Drugs acting on the heart: heart failure and coronary insufficiency

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Learning objectives

After reading this article, you should be able to:

- define heart failure
- list management strategies in acute heart failure
- list drugs used in chronic heart failure
- describe the role of anti-platelet drugs and statins in coronary artery disease

Abstract

Heart failure (HF) and coronary insufficiency are common amongst surgical and critical care patients. Both are chronic conditions interrupted by acute episodes. HF activates neurohormonal mechanisms that worsen renal and cardiac function. Acute heart failure (AHF) commonly presents with dyspnoea as a consequence of systolic and/or diastolic dysfunction. Goals of treatment are symptom relief, to maintain tissue perfusion and optimize cardiac function. Diuretics and vasodilators are used early; positive inotropic drugs are reserved for when other treatment has failed. Chronic heart failure (CHF) is treated using changes in lifestyle and drugs to manage symptoms. ACE inhibitors and beta-blockers are effective in systolic heart failure and are associated with improved mortality. HF with preserved ejection fraction (HFPEF) is less responsive to drug therapy, though outcomes are better than for systolic HF. Coronary insufficiency occurs because of an imbalance of myocardial oxygen balance, leading to symptoms of ischaemic heart disease (IHD). Treatment goals are maintaining coronary blood flow and reducing myocardial oxygen demand. Beta-blockers and anti-platelet drugs improve outcomes; modern anti-platelets are more effective but are associated with risks of haemorrhage. Statins are effective for primary and secondary prevention of myocardial infarction; they have additional anti-inflammatory properties.

Keywords Coronary artery disease; heart drugs; heart failure; heart failure with preserved ejection fraction

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Heart failure

Heart failure (HF) is the inability of the heart to maintain sufficient blood flow to the tissues to meet physiological requirements. It is a clinical syndrome characterized by typical symptoms (breathlessness, ankle swelling, fatigue) alongside objective clinical signs (raised JVP, pulmonary congestion, peripheral oedema). It is caused by structural and/or functional abnormalities of the heart leading to reduced cardiac output or elevated filling pressures.[1] Heart failure may be classified according to the acuity of clinical presentation (acute, sub-acute, chronic, decompensated), or based on the measurement of ejection fraction (heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced EF (HFrEF)). Symptomatic severity of heart failure is classified according the New York Heart Association (NYHA) functional classification (Table 1). The causes and presentation of heart failure should be determined as they govern treatment.

Acute heart failure (AHF)

Acute heart failure (whether new onset or decompensated) is characterized by the development of a rapid onset or change in the signs and symptoms of HF. Diagnosis is based on thorough history and examination accompanied by assessment of the ECG, radiological evidence, serum biomarkers (natriuretic peptides) and early echocardiography. AHF is caused by left ventricular (LV) systolic dysfunction, diastolic dysfunction or, more commonly, a combination of both. Systolic dysfunction is a consequence of impaired myocardial contractility, leading to reduced left ventricular ejection fraction (LVEF) and consequently reduced cardiac output. Diastolic dysfunction is caused by an increase in ventricular stiffness and impaired relaxation, resulting in impaired ventricular filling during diastole; LVEF may be normal. Despite decreased cardiac output, systolic blood pressure may be normal or elevated because of increased systemic vascular resistance. Patients presenting with a systolic blood pressure <90 mmHg have a poor prognosis. Decreased cardiac output leads to tissue hypoperfusion, activating compensatory mechanisms that lead to renal and myocardial dysfunction (Figure 1).

The goals of treatment in AHF are to maintain adequate peripheral perfusion, improve myocardial contractility and reduce fluid overload. Supplemental oxygen should be administered to all hypoxic patients; diuretics should be given early if there are signs of pulmonary congestion and vasodilators if there is dyspnoea at rest. However, it is important to identify the aetiology of the cardiac dysfunction and treat any precipitating factors. For example, in patients with AHF caused by diastolic dysfunction and with normal or high arterial pressure, vasodilators and continuous positive airway pressure (CPAP) or assisted non-invasive ventilation (NIV) should be used and diuretics are indicated only if fluid overload is evident. Conversely, in

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The New York Heart Association (NYHA) classification of heart failure

NYHA class	Description
Class I	No limitation to physical activity
Class II	Slight limitation of physical activity in which ordinary physical activity results in fatigue, palpitations, dyspnoea or anginal pain; the person is comfortable at rest
Class III	Marked limitation of physical activity in which less-than-ordinary activity results in fatigue, palpitations, dyspnoea or anginal pain; the person is comfortable at rest
Class IV	Inability to carry on any physical activity without discomfort but also symptoms of heart failure or the anginal syndrome even at rest, with increased discomfort if any physical activity is undertaken

Table 1

patients with cardiogenic shock, positive inotropic drugs should be given with intravenous fluids guided to maintain cardiac output; however, in patients with isolated right ventricular failure, diuretics are the mainstay of therapy.

There has been much research aimed at developing new treatments for AHF in the last few decades and guidelines have been produced. Several newer drugs have been shown to improve symptoms of AHF, but without convincing effects on long-term outcome. In addition, it is worth noting that there are remarkably few good randomized data to support the use of traditional therapies (Table 2).

Drugs used in AHF

Diuretics

Diuretics are the mainstay of treatment for acute and chronic heart failure, effectively relieving systemic or pulmonary venous congestion. Furosemide (a loop diuretic) blocks the $Na^+/K^+/2Cl^-$ co-transporter at the loop of Henle, inhibiting sodium reabsorption and resulting in diuresis. It also acts as a venodilator to produce early relief from dyspnoea. It should be administered promptly and may also be administered as an infusion, with the aim of a weight reduction of approximately 1 kg per day. The dose should be limited to the smallest amount possible to produce clinical improvement. In those patients already taking furosemide, the intravenous bolus dose should be at least equal to the pre-existing oral dose used at home. The maximum dose should not exceed 100 mg in the first 6 hours as there is no additional benefit and adverse effects (e.g. otoxocity, hyponatraemia, hypokalaemia and dehydration) are more likely.

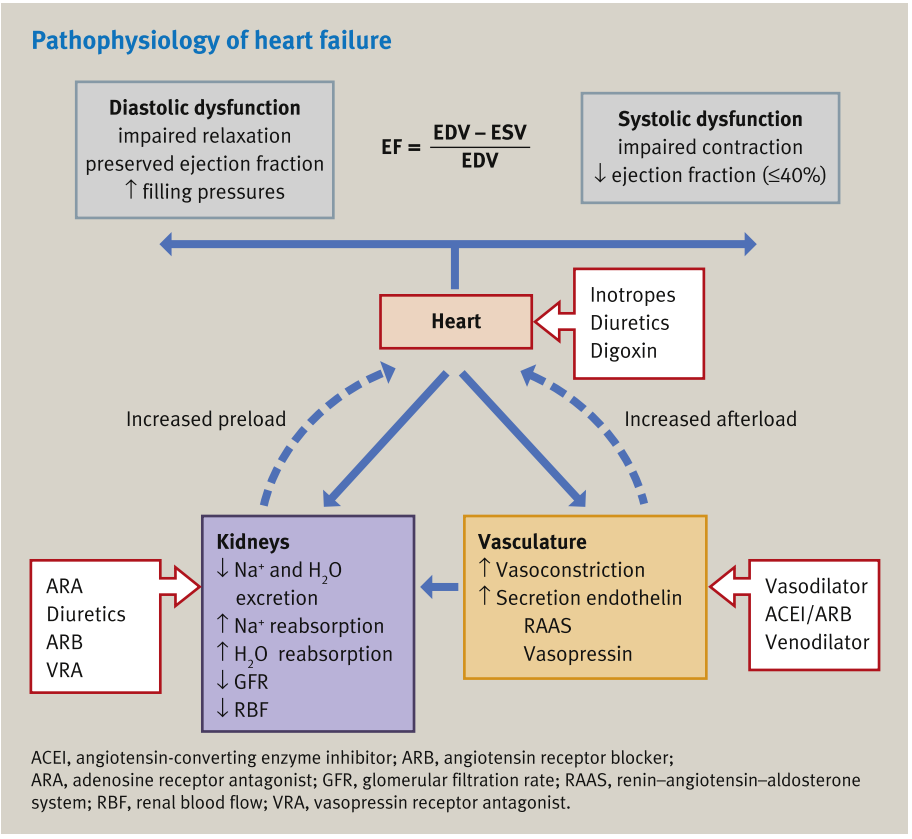

Figure 1 Reduced ejection fraction (EF) varies, depending on the degree of diastolic and systolic dysfunction (EDV, end diastolic volume; ESV, end systolic volume), both tend to co-exist. Heart failure activates compensatory neurohumoral mechanisms within the vasculature and kidneys. Left unchecked, these mechanisms worsen cardiac function, with increased fluid retention increasing venous return (preload), and peripheral vasoconstriction increasing afterload. Pharmacological targets are indicated.

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