

For the Primer, visit [doi:10.1038/nrdp.2017.58](https://doi.org/10.1038/nrdp.2017.58)

➔ Heart failure is a progressive condition in which the heart can no longer supply adequate blood at normal intracardiac pressures to meet the body's metabolic requirements. Heart failure can be classified as either heart failure with reduced ejection fraction (HFrEF) or heart failure with preserved ejection fraction, which each account for ~50% of all cases of heart failure in the United States.

DIAGNOSIS

Transthoracic echocardiogram can be used to determine the left ventricular ejection fraction in individuals with suspected heart failure. An ejection fraction of $\leq 40\%$ in the presence of signs and symptoms of heart failure is sufficient for a diagnosis of HFrEF.

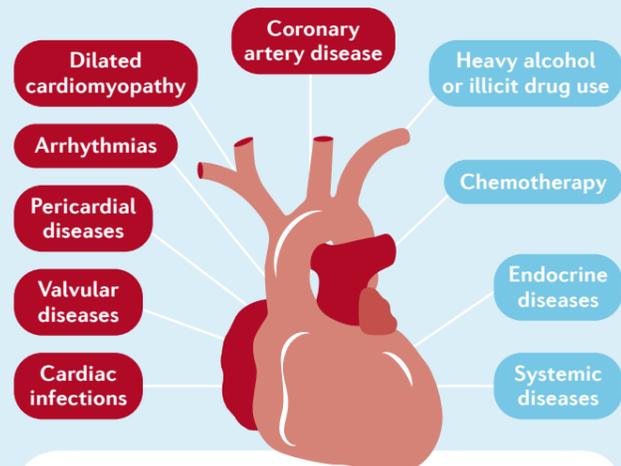
Individuals with confirmed HFrEF, or those at high risk, can be staged using the staging system of the American College of Cardiology Foundation and the American Heart Association

PREVENTION

The main aim in individuals at high risk of heart failure, such as those with certain risk factors, including diabetes mellitus, hypertension or obesity, is to prevent the development of ventricular abnormalities and clinical heart failure. This can be achieved by addressing known risk factors, as well as diet and exercise modification. In asymptomatic individuals with structural heart disease (stage B HFrEF), preventing the development of symptomatic heart failure is key, which can be achieved by screening, close monitoring, pharmacological treatment, disease management strategies and other interventions.

MECHANISMS

HFrEF is the result of an initial injury or disease that affects the heart and results in reduced ventricular contraction. This reduction in ventricular contraction initiates several compensatory mechanisms, including activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS), which regulates arterial blood pressure. Initially, these systems can maintain cardiac output and end-organ perfusion, but chronic activation leads to cardiac hypertrophy, pathological cardiac remodelling and, ultimately, worsening of symptoms.



! The initial event that leads to heart failure can be cardiovascular in origin or can develop in other organs and lead to secondary cardiovascular damage

STAGE A
Individuals at high risk but without structural heart disease or symptoms

STAGE B
Individuals with structural heart disease but with no symptoms

STAGE C
Individuals with structural heart disease and symptoms

STAGE D
Individuals with refractory heart failure requiring specialized interventions

Symptoms include dyspnoea, fatigue, limitations in exercise tolerance and, often, the accumulation of fluid in the lungs, abdomen and lower extremities

Heart failure affects >26 million people worldwide; the global burden of heart failure is increasing and is expected to increase further with the ageing of the world's population

OUTLOOK

Despite the availability of several therapies for HFrEF, patients generally have poor outcomes, underlying the need for new treatments. Accordingly, many therapies are being assessed in clinical trials, including new pharmacological treatments, device-based therapies, gene therapy-based approaches and cell transplantation.

MANAGEMENT Rx

Management of heart failure aims to prevent hospitalization, improve symptoms and improve the quality and duration of life. All patients with symptomatic HFrEF should be initially treated with a combination of pharmacological therapies (including RAAS modulation, a β -blocker and a mineralocorticoid antagonist). Certain patients might be eligible for implantation with a medical device, such as an implantable cardioverter defibrillator or cardiac resynchronization therapy.

Patients with advanced heart failure might require heart transplantation

