Review

High output heart failure

P.A. MEHTA¹ and S.W. DUBREY²

From the ¹Clinical Cardiology, National Heart and Lung Institute, Imperial College, Dovehouse Street, London SW3 6LY, UK and ²Cardiology Department, The Hillingdon Hospital, Field Heath Road, Uxbridge, Middlesex, London UB8 3NN, UK

Summary

The symptoms and signs of heart failure can occur in the setting of an increased cardiac output and has been termed ‘high output heart failure’. An elevated cardiac output with clinical heart failure is associated with several diseases including chronic anaemia, systemic arterio-venous fistulae, sepsis, hypercapnia and hyperthyroidism. The underlying primary physiological problem is of reduced systemic vascular resistance either due to arterio-venous shunting or peripheral vasodilatation. Both scenarios can lead to a fall in systemic arterial blood pressure and neurohormonal activation leading to overt clinical heart failure. In contrast to low output heart failure, clinical trial data in this area are lacking. The use of conventional therapies for heart failure, such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers and certain β-blockers with vasodilatory properties, is likely to further reduce systemic vascular resistance resulting in deterioration. The condition, although uncommon, is often associated with a potentially correctable aetiology. In the absence of a remediable cause, therapeutic options are very limited but include dietary restriction of salt and water combined with judicious use of diuretics. Vasodilators and β-adrenoceptor positive inotropes are not recommended.

Introduction

The syndrome of heart failure is a global clinical problem with at least 10 million patients across Europe¹ and 5 million in the USA² living with the condition. The condition is not confined to the developed world. In the developing world, the epidemiology of heart failure is largely unknown but is likely to evolve in a similar way due to ‘Westernization’ of lifestyle and better control of communicable disease and malnutrition.³,⁴

Heart failure is usually associated with a low cardiac output but less commonly the symptoms and signs of heart failure can occur in the setting of a high cardiac output. Historically this has been termed ‘high output heart failure’.

Low output cardiac failure is well described with a number of pharmacological therapies available which are supported by data from many randomized clinical trials.⁵–¹⁴ In addition, several international consensus guidelines are available for the diagnosis and management of heart failure.¹,¹⁵ However, such clinical evidence and published guidelines do not make reference to high output heart failure.

Definition of high output cardiac state and heart failure

A high cardiac output has been described as being >8 l/min or a cardiac index >3.9 l/min/m².¹⁶ A high
cardiac output state and associated clinical heart failure is associated with several disease states (Figure 1). Some authors suggest the term ‘high output heart failure’ is a misnomer as the heart is intrinsically normal and capable of generating a high cardiac output. Others have suggested that high output heart failure occurs only when there is the presence of underlying heart disease. It is likely that in chronic high output states, heart failure occurs due to eventual deterioration due to the presence, or in most cases the development of heart disease. A persistent high output state may be associated with ventricular dilatation and/or hypertrophy, persistent tachycardia and functional valvular abnormalities, all of which may culminate in heart failure.

Pathophysiology
The underlying primary physiological problem in high output heart failure is of reduced systemic vascular resistance. This occurs due to either systemic arterio-venous shunting or peripheral vasodilatation. Both scenarios can lead to a fall in systemic arterial blood pressure, a feature of low output heart failure. This can lead to sympathetic neural activation, a compensatory rise in cardiac output and neurohormonal activation (including the renin-angiotensin-aldosterone system and vaso-pressin). This process in turn can cause salt and water retention and overt clinical heart failure. Thus, salt and water retention occur both in low and high output heart failure due to a similar neurohormonal response to arterial hypotension. In the former it is due to low cardiac output and in the latter due to reduced systemic vascular resistance.

Diagnosis
Symptoms and signs
In common with low output states, patients with high output heart failure may have a number of symptoms including breathlessness at rest or on exertion, exercise intolerance, fatigue and fluid retention. The signs of typical heart failure may be present including tachycardia, tachypnoea, raised jugular venous pressure, pulmonary rales, pleural effusion and peripheral oedema (Figure 2).
In high output heart failure, patients are likely to have warm rather than cold peripheries due to low systemic vascular resistance and peripheral vasodilatation.

**Investigations**

**Chest radiography**
A chest radiograph is essential in the investigation of heart failure. It is useful in the assessment of cardiomegaly, pulmonary congestion and pleural fluid accumulation. The findings of pulmonary disease and sepsis due to pneumonia may be relevant in the diagnosis of high output heart failure.

**Echocardiography**
Cardiac ultrasound is mandatory in patients with suspected heart failure. In high output states, echocardiography may demonstrate a preserved left ventricular ejection fraction (>45–50%). High output heart failure may occur despite ‘normal’ left ventricular systolic function. Patients may subsequently develop compensatory left ventricular dilatation ± hypertrophy. This may have eventual deleterious consequences with worsening heart failure.

**Venous blood gas**
Invasive haemodynamic measurements in heart failure patients are often not necessary and direct measurement to confirm a high cardiac output may not be available. A mixed venous oxygen saturation (SvO₂) provides an estimate of the body oxygen consumption/delivery ratio and an approximation of cardiac output and organ perfusion. A low SvO₂ (<65%) is associated with an inadequate cardiac output and conversely a high SvO₂ (~>75%) may be due to a high cardiac output state.

**Specific conditions associated with high output heart failure**
A wide spectrum of congenital, acquired and iatrogenic conditions may cause a high output state and lead to the clinical syndrome of heart failure (Figure 1). In many cases this starts as an ‘adaptive’ physiology, such as in an ‘athletes’ heart. It is when this ‘stimulus to change’ is persistent that the adaptation can result in reduced cardiac function. In many cases this is the beginning of a self-perpetuating cycle of deterioration.

**Anaemia**
Severe chronic anaemia can result in physiological adjustment to maintain tissue perfusion and oxygenation. Anaemia can lead to peripheral vasodilatation, at least partly due to increased renal and...
vascular nitric oxide synthase activity and low blood viscosity. Both may lead to low systemic vascular resistance with associated neurohormonal activation and heart failure. Treatment is aimed at correction of the underlying cause of anaemia. Whilst cautious blood transfusion may be necessary, rapid blood volume expansion may worsen pulmonary oedema.

Systemic arterio-venous fistula
Systemic arterio-venous fistulae may cause high output heart failure due to a lowering of the systemic vascular resistance and a compensatory rise in cardiac output.

Acquired arterio-venous fistulae may be iatrogenic or occasionally due to trauma. The creation of arterio-venous fistulae in renal dialysis patients has revealed the extent and timing of associated cardiac adaptation. This includes increase in left ventricular dimensions and a reduction in left ventricular diastolic filling time. An associated increased release of natriuretic peptides has been observed. The degree of increase in cardiac output depends on the physical size and flow magnitude of the fistula. Concomitant chronic anaemia will have an additive effect. Treatment may necessitate reversal or modification of the shunt.

Congenital arterio-venous fistulae, such as in hepatic endotheliomas and lung and/or liver involvement in hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease) may produce a hyperdynamic circulation and subsequent heart failure as described. Arterio-venous malformations may be in the limb with associated hypertrophy (Parkes-Weber syndrome). Heart failure has also been reported in the setting of diffuse arterio-venous malformations associated with Klippel–Trénaunay syndrome. Overall, the ideal treatment is aimed at attempting surgical excision of the causative shunt. However, lesions may be difficult to precisely localize or in some cases so extensive as to prevent complete excision.

Paget’s disease
Paget’s disease is associated with rapid bone formation and resorption that can lead to increased blood flow within bone and the surrounding limb tissue. This may act or indeed cause shunting and lower peripheral vascular resistance. Significant bony involvement (usually defined as >15%) may then lead to heart failure. Both multiple myeloma and fibrous dysplasia (Albright’s disease), by a similar mechanism have been associated with arterio-venous shunting and high output heart failure. Again, concomitant anaemia is likely to exacerbate this process.

Chronic hypercapnia
Chronic hypercapnia is associated with vasodilatation and can potentially lead to systemic hypotension and subsequent adverse neurohormonal response. Hypercapnia is commonly seen in clinical practice due to chronic obstructive pulmonary disease and cor pulmonale. These conditions can lead to fluid retention in the setting of normal/increased cardiac output.

Hyperthyroidism
Thyrotoxicosis is associated with a hyperdynamic circulation. There can be associated tachycardia, left ventricular dilatation and increased cardiac output. The development of heart failure may be predominantly due to ‘tachycardia-mediated cardiomyopathy’ as observed with many other causes of tachycardia including atrial fibrillation.

Sepsis
Sepsis and associated endotoxaemia is a complex and multifactorial process. Severe sepsicaemia is associated with systemic vasodilatation and an increased cardiac output. A number of vasoactive cytokines including tumour necrosis factor-α, interleukins-2, -6, -8 and -15 and inducible nitric oxide synthase have been implicated in this process. The end-result is sometimes significant systemic vasodilatation culminating in arterial hypotension and high output failure.

Beriberi heart disease
This condition is due to severe long-term (>3 months) deficiency of the B vitamin thiamine and is more common in areas of dietary deficiency with high carbohydrate intake (such as the Far East). In the developed world it is most frequently observed in chronic alcoholics due to poor dietary intake of thiamine, impaired thiamine absorption, metabolism and storage. Thiamine deficiency is also associated with malabsorption conditions, dialysis and other causes of chronic protein-calorie under-nutrition. The latter should be suspected in isolated elderly patients. Beriberi heart disease is a cause of heart failure with associated elevated cardiac output, oedema, fatigue and general malaise (‘wet’ beriberi). High output heart failure is possibly due to arteriolar and cutaneous vasodilatation leading to a reduced systemic vascular resistance.
Obesity

Obesity produces an increase in overall blood volume and cardiac output. This is due to the raised metabolic activity of excessive adipose tissue, which leads to compensatory cardiac changes including left ventricular dilatation and eccentric hypertrophy. These adaptive modifications can eventually lead to both systolic and diastolic abnormalities culminating in heart failure or ‘obesity cardiomyopathy’.

Obesity cardiomyopathy is likely to become increasingly prevalent over time due to a rising global epidemic of obesity.

Other causes

There are many other causes of high output heart failure including pregnancy, hepatic disease and carcinoid syndrome. All are related, via a common mechanism, to vasodilatation and a fall in blood pressure.

Treatment

Although the final pathogenesis of salt and water retention is similar in low and high output states, treatment options differ. In low output heart failure, with associated normal or high systemic vascular resistance, circulating vasoconstrictors predominate and are counteracted by neurohormonal antagonists (angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists and β-blockers). Extensive clinical trial data support the use of such therapies with improvement in mortality and morbidity.

The evidence base for the management of high output failure is scarce and generally based on case reports. Clinical trial data in this area are lacking. The use of established vasodilator therapies, such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers and some newer β-blockers with vasodilatory properties (e.g. carvedilol, nebivolol), in patients with low systemic vascular resistance in high output heart failure is likely to lead to further deterioration and is not recommended. In addition the use of β-adrenoceptor positive inotropes is not advisable.

Treatment should be targeted at correcting the cause of low systemic vascular resistance. In addition dietary restriction of salt and water and judicious use of diuretics is advised. Although treatment options are limited for high output heart failure, there are some existing supportive therapies. A number of intravenous vasoconstrictor adrenergic drugs are available including noradrenaline, ephedrine, metaraminol and phenylephrine. These treatments increase systemic vascular resistance by acting on α-adrenergic receptors to constrict peripheral blood vessels. Such therapies may be useful short-term adjuncts in high output heart failure whilst treatment of the underlying aetiology is ongoing. Long-term treatment may be associated with both reduced vital organ perfusion and tachycardia due to β-adrenergic receptor activation (e.g. ephedrine) and is not recommended. Respiratory intervention with high ventilatory peak end-expiratory pressure for resistant pulmonary oedema may also be useful.

Conclusion

Many conditions are associated with high cardiac output physiology. When this becomes chronic the adaptive cardiac changes can fail, resulting in cardiovascular decompensation. Overt high output heart failure, although uncommon, is often associated with a potentially correctable aetiology. There is a notable lack of clinical trial data for this poorly understood condition. In the absence of a remediable cause, therapeutic options are limited. Moreover, many accepted therapies for low output heart failure are in fact contra-indicated.

Conflict of interest: None declared.

References


6. Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Effect of ramipril on mortality and morbidity of survivors of


