# Drugs acting on the heart: heart failure and coronary insufficiency

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## 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 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; inotropes are reserved for when other treatment has failed. Chronic heart failure 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 is less responsive to drug therapy, though outcomes are better than for systolic HF. Coronary insufficiency occurs when myocardial oxygen delivery is inadequate, leading to symptoms of ischaemic heart disease. Treatment goals are maintaining coronary blood flow and reducing myocardial oxygen demand. Beta-blockers and anti-platelet drugs improve outcomes; modern anti-platelet drugs are more effective but 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 that combines symptoms of heart failure (e.g. dyspnoea), signs of fluid retention (e.g. ankle swelling) and objective evidence of structural or functional abnormalities of the heart at rest (e.g. abnormal echocardiogram, third heart sound).[1] Heart failure can be further classified according to the clinical presentation into new onset, transient (symptoms occur over a limited time period) and chronic (including decompensated) heart failure. The cause and

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## Learning objectives

After reading this article, you should be able to:
- define heart failure
- list management strategies for acute heart failure
- list drugs used in chronic heart failure
- describe the role of anti-platelet drugs and statins in coronary artery disease

presentation of heart failure should be sought 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, especially dyspnoea. It 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. Decreased cardiac output leads to decreased blood flow and tissue perfusion which activates neurohormonal mechanisms leading 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 early in the course of treatment. Diuretics are indicated only if there is evidence of fluid overload. Conversely, in 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 1).

### Drugs used in AHF

#### Opioids

Morphine (2.5–5 mg) is recommended in Europe[1] as an early treatment where there is chest pain, dyspnoea or restlessness at
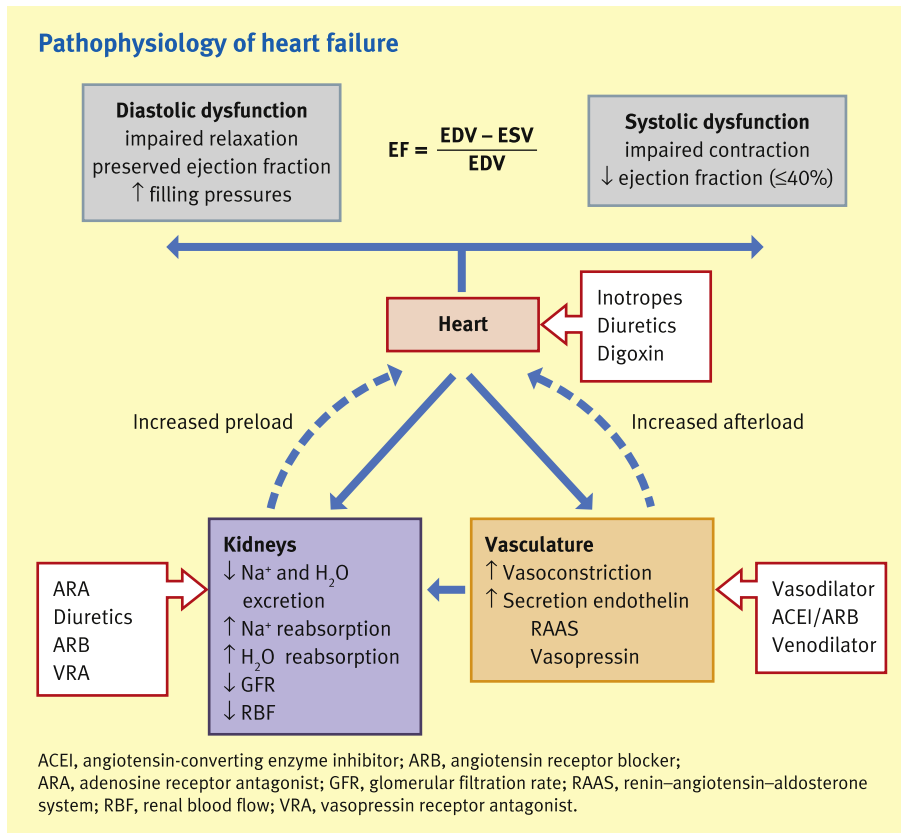
**Figure 1** Reduced ejection fraction (EF) varies, depending on the degree of diastolic and systolic dysfunction (EDV, end diastolic volume; ESV, end systolic volume), both tend to co-exist. Heart failure activates compensatory neurohumoral mechanisms within the vasculature and kidneys. Left unchecked, these mechanisms worsen cardiac function, with increased fluid retention increasing venous return (preload), and peripheral vasoconstriction increasing afterload. Pharmacological targets are indicated.

presentation. Opioids reduce preload through venodilation, reduce afterload and lower heart rate. Dyspnoea and agitation are also improved. Opioids should, however, be used with caution because of their side effects of central nervous and respiratory depression.

**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 $Na^+/K^+/2Cl^-$

### Pharmacological strategies for the emergency management of AHF

| Therapeutic goal | Drug | Mode of action | Side-effects |
|---|---|---|---|
| Systemic congestion | Diuretics e.g. furosemide, metolazone | Diuresis and variable natriuresis | Hypotension, neurohumoral activation, electrolyte abnormalities, renal dysfunction |
| Vasodilation | Nitrates e.g. GTN, SNP | Venodilation, vasodilation | Profound hypotension with vasodilators, ↓coronary perfusion (SNP), headache, metabolite toxicity |
| Cardiac function | Inotropes: β-agonists, PDE-3 inhibitors, levosimendan | Increased force of myocardial contraction + peripheral vasodilation (inodilation) | Increased myocardial oxygen demand, hypotension, arrythmias |
| Cardiac stability | Beta-blockers: emololol, metoprolol digoxin | Reduction in heart rate & sympathetic activity; anti-arrhythmic | Bradycardia, hypotension |

Adapted from Khan SS, Gheorghiade M, Dunn JD, Pezalla E, Fonarow GC. Managed care interventions for improving outcomes in acute heart failure syndromes. *Am J Manag Care* 2008; 14: S273−86.
Key: AHF, acute heart failure; GTN, glyceryl trinitrate; PDE, phosphodiesterase; SNP, sodium nitroprusside.

**Table 1**