Pharmacologic and Surgical Interventions to Improve Functional Capacity in Heart Failure

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KEYWORDS

• Heart failure • Functional capacity • Drugs • Treatments • Surgery • Device

KEY POINTS

- Heart failure is a clinical syndrome of breathlessness, lower extremity swelling, fatigue, and exercise intolerance affecting a large portion of the population worldwide, and associated with premature death.
- Exercise intolerance in heart failure results from, among other things, (1) impaired cardiac contractility, (2) impaired cardiac filling, and/or (3) inappropriate heart rate response.
- Heart failure therapies have multiple goals, including preventing death and hospitalizations and promoting improved symptom control and exercise tolerance.
- Therapies effective in reducing heart failure–related mortality have variable effects on exercise tolerance, with some causing an improvement and some providing no effect or transiently having a negative impact.
- Loop diuretics and aldosterone blockers, although not extensively studied, are routinely used to relieve congestion, improve cardiac filling, and improve exercise tolerance in heart failure.

INTRODUCTION

Heart Failure Syndrome

Heart failure (HF) is a clinical syndrome of breathlessness, lower extremity swelling, fatigue, and exercise intolerance that affects a significant portion of the global population.[1,2] The symptoms and limitations in patients with HF reflect the inability to maintain a cardiac output adequate to the individual's needs and/or the development of inappropriately high cardiac filling pressure leading to pulmonary and/or systemic congestion. Symptoms occurring at rest reflect a severely compromised condition referred to as decompensated HF, which requires urgent care. More often, patients with HF have symptoms occurring with

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exertion, reflecting a situation in which the needs are met when oxygen consumption (V_{O_2}) is at resting levels (ie, approximately 3.5 mL O_2/kg/min) but inadequate when the needs are increased by given level of exertion. Based on the relationship between symptoms and activity levels, the severity of HF is graded into different functional classes: no limitations (New York Heart Association [NYHA] class I), mild limitations (NYHA II), moderate limitations (NYHA III), or severe limitations or symptoms at rest (NYHA IV).[2] The greater the limitations, and the higher the NYHA class, the worse the quality of life and the prognosis in patients with HF. Understanding the determinants of functional limitations in HF is a necessary step to effectively treat HF and improve functional capacity.

Determinants of Functional Limitations in Heart Failure

HF is not synonymous with abnormal cardiac structure but reflects a cardiac function that is impaired or, at least, inadequate for the needs given the delicate balance required by the body to perform the required activities without untoward symptoms. According to the definition given earlier, an individual may have impaired cardiac function with a normal heart if the needs or demands are particularly increased (and outside of the physiologic range) as seen in high-output states, such as severe anemia. However, in most cases, HF is associated with abnormal cardiac structure. Three primary determinants of functional limitations in HF are cardiac contractility, diastolic filling, and heart rate (HR) (Fig. 1).

Left ventricular contractility

The primary central abnormality in HF is an impaired left ventricular (LV) contractility or contractile reserve. Patients with an LV ejection fraction (LVEF) less than 50% (or <40% depending on which definition is used) are referred to as having systolic HF or HF with reduced EF (HFrEF). An LVEF less than 50% is only observed in approximately 50% of patients diagnosed with HF, but the LVEF does not generally correlate with the severity of symptoms. This lack of correlation is expected because the cardiac output (CO) ultimately determines whether the metabolic demands are met, not the LVEF. CO is calculated as LV end-diastolic volume (LVEDV) × LVEF × HR. Therefore, a patient with LVEF of 30% may have the same CO as a patient with LVEF of 60%, if the LVEDV is double. What may be more important is the increase in CO with exertion, but the assessment of LVEF with exertion (contractile reserve) is rarely completed in patients with HF. The CO also depends on the performance of the right ventricle. An abnormal right ventricular (RV) systolic function represents another reason for an inappropriately low CO, even in the presence of normal LVEF.

Left ventricular diastole

The LVEDV is a critical determinant of both stroke volume (stroke volume = LVEDV × LVEF) and CO (LVEDV × LVEF × HR). Impaired LV filling during diastole may lead to an inappropriately small LVEDV and inadequate CO, even in the presence of normal LVEF. The most extreme example of this is the patient with hypovolemic shock in

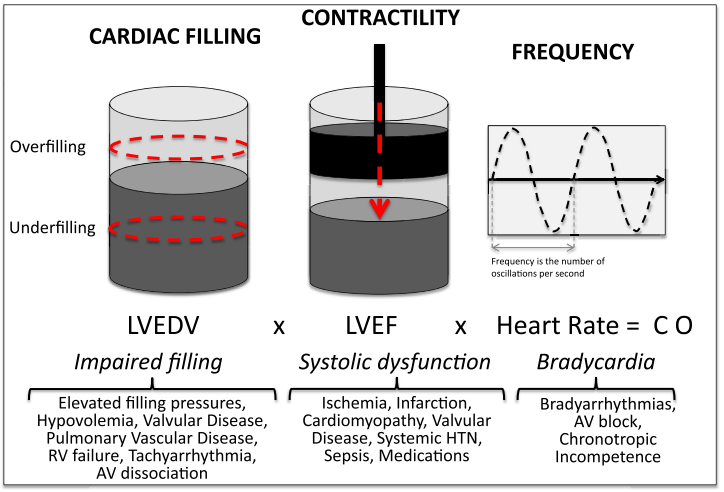

Fig. 1. Cardiac determinants of impaired exercise capacity in HF. An overview of the cardiac determinants of impaired cardiac output (at rest or with exertion) and of impaired exercise capacity in HF. The heart is represented as a cylinder pump with a piston. The filling of the cylinder is important to determine the pump output. The most common conditions leading to impaired cardiac filling are listed. The cardiac contractility is represented by the power of the piston in the engine. If the piston loses power, the pump output is compromised. A list of common conditions leading to impaired systolic function is given. The frequency at which the piston runs determines the output per minute (cardiac output), the frequency may be inappropriately low at rest (bradycardia) or fail to increase with exertion (chronotropic incompetence). AV, atrioventricular; CO, cardiac output; HTN, hypertension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; RV, right ventricular.