Diagnosis and management of heart failure

Guan-Hong Lin1，Chieh Chen 2，Da-Ming Liao3

Division of family medicine, Kaohsiung Armed Forces General Hospital Zuoying

Branch1

Division of family medicine, Hualien Armed Forces General Hospital 2

Dental Department, Puli Christian Hospital 3

Corresponding author: Chieh Chen

guppy5230@yahoo.com.tw

Address: No. 198, Minde 1st Street, Hualien city, Hualien County, Taiwan (R.O.C.)

Tel: 0928-698950

E-mail: guppy5230@yahoo.com.tw

Running title: heart failure

**Abstract**

Heart failure is a condition in which the heart becomes weak and unable to pump blood properly to provide the body with enough oxygen. Common causes of heart failure include coronary artery disease (a previous myocardial infarction), high blood pressure, atrial fibrillation (irregular heart rhythm), and valvular heart disease. Left ventricular ejection fraction (LVEF) is an important basis for the diagnosis, treatment and prognosis of heart failure. The clinical distinctions are HFrEF, HFmrEF, and HFpEF (the cut-off points are ≤ 40%, 41-49%, ≥ 50%), although the cut-off points of these LVEFs are not consistent in different ages and medical societies, and the presence or absence of HFmrEF remains controversial; however, the normal value of LVEF is 52-72% (male) and 54-74% (female). Studies have shown that the mortality rate is the lowest when the LVEF is 60-65%, and both LVEF <60% and LVEF >65% were associated with increased mortality.

**Keywords**: heart failure; HFrEF(heart failure with reduced ejection fraction); HFmrEF; HFpEF(heart failure with preserved ejection fraction).

**Introduction**

Heart failure is a systemic disease, clinically characterized by cardiac hypertrophy, coronary heart disease, and ventricular enlargement; the main groups of heart failure are elderly, female, obese, obstructive sleep apnea, hypertension, and chronic kidney disease CKD, atrial fibrillation, concentric hypertrophy and decreased elasticity of the heart, decreased left ventricular volume LVEDV, increased pressure LVEDP, pulmonary hypertension, etc. [1]; the relationship between heart failure and prognosis is the J curve: the mortality rate is the lowest when the LVEF is 60-65% , increased mortality for both LVEF < 60% and LVEF > 65%. Heart failure does not reflect right heart failure: the majority is secondary to left heart failure and predicts a poor prognosis [2]. The prognosis of heart failure has nothing to do with clinical treatment. Although RCT studies have found that only SGLT2i and MRA are effective for HFpEF[2,3], in clinical practice, doctors will use SGLT2i, MRA, ACEI/ARB/ARNI, type B Sympathetic blockers, diuretics, etc., but the pathophysiology of heart failure is quite diverse (aging, cardiomyopathy, endothelial cell dysfunction, sympathetic nerve stimulation, stimulation of renin-corticosterone system, renal absorption of sodium and water increase) [3].

**Common clinical symptoms of heart failure**

Common clinical symptoms of heart failure include[4]: 1. Dyspnea: Dyspnea occurs immediately after physical activity, and in severe cases, even lying in bed or resting will also feel dyspnea. 2. Lower extremity edema: Typical edema is symmetrical and occurs in both calves or ankles. 3. Orthopnea: Severe heart failure patients will feel dyspnea when lying flat, which can be relieved by sitting up or raising the pillow. 4. Paroxysmal nocturnal dyspnea: The patient is easy to wake up from sleep, breathing hard and wheezing, which needs to be relieved by sitting up or opening the window to breathe fresh air. 5. Cough: A large amount of fluid accumulates in the lung branches and stimulates the mucous membrane. It may be a dry cough, or a large amount of frothy and bloodshot sputum may be coughed up. 6. Brain hypoxia: It may be due to the decrease of cardiac output, which causes insufficient blood flow in the brain, resulting in the inhibition of brain function (such as anxiety, restlessness, memory impairment, nightmares, insomnia or dizziness and other symptoms). 7. Hepatomegaly: Symptoms of right upper quadrant pain are easy to appear. 8. Loss of appetite: Liver stagnation of blood and swelling of the liver caused by right heart failure, resulting in abdominal distension in the right upper abdomen, which affects appetite [4,-6].

**Epidemiology and clinical diagnosis of heart failure**

Heart failure can be divided into three types according to the left ventricular ejection fraction LVEF (Left ventricular ejection fraction)[7]:

1. LVEF≤40%: Heart failure with low systolic fraction HFrEF (Heart failure with reduced ejection fraction) often occurs after coronary artery disease and extensive myocardial damage. In terms of overall treatment, treatment suggestions are mainly given for patients with decreased systolic fraction.

2. LVEF ≥ 50%: This is normal systolic fraction. Heart failure HFpEF (Heart failure with preserved ejection fraction) usually progresses slowly and is related to age and metabolic diseases. 3. LVEF is between 41-49%: common clinical symptoms of heart failure include dyspnea, orthopnea, paroxysmal nocturnal dyspnea, nocturnal cough, reduced cardiopulmonary activity, brain hypoxia, decreased urine and lower extremity edema wait [8]. Heart failure has nothing to do with symptoms: severe symptoms can occur regardless of LVEF. Although patients with HFrEF and HFmrEF can predict the improvement of symptoms by the increase of LVEF, patients with HFpEF cannot predict the improvement of symptoms by the decrease of LVEF [9]. The new definition in 2020 is symptoms/symptoms caused by cardiac structural/functional abnormalities (CXR, electrocardiogram, cardiac ultrasound) combined with increased BNP, systemic/pulmonary congestion (abandoning the Framingham diagnostic criteria)[ ]; according to this definition, severe CKD and Dyspnea caused by fluid overload in dialysis patients is not CHF (because the symptoms can be improved by large amounts of diuretics or dialysis). There are several disadvantages in using LVEF to distinguish heart failure; first, the normal value is unknown: although the normal value of LVEF is traditionally considered to be 52-72% (male), 54-74% (female)[10], secondly, different measurement methods (heart Ultrasound, single photon emission computed tomography (SPECT, MRI) results are not consistent: even the inter-measurement variability of the same method can cause differences in classification, and the results of ultrasound are also inconsistent between different examiners[11].

**Newest Clinical recommendations for heart failure**

In 2022, the treatment guidelines for the HFrEF population will be guided by drug therapy (guideline-directed medical therapy), and a total of 4 drugs are recommended for the treatment of heart failure[12]: SGLT2 inhibitor (originally used to treat diabetes), ACEI (Angiotensin converting enzyme inhibitor) /ARB (Angiotensin II receptor blocker)/ARNI (angiotensin receptor neprilysin inhibitor), beta-blocker, MRA (Mineralocorticoid receptor /aldosterone antagonist)[13]; generally clinically, angiotensin converting enzyme inhibitor/angiotensin will be given depending on the severity Receptor blockers are used to dilate peripheral arteries and veins to reduce vascular resistance, thereby reducing the load on the heart and reducing water retention [13]. Beta blockers: reduce cardiac work and ease the burden on the heart [14-16]. Diuretics: The function is to excrete excess water in the body to reduce the burden on the heart [17]. Foxglove: The function is to make the heart contract more powerfully, which can improve the patient's symptoms, but cannot prolong the survival. When combined with atrial fibrillation, it can slow down the heartbeat and reduce palpitations, but it may cause bradycardia[18-20]. For patients with heart failure, the first choice for the treatment of EF between 41-49% is diuretics, followed by SGLT2i (drugs for diabetes, which is also effective for heart failure), antihypertensive drugs: ACEi, ARB and AENI, MRA, type B Sympathetic blockers, etc.[21,22].

**Conclusion**

Heart failure is due to abnormal systolic or diastolic function of the heart, and the heart cannot output enough blood to meet the metabolic needs of various organs in the body. With the development of the disease, patients are often hospitalized due to the deterioration of symptoms, which affects the quality of life; therefore, slowing the deterioration of the disease, reducing mortality, and improving disease-related symptoms are the main goals of the treatment of heart failure [1,22]; according to the statistics data of the National Health Insurance, about 22,000 people in Taiwan are hospitalized every year due to severe heart failure. Without stable and regular treatment or changes in lifestyle, the rate of rehospitalization within 3 months is as high as 30%, and the mortality rate within 5 years is close to 50%, which is higher than the mortality rate of many cancers.

**Reference**

1. Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2022; 2022(145): e895-e1032.
2. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: Executive summary: a report of the American College of Cardiology/American heart association joint Committee on clinical practice guidelines. Journal of the American College of Cardiology 2022; 79(17): 1757-80.
3. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology 2022; 79(17): e263-e421.
4. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. New England Journal of Medicine 2020; 383(15): 1413-24.
5. Kaplinsky E. DAPA-HF trial: dapagliflozin evolves from a glucose-lowering agent to a therapy for heart failure. Drugs in Context 2020; 9: 1-7.
6. McMurray JJ, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381: 1995-2008.
7. Xanthopoulos A, Giamouzis G, Skoularigis J, Triposkiadis F. Heart failure with reduced, mildly reduced, or preserved left ventricular ejection fraction: Has reasoning been lost? World Journal of Cardiology 2022; 14(7): 438-45.
8. Triposkiadis F, Giamouzis G, Kitai T, Skoularigis J, Starling RC, Xanthopoulos A. A holistic view of advanced heart failure. Life 2022; 12(9): 1298.
9. Triposkiadis F, Starling RC. Chronic heart failure: diagnosis and management beyond LVEF classification. Journal of Clinical Medicine 2022; 11(6): 1718.
10. Budde H, Hassoun R, Mügge A, Kovács Á, Hamdani N. Current understanding of molecular pathophysiology of heart failure with preserved ejection fraction. Frontiers in Physiology 2022; 1384.
11. Ferreira JP, Packer M, Butler J, Zannad F. Reconsidering the ejection fraction centric view of pharmacologic treatment for heart failure. European Journal of Heart Failure 2022.
12. Khan MS, Shahid I, Fonarow GC, Greene SJ. Classifying heart failure based on ejection fraction: imperfect but enduring. European Journal of Heart Failure 2022.
13. Lund LH, Pitt B, Metra M. Left ventricular ejection fraction as the primary heart failure phenotyping parameter. European Journal of Heart Failure 2022; 24(7): 1158-61.
14. Severino P, D’Amato A, Prosperi S, Dei Cas A, Mattioli AV, Cevese A, et al. Do the current guidelines for heart failure diagnosis and treatment fit with clinical complexity? Journal of Clinical Medicine 2022; 11(3): 857.
15. Lauritsen J, Gustafsson F, Abdulla J. Characteristics and long‐term prognosis of patients with heart failure and mid‐range ejection fraction compared with reduced and preserved ejection fraction: a systematic review and meta‐analysis. ESC heart failure 2018; 5(4): 685-94.
16. Liang M, Bian B, Yang Q. Characteristics and long‐term prognosis of patients with reduced, mid‐range, and preserved ejection fraction: a systemic review and meta‐analysis. Clinical cardiology 2022; 45(1): 5-17.
17. Karamichalakis N, Xanthopoulos A, Triposkiadis F, Paraskevaidis I, Tsougos E. Reshaping treatment of heart failure with preserved ejection fraction. Journal of Clinical Medicine 2022; 11(13): 3706.
18. Latado AL. Prognosis of heart failure with mid-range ejection fraction: A story or a version? Arquivos Brasileiros de Cardiologia 2022; 118: 701-2.
19. Wehner GJ, Jing L, Haggerty CM, Suever JD, Leader JB, Hartzel DN, et al. Routinely reported ejection fraction and mortality in clinical practice: where does the nadir of risk lie? European heart journal 2020; 41(12): 1249-57.
20. Triposkiadis F, Butler J, Abboud FM, Armstrong PW, Adamopoulos S, Atherton JJ, et al. The continuous heart failure spectrum: moving beyond an ejection fraction classification. European heart journal 2019; 40(26): 2155-63.
21. Pellikka PA, She L, Holly TA, Lin G, Varadarajan P, Pai RG, et al. Variability in ejection fraction measured by echocardiography, gated single-photon emission computed tomography, and cardiac magnetic resonance in patients with coronary artery disease and left ventricular dysfunction. JAMA network open 2018; 1(4): e181456.
22. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Heart Journal-Cardiovascular Imaging 2015; 16(3): 233-71.