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Heart failure

Chapter: Heart failure

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Summary



Heart failure is a common presentation of neonates and children with congenital heart disease and is the most important long-term complication in adults. It may be due to residual lesions and/or the complex circulation which are present even after repair. The

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mechanisms of heart failure are often different from normally built hearts and this will influence optimal treatment approaches. Several interventions (surgical, transcatheter, or pharmacological) can improve patient outcome and assist devices and heart transplantation are options in severe refractory cases.

Introduction



With the increasing number of adult survivors with complex congenital heart disease, the prevalence of clinical heart failure has increased to approximately 20%. It is dependent on the underlying disease complexity,^{1,2,3} and patients with a systemic right ventricle, residual valvar dysfunction, a single ventricle, or pulmonary hypertension are at particularly high risk.⁴ Importantly, heart failure has emerged as the leading cause of death in the adult congenital heart disease population.^{5,6} Early diagnosis is important, as mortality is increased fivefold after first heart failure admission.⁶ The diagnosis of heart failure is based on clinical signs, together with imaging studies and biomarkers. Patients often deny symptoms, even though exercise capacity is almost always decreased when tested objectively.

Pathophysiology of heart failure



The pathophysiology of heart failure after repair of congenital heart disease is more complex than in a structurally normal heart, and it is often not appropriate to extrapolate from clinical trial evidence of treatment benefit with conventional medical therapies. The situation is further complicated by interaction between the impact of the underlying congenital heart lesion and acquired cardiovascular risk factors which increase with ageing. Understanding of the mechanisms is thus important for risk assessment and appropriate treatment. The pathway towards heart failure in patients with repaired congenital heart disease can be considered as a three-step process² (Figure 17.16.1). The residual lesions after corrective surgery and the impact of repeated interventions often result in a suboptimal haemodynamic result and decreased myocardial function. Furthermore, evidence has emerged that genes responsible for cardiac morphogenesis may also play a key role in the regulation of myocardial function and the response to physiological stress.^{7,8,9} In these vulnerable hearts, the imperfect haemodynamic result after repair stresses the heart for a prolonged period of time (Box 17.16.1). During this period, patients are often asymptomatic, but the persisting volume load and/or pressure load results in changes in molecular signalling as well as remodelling of the extracellular matrix and mitochondrial function.¹⁰ Furthermore, arrhythmias often trigger heart failure symptoms and ventricular dyssynchrony is increasingly recognized as a possible contributor to decreased ventricular function.^{11,12} Next, neurohormonal activation comes into play, with elevation of natriuretic peptides, increases in the renin-aldosterone system, increased

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sympathoadrenergic tone, and activation of the endothelin pathway.¹³ In repaired congenital heart disease, this results most often in impaired systolic function, although heart failure with preserved ejection fraction is increasingly recognized, as in a restrictive right ventricular physiology in patients with pulmonary atresia or in the context of Shone complex, ventricular septal defect, and major aortopulmonary collateral arteries.

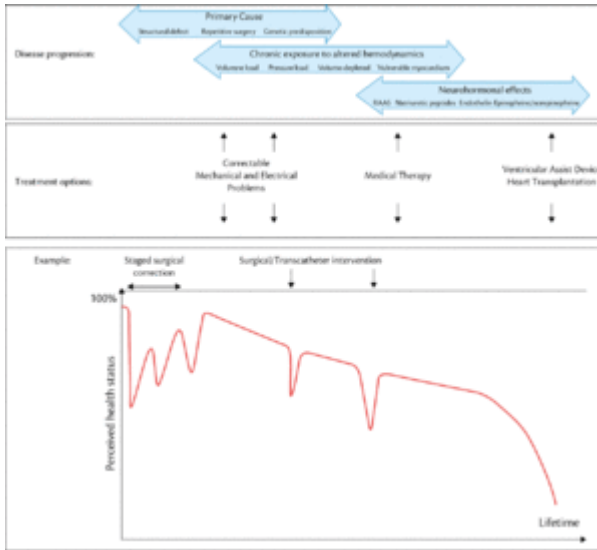


Figure 17.16.1

The pathway towards heart failure in patients with repaired congenital heart disease can be considered as a three-step process.

Box 17.16.1 Reasons for heart failure in congenital heart disease

- ◆ Secondary to (repetitive) surgical intervention: limited myocardial protection during bypass, ventriculotomy, and coronary kinking after re-implantation of coronary arteries.
- ◆ Chronic pressure overload:
 - Left ventricle: sub-, supra- or valvular aortic stenosis, coarctation of the aorta, systemic hypertension.
 - Right ventricle: severe right ventricular outflow tract obstruction, pulmonary hypertension (e.g. Eisenmenger syndrome), or systemic pressure load on the right ventricle (e.g. congenitally corrected transposition of the great arteries, dextro-transposition of the great arteries after atrial switch repair (Mustard/Senning)).

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- Secondary effect: altered geometry and function of the pressure-loaded right ventricle leads to a loss of normal right ventricular morphology and impaired ventricular and tricuspid valve function.

◆ Chronic volume overload:

- Left ventricle: aortic valve regurgitation, ventricular septal defect, patent ductus arteriosus, mitral valve regurgitation.
- Right ventricle: atrial septal defect, supratricuspid left-to-right shunt lesions, tricuspid and pulmonary valve regurgitation (e.g. Ebstein's malformation and after tetralogy of Fallot, respectively).
- Volume under-load after initial volume overload (e.g. Fontan repair).
- Secondary effect: altered geometry and function of the subpulmonary ventricle interfering with diastolic filling of the systemic ventricle (e.g. severe pulmonary regurgitation in tetralogy of Fallot leading to enlargement of the right ventricle and septal shift to the left ventricle).

◆ Inherent to the underlying defect:

- Congenital coronary artery abnormalities: functional ischaemia due to single coronary artery, anomalous origin and/or course of the coronary arteries, extrinsic compression by a dilated pulmonary artery, chronic hypoxia (ventricular septal defect with pulmonary stenosis).

◆ Concomitant presence of cardiomyopathies with a genetic background:

- Altered myocardial architecture: non-compaction.
- Possible genetic and developmental factors may turn the myocardium vulnerable to systolic dysfunction.

◆ Concomitant acquired ischaemic heart disease and ventricular dysfunction: due to cardiovascular risk factors (arterial hypertension, hyperlipidaemia, diabetes mellitus, obesity, smoking) as well as tachyarrhythmias.



Neurohormonal activation in patients with congenital heart disease and heart failure

As in acquired heart disease, heart failure initiates various compensatory mechanisms with increased neurohormonal activation. The resultant vasoconstriction and increased plasma volume reduce symptoms in the short term but are deleterious in the long run. Neurohormonal activation influences outcome and is a therapeutic target in patients with acquired heart disease.^{14,15,16,17} In patients with congenital heart disease, there is a stepwise increase related with New York Heart Association functional class and ventricular dysfunction. However, even in patients in functional class I without evidence of decreased ventricular function, neurohormonal parameters can be elevated.¹³ Therefore, extrapolation of the guidelines for heart failure in acquired heart disease and initiation of neurohormonal antagonism is reasonable, at least in the failing left ventricle. The goal of treatment of heart failure should be symptom relief or prolonged survival, or both of these. However, no studies have yet shown a survival benefit of starting therapy with neurohormonal blockade in any group of congenital heart disease patients. Whether extrapolation of neurohormonal blockade is justified in right ventricular failure is even less well established. Theoretically, in patients with a systemic right ventricle and neurohormonal activation, neurohormonal blockade should be considered.¹⁸

End-organ dysfunction



Chronic kidney dysfunction is frequent,¹⁹ and elevated systemic venous pressure may give rise to increased liver stiffness and liver cirrhosis, as well as to protein-losing enteropathy.^{20,21} Rarely, plastic bronchitis is encountered after Fontan repair.²² Haematological disturbances, such as thrombocytopenia, are often encountered²³ and cyanosis (e.g. Eisenmenger's syndrome) leads to an increased haematocrit, which can result in symptoms of hyperviscosity.²⁴ Threshold for phlebotomy however, should be high, as low iron reserves have been shown to increase mortality.²⁵

Therapeutic implications



Therapy in heart failure consists of four main steps:

- ◆ Timely detection of triggers that might provoke heart failure.
- ◆ Timely repair of haemodynamic and electrical disturbances that result in decreased cardiac function.
- ◆ Initiation of pharmacological treatment.
- ◆ Referral for left ventricular assist device and heart transplantation (combined with or without lung/liver transplant).

Early detection and timely structural and electrical repair

Invasive evaluation plays a crucial role and may identify elevated pressures and residual lesions as possible contributors to symptoms and heart failure pathophysiology. Percutaneous interventions play an increasingly important role in haemodynamic optimization in adult congenital heart disease patients, but early degeneration, endocarditis, and subsequent re-intervention are of concern, especially after valve replacement.²⁶ Early relief of the haemodynamic stress on the myocardium might prevent the evolution towards heart failure. Examples include closure of atrial septal defects, and correction of pulmonary valve regurgitation in repaired tetralogy of Fallot by percutaneous pulmonary valve implantation. Although morphological and functional parameters remain good after haemodynamic optimization, the true long-term effects on patient survival are not yet established.

Initiation of pharmacological treatment

The European Working Group on Grown Up Congenital Heart Disease and European Heart Failure Association consensus statement in 2016 proposed treatment standards for heart failure.¹⁸ The rationale for heart failure treatment in the systemic left or right ventricle is described in the second paragraph (Neurohormonal activation in patients with congenital heart disease and heart failure) and treatment is largely in line with that of heart failure due to acquired heart disease. However, care should be taken, especially in patients with cyanotic heart disease, because systemic afterload reduction may increase right-to-left shunt and hence decrease oxygen saturation. Of note, prevention of iron depletion has been shown to be important in patients with Eisenmenger syndrome as iron-depleted patients do significantly worse than iron-repleted patients.²⁵ Furthermore, even more than in acquired heart disease, control of cardiovascular risk factors plays a vital role in patient care.

Referral for assist device and heart transplantation

Despite optimal non-pharmacological and pharmacological treatment, patients may progress towards refractory, severe heart failure and become candidates for a left ventricular assist device or heart transplantation. Ventricular assist devices are less often used in patients with congenital heart disease, due to difficult anatomy, higher incidence of right-sided heart failure, pulmonary hypertension, or residual shunts.^{27,28} Despite 10-year survival rates similar to those of patients with ischaemic or dilated cardiomyopathy, listing of patients for heart transplantation is difficult, as no good predictive models for survival without transplant are available. Their anatomical complexity and previous multiple surgeries increase the technical difficulty of transplantation as well as early risk.

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