Universal Definition and Classification of Heart Failure

By Theodore J. Berei, Pharm.D., MBA, BCCP

Reviewed by James C. Coons, Pharm.D., FCCP, FACC, BCCP; and Evan J. Peterson, Pharm.D., BCCP

LEARNING OBJECTIVES

1. Account for how heart failure (HF) is diagnosed using signs, symptoms, and other objective markers.
2. Distinguish between existing definitions of HF related to ejection fraction and staging and the updated universal definition and classification of HF.
3. Evaluate how changes to the definition of HF will affect future clinical research and therapeutic approaches.

ABBREVIATIONS IN THIS CHAPTER

EF	Ejection fraction
GDMT	Guideline-directed medical therapy
HF	Heart failure
HFimpEF	HF with improved EF
HFmrEF	HF with mildly reduced EF
HFpEF	HF with preserved EF
HFrEF	HF with reduced EF
LVEF	Left ventricular EF
UHF	Universal definition and classification of HF

Table of other common abbreviations.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome with a great deal of ambiguity and lack of consensus regarding its clinical definition and diagnosis. Current cardiovascular organizational guideline definitions encompass a variety of approaches to defining HF, with some focused more overtly on diagnostic parameters related to hemodynamic characterization of this patient population and others focused on the hallmark features of HF as a clinical syndrome. Clinicians are ultimately left to process these individual definitions into their own interpretation of HF, which can lead to misdiagnosis and lack of appropriate treatment for patients. The recently released 2021 universal definition and classification of HF (UHF) consensus statement by the Heart Failure Society of America (HFSA), the Heart Failure Association of the European Society of Cardiology (HFA), and the Japanese Heart Failure Society (JHFS) aims to provide both a uniform and a contemporary definition of HF using the most recently available clinical evidence (Bozkurt 2021).

Homogenizing the clinical definition of HF will serve a variety of critical purposes. Given the ever-expanding prevalence of HF, it is hoped that a singular definition will help clinicians properly identify and treat patients at risk of or with overt HF (Virani 2020). Communication within and outside the medical sphere will also be streamlined, empowering shared decision-making among the medical team and with patients. A universal definition, finally, will offer the ability to frame clinical research, trial design, and registries in unison with a universally accepted approach to the diagnosis and architecture of distinct HF phenotypes. Although this definition will undoubtedly require further revision as scientific understanding of HF phenotypes and risk factors improves, it offers a starting point on which to build.

EXISTING DEFINITIONS OF HF

The preexisting framework for the diagnosis of HF considers many factors, including the presence of structural and/or functional cardiac disease and dysfunction, clinical signs and symptomatology, pathogenic serum biomarker concentrations, and abnormal results from imaging studies. Table 1 provides existing guideline definitions from the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), HFSA, ESC, HFA, and JHFS (Tsutsui 2019; Yancy 2017; Ponikowski 2016). Heart failure is a clinical syndrome that requires not only the presence of patient symptomatology, but also an underlying structural or functional defect contributing to the elevation in intracardiac pressures, often with accompanying congestion. Compared with early definitions from pioneers in the field (Denolin 1983; Wagner 1977) that primarily focused on the heart's inability to pump blood commensurate to metabolic requirements because of pathophysiologic cardiac abnormalities, the current definitions offer scarcely more nuance.

Many underlying causes can lead to clinical disease, and there is no established benchmark test for clearly identifying patients with HF. A unifying diagnosis can be challenging compared with other disease states having a more standardized diagnostic approach. Consequently, there is concern that many patients have active HF that is undiagnosed. Therefore, a clearer definition of HF will provide clinicians with a more straightforward approach to making an accurate diagnosis. After diagnosis, the underlying cause must be determined because therapeutic approaches may differ and reversible causes may need to be addressed (e.g., valvular disease, tachycardia-mediated cardiomyopathies, drug-induced cardiomyopathies).

As important as defining clinical HF in an accurate and actionable format is having defined staging and classification criteria from which therapeutic modalities can be formulated. To date, clinical trials have used both ejection fraction (EF) classification (see Table 1) and staging (Table 2) to develop guideline-directed device and pharmacotherapy-based approaches. Prognostically, these classifications are important because they can inform shared decision-making with patients and lead to appropriate discussions of goals of care early during treatment.

Classification According to EF

Left ventricular ejection fraction (LVEF), typically gathered from transthoracic echocardiography (TTE), is organized into three main phenotypes, with different nomenclature depending on the organizational guideline (Table 1). Globally, HF with reduced ejection fraction (HFrEF) is defined as an EF less than 40%, with the American guidelines slightly differing, distinguishing HFrEF as 40% or less. Of the many EF phenotypes, evidence for use of device and pharmacotherapy is most robust within this grouping, and HFrEF accounts for almost one-half of all patients living with HF (Yancy 2017).

Both the ACCF/AHA/HFSA and the JHFS mention HF with improved EF (HFimpEF), which they define as a baseline EF of 40% or less with a 10-point or greater increase from baseline and a repeat EF measurement greater than 40%. Withdrawal of guideline-directed medical therapy (GDMT) in these patients is generally not advised as recent evidence has demonstrated a greater risk of relapse to HFrEF than those receiving uninterrupted therapy (Halliday 2019).

All three guidelines (i.e., ACCF/AHA/HFSA, ESC/HFA, and JHFS) agree that HF with preserved ejection (HFpEF) is an EF of 50% or greater. Therapeutic approaches within this class are more limited, though mineralocorticoid receptor antagonists (Pitt 2014), angiotensin receptor-neprilysin inhibitors (Solomon 2019), and sodium-glucose cotransporter-2 inhibitors (Anker 2021) are potential therapies.

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- General knowledge of the pathophysiology that leads to heart failure (HF) and the variety of causes leading to cardiac dysfunction
- Understanding of contemporary classifications of HF and use of ejection fraction as a parameter for clinical trial enrollment and design

Table of common laboratory reference values.

ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- Journal of Cardiac Failure. Universal Definition and Classification of Heart Failure
- American College of Cardiology, American Heart Association, Heart Failure Society of America. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure
- Japanese Cardiology Society/Japanese Heart Failure Society. JCS 2017/JHFS 2017 Guideline on Diagnosis and Treatment of Acute and Chronic Heart Failure
- Canadian Cardiovascular Society. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure
- European Society of Cardiology, Heart Failure Association of Europe. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
- American Heart Association/American College of Cardiology/Heart Failure Society of America. 2022 Guideline for the Management of Heart Failure

Table 1. Guideline Definition and Classification of HF by Major Cardiovascular Societies

Organization	Definition	Classification
ACCF/AHA/HFSA (2013/2017)	HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood	HFrEF: ≤ 40% HFpEF: ≥ 50% Borderline: 41%–49% Improved: > 40%
ESC/HFA (2016)	HF is a clinical syndrome characterized by typical symptoms (e.g., breathlessness, ankle swelling, and fatigue) that may be accompanied by signs (e.g., elevated jugular venous pressure, pulmonary crackles, and peripheral edema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress	HFrEF: < 40% HF mid-range EF: 40%–49% HFpEF: ≥ 50%
JHFS (2017)	HF is a clinical syndrome consisting of dyspnea, malaise, swelling, and/or decreased exercise capacity because of the loss of compensation for cardiac pumping function as the result of structural and/or functional abnormalities of the heart	HFrEF: < 40% HF mid-range EF: 40%–50% HFpEF: ≥ 50% HFpEF improved: ≥ 40% with prior EF < 40%

EF = ejection fraction; HF = heart failure; HFimpEF = HF with improved EF; HFpEF = HF with preserved EF; HFrEF = HF with reduced EF.

Information from: 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; Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129-200; Tsutsui H, Isobe M, Ito H, et al. JCS 2017/JHFS 2017 guideline on diagnosis and treatment of acute and chronic heart failure. Circ J 2019;83:2084-184.

Patients with an EF of 41%–50% without previous HFrEF are classified as having HF with a mid-range ejection, though international guidelines vary slightly. The ACCF/AHA/HFSA guidelines, using an EF range of 41%–49%, sub-classify this as borderline HFpEF. The European and Japanese guidelines consider this HF with a mid-range EF (ESC/HFA: 40%–49%, JHFS: 40%–50%). Although clinical research is in its infancy for this phenotype, current data suggest therapeutic responses to typical HFrEF GDMT (Heidenreich 2022).

Classification According to Staging

Heart failure is most commonly classified using the ACCF/AHA and NYHA classification schemas (see Table 2). The ACCF/AHA staging incorporates both patient symptomatology and pathophysiologic processes, including high-risk comorbidities, that may lead to or be contributing to active HF. Staging nomenclature ranges on a continuum from A to D. The NYHA classification incorporates a numeric grading scheme ranging from I to IV, solely focusing on patient symptomatology without mention of high-risk factors or preexisting structural or functional cardiac deficits.

Biomarkers as a Tool to Support HF Diagnosis

Although HF can be diagnosed from identifying a structural or functional substrate causing cardiac dysfunction together with corresponding patient symptoms, both biomarkers and hemodynamic monitoring often play a key role in developing a unified diagnosis. The usefulness of biomarkers, particularly high-sensitivity assays, has significantly grown as a tool for disease diagnosis and prognostication. Both BNP and N-terminal pro-BNP (NT-proBNP) play a key role in patients with HF, often signaling worsening disease. These peptides are released in response to ventricular stretching as the body's compensatory mechanism to curb rising cardiac filling pressures. Contemporary clinical guidelines give class I recommendations to use either biomarker to support a clinical diagnosis of HF, assess disease severity, and establish the prognosis, though BNP is not formally part of any preexisting HF definitions (Yancy 2017). Several studies have assessed the usefulness of BNP and NT-proBNP reduction as markers of response to GDMT, finding an association between curbed left ventricular remodeling, increased LVEF, and reduction in a variety of morbidity-related outcomes (Januzzi 2019; Felker 2017).

Unlike measuring troponin to diagnose myocardial infarction or measuring A1C to diagnose diabetes, data remain unclear on BNP or NT-proBNP as an individual means of HF diagnosis. Investigators have proposed potential diagnostic thresholds for BNP (Cleland 2021), though this remains unvalidated in clinical practice. Of note, at baseline, BNP is often higher in women than in men, and with age and declining renal

Table 2. Former Staging/Classification of HF Compared with UHF

Former Definition	Universal Definition
Inability of the heart to pump blood to the body to satisfy metabolic demands and prevent tissue hypoperfusion, ultimately leading to clinical signs and symptoms of congestion	Clinical syndrome with signs/symptoms caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide concentrations and/or objective evidence of pulmonary or systemic congestion
Staging *ACC/AHA* • Stage A: Patients at risk of HF who have not yet developed structural heart changes • Stage B: Patients with structural heart disease who have not yet developed symptoms of HF • Stage C: Patients who have developed symptomatic HF • Stage D: Patients with refractory HF requiring advanced intervention *NYHA* • Functional class I: No limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea • Functional class II: Slight limitation of physical activity. Comfortable at rest; ordinary physical activity results in fatigue, palpitation, dyspnea • Functional class III: Marked limitation of physical activity. Comfortable at rest; less-than-ordinary activity causes fatigue, palpitation, or dyspnea • Functional class IV: Unable to carry on any physical activity without discomfort. Symptoms of HF at rest. If any physical activity is undertaken, discomfort increases	• At-risk (stage A): Patients at risk of HF but without current or prior symptoms or signs of HF and without structural or biomarker-based evidence of heart disease • Pre-HF (stage B): Patients without current or prior symptoms or signs of HF, but evidence of structural heart disease or abnormal cardiac function, or elevated natriuretic peptide concentrations • HF (stage C): Patients with current or prior symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality • Advanced HF (stage D): Patients with severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite GDMT, refractory to or intolerant of GDMT requiring advanced therapies *Of note, NYHA functional classifications are maintained in the UHF definition*
EF Classification • HFrEF: EF ≤ 40% • HFmrEF: EF 41%–49% • HFpEF: EF ≥ 50%	• HFrEF: EF ≤ 40% • HFmrEF: EF 41%–49% • HFpEF: EF ≥ 50% • HFimpEF: Baseline EF ≤ 40% with ≥ 10-point increase from baseline and repeat measurement of EF > 40%

EF = ejection fraction; GDMT = guideline-directed medical therapy HFREF = HF with reduced ejection fraction; HFmrEF = HF with mildly reduced EF; NYHA = New York Heart Association; UHF = universal definition and classification of HF.

Information from: 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; Bozkurt B, Coats AJ, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Eur J Heart Fail 2021;23:352-80.

function, BNP often accumulates, given decreased clearance. Many additional clinical factors can also affect BNP concentrations, which should be considered when using this tool (Bozkurt 2021). An inverse relationship exists between serum BNP/NT-proBNP concentrations and BMI (Bachmann 2021). Future research aims to add clarity to the usefulness of biomarkers as the sole means of diagnosing patients on the HF continuum, but for now, they should be used to complement existing diagnostic approaches.

NEW UHF GUIDELINES

Previous definitions of HF did not clearly delineate between patients on the HF continuum and those with comorbidities and/or structural defects at risk of developing active disease. The newly proposed contemporary definition (see Figure 1) aims to provide a simplified approach, with universal applicability, to identify these patients without sacrificing diagnostic sensitivity and specificity (Bozkurt 2021). The new UHF defines HF as a clinical syndrome with symptoms and/or signs

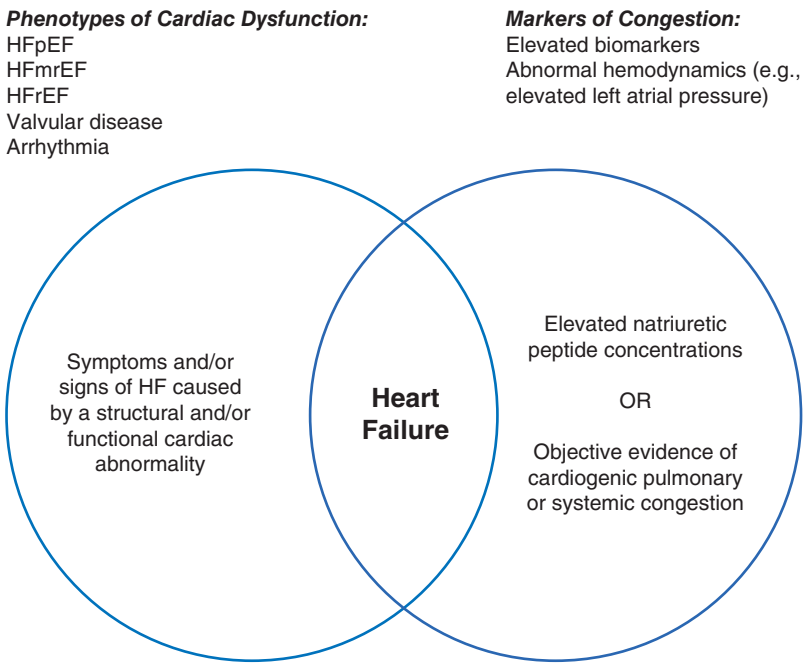

Figure 1. Graphic representation of the new universal definition of heart failure.

HF = heart failure; HFmrEF = HF with mildly reduced ejection fraction; HFpEF = HF with preserved ejection fraction; HFrEF = HF with reduced ejection fraction.

Information from: Bozkurt B, Coats AJ, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Eur J Heart Fail 2021;23:352-80.

of HF caused by a structural and/or functional cardiac abnormality that must be corroborated by either elevated natriuretic peptide concentrations or objective evidence of cardiogenic pulmonary or systemic congestion as revealed by diagnostic modalities (e.g., invasive hemodynamics, elevated jugular venous pressure, dilated superior vena cava on ultrasonography). The UHF defines elevated natriuretic peptide concentrations as BNP 35 pg/mL or greater and NT-proBNP 125 pg/mL or greater for ambulatory patients and BNP 100 pg/mL or greater and NT-proBNP 300 pg/mL or greater for decompensated patients. This updated definition provides a foundation on which more accurate sub-classification and staging can take place.

The UHF offers a streamlined four-stage approach (Figure 2) that encompasses the spectrum of those at risk of HF to those with advanced disease requiring mechanical support and/or transplantation. The four stages are at-risk (stage A), pre-HF (stage B), HF (stage C), and advanced HF (stage D). Individuals with comorbidities, particularly atherosclerotic cardiovascular disease, hypertension, type 2 diabetes, obesity, exposure to cardiotoxins, and/or a family/genetic history, are considered in the at-risk stage. This is a distinct difference, particularly from the ACCF/AHA stage A criteria, in which someone with risk factors would be labeled as having "HF," which semantically could be confusing to the patient. Those with pre-HF staging, like those with ACCF/AHA stage B, may have structural cardiac abnormalities. In addition, abnormal cardiac function or elevated biomarkers may be used to subsequently categorize patients' diseases as pre-HF as long as patients are without current or prior HF symptoms. Similarly, the ACCF/AHA stage B criteria may imply someone has "HF," whereas the UHF implies what may eventually occur. Applying a more accurate label to a patient's current state and clinical trajectory at a specific time ultimately allows for tailored discussions of goals of care and informed, shared decision-making.

The implications for pharmacotherapy and device therapy also vary greatly between those at risk of developing HF and those with clinical disease. Heart failure (stage C) requires patients to have either current or past HF symptoms together with a structural/functional cardiac abnormality. This stage is further sub-divided into persistent HF (patients who remain symptomatic despite intervention) and HF in remission (patients with resolution of signs or symptoms of HF together with resolution of previously present structural and/or function heart disease after a phase of symptomatic HF). Of note, the UHF guidelines do not recommend

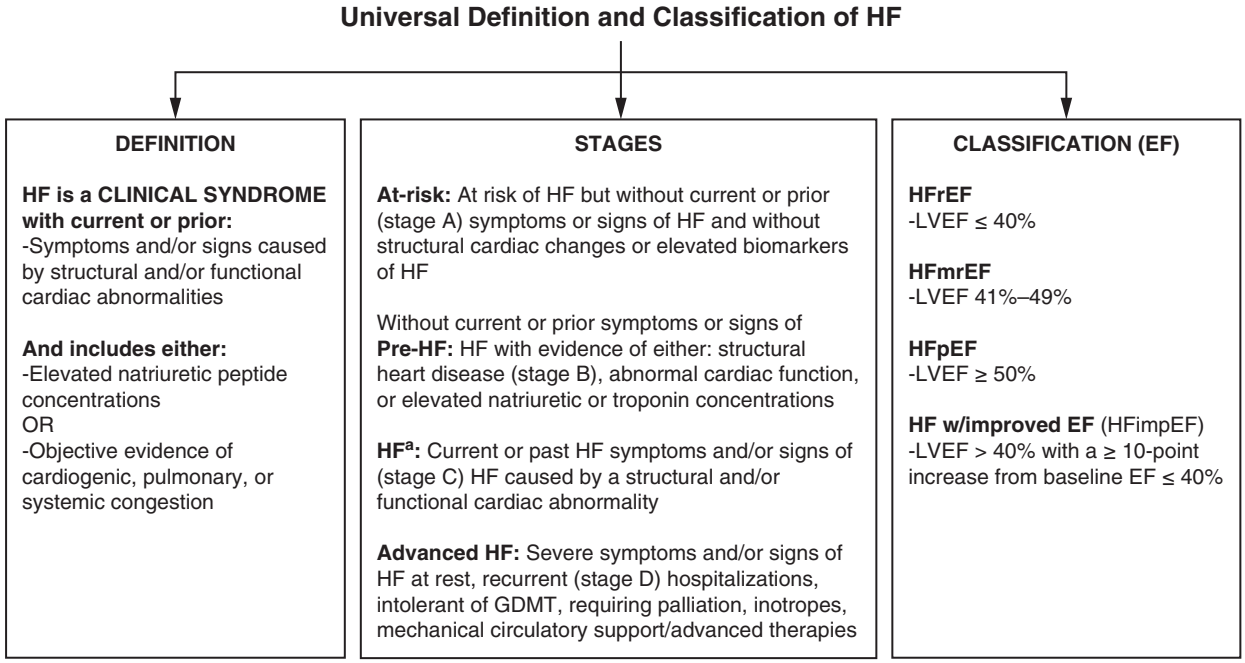

Figure 2. Diagrammatic representation of the new universal definition and classification of heart failure.

[a]Sub-categorized into two distinct trajectories: persistent HF (replaces use of the term *stable HF*) and HF in remission (replaces use of the term *recovered HF*).

GDMT = guideline-directed medical therapy; LVEF = left ventricular ejection fraction.

withdrawing pharmacotherapy in patients whose disease is considered to be in remission. Patients with advanced HF (stage D) have severe symptoms at rest and are refractory to or intolerant of typical GDMT, requiring inotropic support, mechanical circulatory support, transplantation, or palliation.

The harmonized UHF staging allows for linear movement from at-risk to pre-HF and pre-HF to either HF or advanced HF. Patients with HF, however, cannot move backward in their trajectory and will instead transition between persistent HF and HF in remission. As such, patients with advanced HF can move back to HF staging, though rarely, pending clinical response to therapies. Those requiring durable mechanical support or home inotropes, even if asymptomatic after such therapies are initiated, will maintain the advanced HF staging.

Like in previous guidelines, LVEF in UHF is used to classify patients' disease once staging has been determined. Past and current research efforts have largely focused on determining the prognosis for these specific LVEF phenotypes together with their response to therapeutic interventions. There are four distinct LVEF classes, three of which – HFrEF (LVEF 40% or less), HFpEF (LVEF 50% or greater), and HFimpEF (EF greater than 40% with a 10-point or greater increase from baseline EF of 40% or less) – remain unchanged from the 2017 ACCF/AHA/HFSA guidelines. Heart failure with mildly reduced EF (HFmrEF, 41%–49%) replaces borderline HF.

Combined with the staging and classification of patients within the HF continuum, particularly those with symptomatic HF, is the unwavering need for identifying the underlying cause of disease. Addressing reversible causes, in addition to device and pharmacotherapy, will thwart further cardiac dysfunction and allows patients to potentially achieve remission. Similarly, using this contemporary framework in all clinical settings will allow for early identification of patients at risk of developing clinical disease.

CONCLUSION

The new UHF aims to streamline the diagnosis of HF while ensuring patients at risk of developing HF or with pre-HF are identified sooner to increase the potential for early intervention. Although the UHF does not replace preexisting staging criteria, it offers clinicians a new framework to clinically delineate patients across the spectrum of this syndrome. At the same time, the UHF recognizes the importance of consistency when it comes to medical vernacular among health care providers and patients. Having distinct staging across the risk continuum may empower patients and those caring for them to play an even more active role in managing their health. This is further reinforced through a change from using "failure" to "function." (Bozkurt 2021). Use of the UHF will also directly affect clinical research aimed at discovering

Patient Care Scenario

J.M. presents to your outpatient heart function (formerly "heart failure") clinic this afternoon for a follow-up. His medical history is significant for HF, an MI (3 years prior with two drug-eluting stents placed), hypertension, type 2 diabetes, hyperlipidemia, and obstructive sleep apnea. He endorses no HF symptoms at rest, when doing daily activities, or while exercising. His annual ECHO reveals an EF of 55% (formerly 20% after his MI). J.M.'s current medications include sacubitril/valsartan 97 mg/103 mg twice daily by mouth, spironolactone 25 mg once daily by mouth, dapagliflozin 10 mg once daily by mouth, metformin immediate release 500 mg twice daily by mouth, amlodipine 5 mg once daily by mouth, metoprolol succinate 150 mg once daily by mouth, aspirin 81 mg once daily by mouth, and rosuvastatin 20 mg once daily by mouth. As you write the progress note for your encounter with J.M., which would be the most appropriate stage and classification to document for J.M.'s current heart function?

A. Advanced HF/HF with mildly reduced EF (HFmrEF)

B. Advanced HF/HF with improved EF (HFimpEF)

C. Persistent HF/HFimpEF

D. HF in remission/HFimpEF

ANSWER

J.M. has HF in remission/HFimpEF (Answer D is correct). The recently released UHF document (see Figure 2) now defines HF by staging and classification. Because this patient does not appear to be experiencing HF symptoms at rest, has not had multiple recent HF-related hospitalizations, and is not receiving any form of mechanical circulatory support, he would not fit into the advanced HF staging. Furthermore, because the patient was previously diagnosed with clinical HF, he would also not fit into the pre-HF or at-risk stage, leaving him in the HF stage. Heart failure is further categorized into both persistent HF and HF in remission. Because J.M. has had a greater than a 10% increase in EF – given his current EF of above 40% – and no signs or symptoms of HF, his disease would be staged as HF in remission, with a classification of HFimpEF.

1. Bozkurt B, Coats AJ, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Eur J Heart Fail 2021;23:352-80.
2. 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.

therapeutic approaches and refining the implementation of necessary practice changes for the prevention and treatment of HF. Future research will not only focus on the treatment of those with HF, but also further address questions to help curb disease progression in those with at-risk or pre-HF staging. Further developing our current knowledge of specific phenotypes within this staging will also shed light on which patients are best suited for preexisting and forthcoming therapies.

Practice Points

The UHF offers a new perspective on how clinicians can characterize patients on the risk continuum for HF. In recognizing the importance of how medical vernacular may be interpreted by patients and providers, the UHF empowers clinicians with a clear diagnostic framework. The UHF also provides patients with a more accurate assessment of their current clinical status, with the ability for early intervention with appropriate diagnosis. Other highlights of the UHF include the following:

- **Defines HF as a clinical syndrome with signs/symptoms caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide concentrations and/or objective evidence of pulmonary or systemic congestion.**
- **Identifies four distinct stages: at-risk (stage A), pre-HF (stage B), HF (stage C), and advanced HF (stage D)**
- **Those with HF (stage C) or advanced HF (stage D) are also categorized by EF (See *Figure 2*)**
- **Those with persistent HF (patients who remain symptomatic despite intervention) and HF in remission (patient with resolution of signs or symptoms of HF along with resolution of previously present structural and/or function heart disease after a phase of symptomatic HF) are also included in the UHF guideline.**

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Self-Assessment Questions

Questions 1–3 pertain to the following case.

P.L., a 58-year-old man, presents to a family medicine clinic for his annual physical examination. His medical history is significant for hypertension, type 2 diabetes, and coronary artery disease secondary to a myocardial infarction (MI) (two drug-eluting stents placed to the left anterior descending artery) 3 years ago. P.L. reports feeling more rundown than usual together with extreme fatigue from his daily 2-mile jog, which he used to do without issue. He reports progressive dyspnea recently, and his physical examination reveals noticeable lower extremity edema. His average blood pressure in the clinic is 114/72 mm Hg. All of his laboratory values are within normal limits. P.L.'s home drugs include aspirin 81 mg once daily by mouth, rosuvastatin 20 mg once daily by mouth, metformin 500 mg twice daily by mouth, and chlorthalidone 25 mg once daily by mouth. An ECHO reveals an ejection fraction (EF) of 55% with significant left ventricular hypertrophy and thickening of the ventricular wall.

1. Which one of the following best evaluates P.L.'s heart failure (HF) stage?

   A. Advanced HF
   B. Pre-HF
   C. HF in remission
   D. Persistent HF

2. Which one of the following best evaluates P.L.'s HF classification?

   A. HF with reduced EF (HFrEF)
   B. HF with improved EF (HFimpEF)
   C. HF with preserved EF (HFpEF)
   D. HF with mildly reduced EF (HFmrEF)

3. P.L. is referred to your heart function clinic. A repeat ECHO reveals an EF of 50%. A right heart catherization is completed, demonstrating cardiac output 4.2 L/minute (4–6 L/minute), systemic vascular resistance 1200 peripheral resistance units (normal range: 800–1200 dynes/seconds/cm^{-5}), central venous pressure 12 mm Hg (normal range: 4–10 mm Hg), and left atrial pressure 16 mm Hg (normal range: 8–12 mm Hg). According to the new universal definition and classification of HF (UHF), which one of the following is most needed to make a unifying HF diagnosis for P.L.?

   A. Left atrial pressure
   B. D-dimer
   C. EF
   D. Diabetes diagnosis

4. A 53-year-old woman presents to your heart function clinic after a recent hospitalization for decompensated HF. Her EF was 45% on admission and 55% at discharge. The patient's medical history includes hypertension, type 2 diabetes, morbid obesity, and obstructive sleep apnea. Her home drugs include metformin extended release 1500 mg once daily by mouth, glipizide 5 mg twice daily by mouth, amlodipine 5 mg once daily by mouth, and spironolactone 25 mg once daily by mouth. The patient reports paroxysmal nocturnal dyspnea but otherwise maintains she is symptom free. Physical examination reveals no edema in the lower extremities or rales on auscultation. A BNP results at 65 ng/L (normal range: 0-100 ng/L). The patient's repeat ECHO at the 6-month follow-up reveals an EF of 45%. She continues to have nocturnal dyspnea and now also has noticeable lower extremity edema. Which one of the following best characterizes this patient's stage/classification?

   A. Persistent HF, HFpEF
   B. Persistent HF, HFrEF
   C. Persistent HF, HFmrEF
   D. Advanced HF, HFmrEF

5. You are granted access to a large Medicare data set with 15 years of retrospective data from which you can extract BNP concentrations and incident HF. Using a BNP threshold of 100 ng/L for identifying patients with incident HF, you identify 123,000 patients with a BNP of 100 ng/L or greater out of 2.37 million total patients without previously diagnosed HF. Of the 123,000 patients, 100,000 are eventually diagnosed with HF. According to these data, which one of the following best depicts the specificity of using BNP as a diagnostic tool for HF?

   A. 68%
   B. 98.9%
   C. 9.89%
   D. 95.7%

Questions 6 and 7 pertain to the following case.

P.W., a man, returns to a heart function clinic for a follow-up after a recent escalation in his guideline-directed medical therapy (GDMT). He reports that he no longer becomes short of breath when walking around at work or at home. P.W.'s peripheral edema has also improved since his last visit 4 months ago. A review of his most recent laboratory and imaging results reveals marked improvement in the patient's BNP (from 2200 ng/L to 546 ng/L) and left ventricular EF (LVEF) (from 20% to 35%), though he still has signs of structural disease (elevated left ventricular end-diastolic volume on ECHO).

6. Which one of the following best classifies P.W.'s HF according to the previous guidelines versus the new UHF?

   A. Recovered HF; HF in remission
   B. Stable HF; HF in remission
   C. Recovered HF; persistent HF
   D. Stable HF; persistent HF

7. Considering P.W. and the new trajectory terms in the UHF, which one of the following is most likely to be an advantage of the new term *HF in remission*?

   A. Signifies to the patient and provider that treatments may be discontinued immediately.
   B. May keep providers vigilant in treating HF, even when patients' symptoms improve.
   C. Is more objective because it only requires improvement in HF signs, not symptoms.
   D. Is more patient-centric because it only requires improvement in HF symptoms, not signs.

8. A man presents to the ED as a referral from his primary care physician (PCP). During the initial visit to the PCP, the patient was concerned about chest pressure. An ECG in that office was non-revealing, but the patient's BNP was slightly elevated at 125 pg/mL. The patient has no contributory cardiac history, but his father died of an MI in his 40s. The patient now endorses nothing other than chest tightness subjectively. A physical examination in the ED is non-revealing, as is a basic metabolic panel and chest radiography. His other medical history includes chronic kidney disease (stage 4) and non-Hodgkin lymphoma (in remission). The cardiology team is consulted by the ED provider, who is puzzled by the patient's elevated BNP. A bedside TEE reveals an EF of 65%, normal left ventricular wall thickness, and no valvular disease. Which one of the following HF classifications best evaluates this patient's disease?

   A. HFpEF
   B. HFimpEF
   C. No HF
   D. HF with a borderline EF

Questions 9–14 pertain to the following case.

Z.B., a 42-year-old man, presents to the cardiac ICU with decompensated HF. His medical history includes a bicuspid aortic valve with moderate aortic stenosis and asthma. At home, Z.B. uses albuterol as needed and occasionally takes furosemide 20-mg tablets if he feels "puffy." His LVEF in the cardiac ICU, as measured by a bedside ECHO, is 20% (previously 55% a year ago) with a dilated left ventricle and severe aortic stenosis. Z.B. is massively volume overloaded with 4+ pitting edema, audible wheezing, and significant cardiomegaly on radiography, together with a BNP of 950 pg/mL. The patient is initiated on sodium nitroprusside and furosemide infusions but continues to clinically deteriorate. An intra-aortic balloon pump is inserted at the bedside, and a dobutamine infusion is initiated, temporarily stabilizing Z.B.'s condition.

9. According to the UHF, which one of the following HF stages best evaluates Z.B.'s disease?

   A. Advanced HF
   B. HF
   C. Pre-HF
   D. At-risk

10. Z.B., in consultation with the cardiothoracic surgical team, agrees to have his bicuspid aortic valve replaced with a bioprosthetic valve, given the severity of his HF. He successfully recovers from the operation and is nearing discharge. Z.B. has no signs or symptoms of HF, and his physical examination is non-revealing. His ECHO now reveals an EF of 40% with resolved aortic stenosis and a mildly dilated left ventricle. He is initiated on aspirin 81 mg orally once daily, lisinopril 20 mg once daily, metoprolol succinate 25 mg once daily, and spironolactone 25 mg once daily. According to the UHF, which one of the following HF stages best characterizes Z.B.'s disease?

    A. Advanced HF
    B. HF
    C. Pre-HF
    D. At-risk

11. Which one of the following classifications best characterizes Z.B.'s disease?

    A. HFrEF
    B. HFmrEF
    C. HFpEF
    D. HFimpEF

12. One month after his hospital discharge, Z.B. comes to the heart function clinic. His LVEF is now 60% (no left ventricular dilation noted on ECHO), and he continues to be free of HF symptoms. Which one of the following best characterizes Z.B.'s disease?

    A. HFimpEF, HF in remission
    B. HFmrEF, HF in remission
    C. HFpEF, HF in remission
    D. HFpEF, persistent HF

13. Z.B. asks why he needs to take lisinopril, metoprolol succinate, and spironolactone if his HF is "doing better" and he is symptom free. Considering the UHF, which one of the following is the best response to give Z.B.?

    A. We can taper off your HF medications because you are no longer symptomatic.
    B. We can taper off your HF medications because you have no signs of HF.

C. We cannot taper off your medications because you are still considered to have HF.
D. We can taper off your medications because you are no longer considered to have HF.

14. Z.B. decides to stop his HF pharmacotherapy. Six months later, he presents to the clinic with a 13.6-kg (30-lb) weight gain since his last visit. He has 2+ pitting edema and a noticeable jugular venous pressure and reports waking up in the middle of the night short of breath. A repeat ECHO reveals an EF of 40% with a moderate to severely dilated left ventricle. Which one of the following best characterizes Z.B.'s disease?

A. HFrEF, persistent HF
B. HFmrEF, persistent HF
C. HFrEF, HF in remission
D. HFmrEF, HF in remission

15. You are the primary investigator on a clinical trial assessing the efficacy of continued GDMT in patients formerly with HFrEF whose disease is now considered in remission. Which one of the following 55-year-old women with no signs or symptoms of HF is most likely to be excluded from your trial?

A. Patient with elevated troponin
B. Patient with elevated D-dimer
C. Patient with elevated blood pressure
D. Patient with elevated BNP