At-risk for HF, patients at risk for HF but without current or prior symptoms or signs of HF and without structural or biomarkers evidence of heart disease; • Pre-HF, patients without current or prior symptoms or signs of HF, but evidence of structural heart disease or abnormal cardiac function, or elevated natriuretic peptide levels; • HF, patients with current or prior symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality; • Advanced HF, patients with severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite GDMT, refractory or intolerant to GDMT, requiring advanced therapies.	Pre-symptomatic stages (at risk for HF and pre-HF) are no longer covered under the universal definition as having HF—the definition of "HF" being restricted to the symptomatic clinical condition—thus clarifying population estimates of "HF"(referring to the clinically manifest condition rather than its risk factors), while preserving the emphasis on prevention of HF in at risk and pre-HF populations.
Classification according to LVEF: • HFrEF, LVEF <40%; • HFmrEF or HF borderline EF, LVEF 40% to 49%; and • HFpEF, LVEF ≥50%	Classification according to LVEF: • HFrEF, LVEF ≤40%; • HFmrEF, LVEF of 41%−to 49%; • HFpEF, LVEF ≥50%; and • HFimpEF: baseline LVEF ≤40% with ≥10-point increase from baseline and second measurement of LVEF >40%	The universal definition proposes LVEF categories that define groups where treatment differs, replacing "mid-range" with "mildly reduced" in HFmrEF given emerging evidence that patients with HFmrEF may benefit from neurohormonal blockade proven to improve outcomes in patients with more "reduced" EF and in contrast to those with HFpEF. Furthermore the universal definition emphasizes the importance of the *LVEF trajectory*—GDMT can improve LVEF in HFrEF; conversely a significant decrease in the LVEF over time is a poor prognostic factor calling for consideration of intensification of therapy.
	Other terms: • "New onset/de novo HF," referring to the patient who newly transitioned from pre-HF to HF; • "Worsening HF," where there is deterioration of HF signs and symptoms despite ongoing therapy, requiring hospitalization or outpatient escalation of therapy; • "Persistent" for lack of improvement, to be recognized as a marker of worse prognosis prompting clinicians to further optimize therapy; • "In remission" for patients who have resolution of symptoms and signs of HF along with resolution of previously present structural/functional heart disease after a phase of symptomatic HF.	Highlighting both the *clinical trajectory* (ie, improving vs stalled or persistent vs worsening) and the stage of the patient's natural history ideally facilitates optimal management. The universal definition specifically recommends the terminology "in remission" in preference to "recovered", and "persistent" avoiding the term "stable" —as a caution against therapeutic complacency or inappropriate withdrawal of therapy.

GDMT, guideline-directed management and therapy; HF, heart failure; HFimpEF, heart failure with improved ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction.

which requires symptoms. Yet the term pre-HF still conveys the continuum of risk and encourages the discovery of more HF preventive approaches. The further terms "de novo" vs "worsening," and "improving" vs "persistent" vs "in remission" to describe the patient's clinical trajectory all represent major steps forward in precise, more standardized nomenclature (Table 1).

However, this new definition remains imperfect. The classification schemes according to ejection fraction lack biological premise and may once again represent convenience sampling (Table 1). Recent investigations now challenge the upper thresholds for HF with reduced ejection fraction, showing that the "cut-point" for HF with preserved ejection fraction may begin at a left ventricular ejection

fraction of 0.57.[1] The recognition of a population with a "mildly reduced" ejection fraction helps to move the left ventricular ejection fraction cut-point higher and enlarge the treatment population who may potentially benefit from neurohormonal blockade[2]; nonetheless, the cut-point of 50% hardly seems high enough, especially in women, the elderly, and in some racial/ethnic groups.[3] Moreover, what is the biological foundation for HF with an improved ejection fraction? The clinical observations are noted and now widely reported, but is the correct delta of 10 or more "points" and is there evidence that outcomes are better if the peak improvement is greater than 40% when a number less than 40% might represent a 100% increase in ventricular function over baseline? What is the proven natural history for this important new phenotype?

An even more basic argument is the singular focus on ejection fraction. Contemporary echocardiographic imaging laboratories provide robust descriptions of ventricular strain and cardiac MR suites routinely provide extracellular fraction, T1, T2, times and accurate volumetric measurements. A classification scheme limited to ejection fraction remains a handicap, but a more novel scheme that enhances ejection fraction via new measures of ventricular performance might, once again, better partition patients achieving greater homogeneity and better targets for clinical care and for clinical science.

This new definition is a milestone in HF. It is universal, it is broadly applicable, it embraces more of what we know, and many can use it. The list of signatory organizations endorses the potential for widespread international adoption. However, does it fully "define" HF? Certainly, the definition per se is a step forward, particularly with the inclusion of natriuretic peptide elevation and the refinement of the stages of HF is important; yet the classification scheme revisits old standards that were never standardized. The hope is that we use this new definition and classification scheme and continue a process of scientific inquiry, discovery and further refinement of the definition, stages, and classification schemes. Patients expect diagnostic clarity, physicians need guidance, investigators desire directions, and this new universal definition is responsive to those needs and expectations.

Declaration of Competing Interest

None relevant to present work.

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