



Management of acute heart failure in adult patients with congenital heart disease

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Published online: 25 December 2017
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Abstract

Heart failure is an increasing reason for hospitalization and the leading cause of death in patients with adult congenital heart disease (ACHD). Recently, the European Society of Cardiology and the American Heart Association published consensus documents on the management of chronic heart failure in ACHD patients. However, little data and/or guidelines are available for the management of (sub)acute heart failure. The ACHD population is heterogeneous by definition and often has complex underlying anatomy, which could pose a challenge to the physician confronted with the ACHD patient in (sub)acute heart failure. Recognizing the underlying anatomy and awareness of the possible complications related would result in better treatment, avoid unnecessary delays, and improve outcomes of the ACHD patient with (sub)acute heart failure. This review focuses on the management of (sub)acute heart failure in ACHD with specific attention to lesion-specific issues.

Keywords Adult congenital heart disease · Heart failure · Systemic right ventricle · Fontan · Tetralogy of Fallot · Cyanotic congenital heart disease

Introduction

Survival of patients born with congenital heart defects has improved significantly over the past decades. Nowadays, due to advances in cardiac surgery, intensive care, and diagnostic capabilities, 88% of children with congenital heart disease (CHD) survive into adulthood [1]. An improved survival of patients with moderate- and complex-congenital heart defects and increasing age of the adult CHD populations will dramatically change the profile of the adult CHD patient, with

symptomatic heart failure episodes and end-stage heart failure becoming more prevalent [2–4]. The hospital admission rate of patients with CHD is twice that of the general population, with 50% of patients being hospitalized and 16% being admitted to the intensive care unit (ICU) over a 5-year period [5, 6]. Approximately 7% of admissions reported are due to heart failure [5], but heart failure is the leading cause of death in the CHD population [4]. The aim of this article is (1) to define (sub)acute heart failure in adult patients with CHD, (2) to identify the Achilles heel of the circulation (which will depend on the type of underlying heart defect and may include the heart, the lungs, and/or the vascular connections), and (3) to review the initial evaluation and management of the patients admitted with (sub)acute heart failure and CHD. Specific attention will be paid to factors that differ from the non-congenital patient with acute decompensated subaortic left ventricular failure in a biventricular circulation.

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Definition

The ESC guidelines define heart failure as signs and symptoms caused by a structural and/or functional cardiac

abnormality resulting in reduced cardiac output and/or elevated intracardiac pressures at rest or during stress [7]. In CHD, there is emerging evidence of increased neurohormonal activation [8, 9], high circulating inflammatory cytokine levels [10], and decreased autonomous nervous activity [11] supporting the notion of a “heart failure state” with recurrent symptomatic exacerbations [3]. However, given the unique vascular connections and configuration of the circulation, the subaortic ventricle is often not the predominant hemodynamic problem in patients with CHD. Therefore, a structural and/or function *cardiovascular* abnormality leading to reduced cardiac output and/or increased filling pressures is probably more appropriate.

Traditionally, heart failure is divided into heart failure with reduced ejection fraction (HF-rEF) and heart failure with preserved ejection fraction (HF-pEF), based upon measured EF higher or lower than 40–45% of the subaortic left ventricle. Effective therapies have been demonstrated in patients with HF-rEF (EF \leq 35%) having a biventricular circulation and a left ventricle (LV) as the subaortic ventricle [12]. This distinction may still be important in the subset of CHD patients with a biventricular circulation and the LV as the subaortic ventricle. In adult congenital heart disease (ACHD), patients with a failing subaortic or subpulmonary right ventricle—although cardiac dysfunction is often present—this distinction is no longer valid [3, 13].

For the purpose of this article, we describe (sub)acute cardiovascular failure as CHD patients who present suddenly (acute) or gradually (subacute) with signs and symptoms of cardiovascular failure requiring hospital admission. Cardiovascular failure after cardiac surgery or cardiovascular failure in young children is beyond the scope of this article. The distinction between mild, moderate, and severe CHD is based upon the 32nd Bethesda Conference [2].

Identifying the “Achilles heel” of the circulation

The heart (myocardial structure and function, valves, conduits)

Patients with simple CHD have a biventricular circulation with the LV as the subaortic ventricle. These patients usually have good overall prognosis [4] and treatment of (sub)acute heart failure is not different from heart failure in patients without CHD [12].

Patients with CHD of moderate severity also have a biventricular circulation with the RV as the subpulmonary ventricle and the LV as the subaortic ventricle. It is crucial to evaluate and identify persistent hemodynamic defects and

residual post-repair lesions as they often represent the “Achilles heel” of the circulation. In patients with ventricular septal defect (VSD), (persistent) left-to-right shunt, aortic valve regurgitation (due to aortic cusp prolapse into the defect), LV septal dyskinesia, and left ventricular outflow obstruction (LVOT) may persist or evolve after repair. Patch dehiscence in the setting of endocarditis is particularly poorly tolerated. Patients with atrioventricular septal defect (AVSD) often have persistent left and/or right AV valve regurgitation as well as LVOT obstruction [14]. Patients who had shunt lesions such as partial or total anomalous pulmonary venous connection (PAPVC/TAPVC) or sinus venosus atrial septal defect may have residual RV dilatation and/or dysfunction. Right-sided lesions, such as pulmonary regurgitation, pulmonary valve stenosis, and right ventricular outflow tract obstruction, represent a volume and/or pressure load to the RV that may precipitate failure of the ventricle [15, 16]. In CHD, patients with a subpulmonary ventricle to pulmonary artery conduit, recurrence of stenosis, regurgitation, and/or infection are frequent [17]. In patients with tetralogy of Fallot, pulmonary regurgitation, pulmonary valve stenosis, RV dysfunction, or LV dysfunction may be present either in isolation or simultaneously, each with a certain degree of severity.

Patients with CHD of complex severity may have a biventricular or univentricular circulation and the subaortic ventricle may either be the LV or RV. They represent a truly unique group of patients to which none of the currently published practice guidelines apply.

Eisenmenger syndrome

Eisenmenger syndrome represents the extreme end of pulmonary arterial hypertension associated with CHD. It is a clinical phenotype characterized by suprasystemic pulmonary artery pressures in patients with shunt lesions leading to pulmonary vascular disease causing shunt reversal and central cyanosis [18].

Although deterioration of the RV is much slower in Eisenmenger patients when compared to patients with idiopathic PAH [19], preservation of RV function is a major determinant of survival [20]. Clinical signs of right heart failure [21], the degree of right ventricular hypertrophy on electrocardiography [22], and qualitative echocardiographic assessment of right ventricular function [23] have been related with adverse outcome. Quantitative assessment of longitudinal right ventricular function using tricuspid plane annular systolic excursion (TAPSE) showed that patients with TAPSE $<$ 16 mm had a worse prognosis [24, 25].

Fontan circulation

The Fontan circulation provides definite palliation for patients born with a single anatomical or functional ventricular chamber. In the Fontan circulation, the systemic and pulmonary

circulations are connected in series without the presence of a subpulmonary ventricle to add forward energy to flow through the lungs [26]. The systemic ventricle usually evolves from volume overloaded, dilated, and/or hypertrophied when shunted or banded to overgrown and preload insufficient after a cavopulmonary connection [27]. Although classic indices of ventricular function are difficult to evaluate in Fontan patients, impaired systemic ventricular function will limit cardiac output and affect prognosis [28]. It may be even more difficult to identify patients with impaired diastolic dysfunction but preserved systolic ventricular function [29, 30]. Although controversial, there is little evidence to support a poorer outcome of patients with a single RV when compared to a single LV [31–33].

Subaortic right ventricle: ccTGA and complete TGA with Mustard/Senning repair

Patients with congenitally corrected transposition of the great arteries (ccTGA) and complete TGA who underwent atrial rerouting (Mustard or Senning repair) have a biventricular circulation with the morphological RV as the subaortic ventricle. In contrast to the LV who has three muscle layers, the RV only has two muscle layers. The circumferential layer is responsible for torsion of the LV, necessary for adequate pumping and filling of the LV [34]. Although intuitive, robust evidence that the RV is unable to support the systemic circulation is controversial [35]. Nevertheless, Graham et al. reported more than 50% of patients with congestive heart failure by the age of 45 [36]. Concerns regarding eventual RV failure led to a transition to the arterial switch procedure for patients with complete TGA. Moderate RV dysfunction has been reported in 10 to 20% of patients [37–39]. A key player in the evolution to clinical overt heart failure is the presence of tricuspid regurgitation [38, 39], especially as Ebstein-like tricuspid malformations are the most common cardiac abnormality related with ccTGA [40]. Although echocardiographic parameters suggest “RV dysfunction,” they may rather represent an adaptive response to changed loading conditions [41, 42] and partly explain the difficulties in defining cardiovascular failure and the failure of pharmacological therapy in this population [43–45]. Finally, in patients with TGA after atrial switch procedure, capacitance and conduit function of the baffles is impaired [42]. Therefore, these patients poorly tolerate fast heart rate (for example in the setting of atrial fibrillation and a fast ventricular response) as the decrease in diastolic filling time will limit ventricular filling, decrease cardiac output, and may even cause hemodynamic collapse.

The lungs (pulmonary vasculature)

The pulmonary vascular system, while being constrained by the chest cavity, maximizes the surface area for gas exchange, while minimizing the resistance to decrease the work that the subpulmonary ventricle needs to perform [46, 47]. Evaluation

of the pulmonary circulation is of utmost importance in patients presenting with subpulmonary RV failure and patients with Fontan circulation.

Some CHD patients will have elevated pulmonary vascular resistance, which is due to elevated pulmonary blood flow (intra- or extracardiac left-to-right shunt, palliative shunts, non-pulsatile flow instead of laminar flow) [48, 49]. The increased pulmonary vascular resistance represents an increased load to the subpulmonary circulation (which could be either the RV in a biventricular system or the venous system in a Fontan circulation). Pulmonary hypertension in CHD is associated with a 2-fold increase in all-cause mortality [50].

It remains crucial in the assessment of afterload to the subpulmonary circulation to distinguish increased afterload (1) at the level of the RVOT (subvalvular, valvular, and/or supra-valvular), (2) due to pulmonary vascular disease, (3) due to baffle stenosis or pulmonary vein stenosis, and (4) due to increased left atrial pressures (subaortic ventricular dysfunction or subaortic atrioventricular valve dysfunction) as it has important implications for treatment.

Thrombus formation is a major concern in patients with a Fontan circulation, occurring in about 25% of patients, especially in patients with a right atrium to pulmonary artery Fontan connection or patients with a history of atrial arrhythmias [51, 52]. Pulmonary embolism may result in ventilation/perfusion mismatch or a significant increase in pulmonary vascular resistance, both of which are poorly tolerated by Fontan patients. Likewise, pulmonary artery thrombus is present in about 25% of patients with Eisenmenger physiology [53, 54].

Shunts and collaterals

In patients with complex CHD, it is important to consider the presence/persistence of shunts and collaterals as they may cause additional volume and/or pressure load. Pre-tricuspid shunt lesions, such as atrial septal defects and abnormal pulmonary venous drainage, result in a volume load of the pulmonary circulation, which may eventually cause pulmonary vascular disease with increased pulmonary artery pressures [55]. Post-tricuspid shunt lesions, such as VSD and patent ductus arteriosus, cause volume load of the LV and may also give rise to pulmonary vascular disease. In Fontan patients, a spontaneous or surgically created fenestration may cause right-to-left shunt with arterial desaturation. Aorta-pulmonary arterial collaterals should be considered in CHD patients who have/had low pulmonary blood flow (pulmonary atresia, patients with single-ventricle physiology, patients with Glenn shunts or Fontan circulation). These may cause left-to-right shunting resulting in pulmonary vascular disease, increased systemic ventricular filling pressures, and systemic ventricular volume load. In CHD, patients with chronically elevated venous pressure, venous-venous collaterals can occur (Fontan patients, patients with Glenn shunt) [56]. These collaterals cause right-to-left shunt

with cyanosis. Patients who lack circulating hepatic factor in the pulmonary blood flow (in case of classic Glenn connection) are more prone to form pulmonary arteriovenous malformations causing an intrapulmonary right-to-left shunt [57].

Especially during (sub)acute deterioration of patients with right-to-left shunts (Eisenmenger, Fontan with fenestration and/or collaterals, univentricular heart physiology), the ratio of SVR to PVR should be taken into account. Any state that decreases SVR and/or increases PVR will result in increased right-to-left shunting, systemic arterial desaturation, and worsening of cyanosis. Care should be taken to avoid and treat septicemia, elevated temperatures, and medical therapies that could reduce afterload.

Endocarditis

Endocarditis is more prevalent in patients with CHD with an incidence of 1.3 per 1000 patient years, and even more prevalent in patients with valve-containing prosthetic material [58]. It should be noted that endocarditis risk depends on the type of valve, ranging from 1% per year in homograft conduits to 2–3% per year for Contegra conduits or Melody valves [59]. Heart failure during infective endocarditis is an important risk factor for mortality in patients with CHD [60].

Initial evaluation

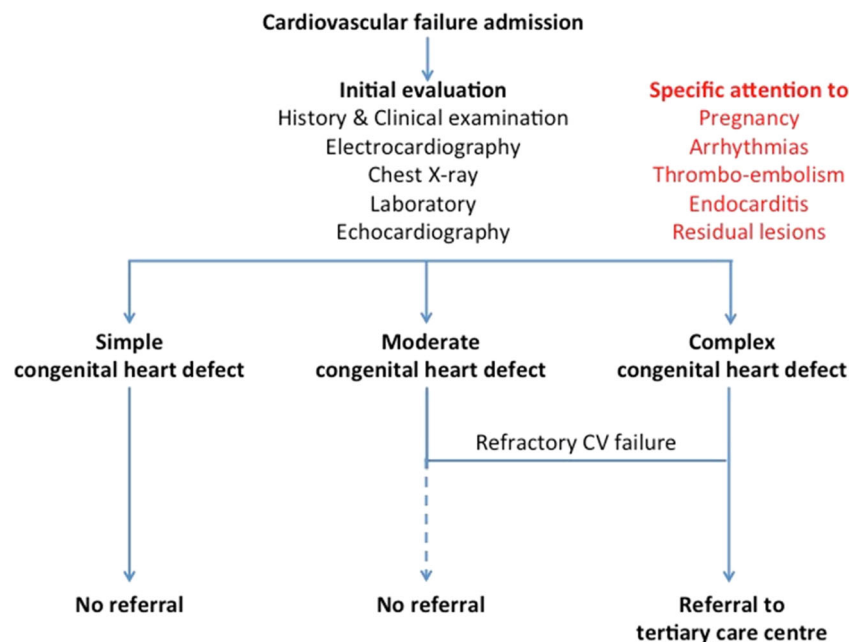
The initial assessment of CHD patients with (sub)acute cardiovascular failure is similar to what is proposed in the ESC heart failure guidelines [7] albeit complicated by the underlying

anatomy and physiology. Distinguishing between subaortic and subpulmonary ventricular failure, the presence/absence of shunts and the presence/absence of pulmonary vascular disease has direct consequences for the management of these patients. It includes confirmation of cardiovascular failure, the identification of precipitating causes (such as anemia, hyper- or hypothyroidism, infectious disease (specifically endocarditis), mechanical causes, and even pregnancy), and evaluation of the severity of the patient's condition. In patients with CHD, there may be an underlying hemodynamic lesion causing or exacerbating heart failure. These depend on the type of underlying heart defect and have been discussed above. Key in the initial evaluation is the assessment of lactate, diuresis, and mental function as markers of circulatory failure Fig. 1.

Oxygenation and ventilation (pulse oxymetry, arterial blood gas)—fluid overload (chest X-ray and biomarker B-type natriuretic peptide (BNP) and NT-proBNP)

In patients with cyanotic CHD, it is important to check saturation measured at the last outpatient clinic visit for comparison. Although there are some concerns regarding the accuracy of pulse oxymetry in patients with cyanotic CHD and elevated hematocrit levels, it remains reliable until a saturation of 80% [61]. In case of differential cyanosis (PDA-Eisenmenger), care should be taken to follow saturation in the lower extremities. We advocate a low threshold for arterial blood gas (and if available mixed venous blood gas) analysis, because of more reliable and more complete results. A chest X-ray is cheap, easily accessible and provides information about pulmonary

Fig. 1 Initial evaluation and location of care for patients with congenital heart disease, admitted due to cardiovascular failure



venous congestion. Biomarkers, such as BNP and NTproBNP, are related with adverse outcome in stable ACHD outpatients [62, 63] and in ACHD patients with heart failure [64].

Blood pressure and heart rhythm/rate (ECG)

Low blood pressure with signs of reduced peripheral and vital organ perfusion requires immediate attention. Both tachy-arrhythmias and brady-arrhythmias can easily disrupt the delicate hemodynamic balance in patients with CHD.

Intraatrial reentrant tachycardia and atrial fibrillation are very frequent in CHD patients due to previous atriotomy, but especially frequent in patients with complete TGA who underwent Mustard or Senning repair and patients with Fontan physiology [38, 65]. As these patients are preload dependent (due to atrial baffles and the absence of a subpulmonary ventricle, respectively), they are especially sensitive for atrial arrhythmias with a rapid ventricular response. Ebstein's anomaly is often related with the occurrence of a Kent bundle [66]. Ventricular tachycardia is most typically encountered in patients with tetralogy of Fallot, but may also occur in patients with TGA or Ebstein anomaly and is sometimes—but not always—related with hemodynamic deterioration of the circulation [67, 68].

Brady-arrhythmias include sinus node dysfunction and atrioventricular block. Sinus node dysfunction is frequent in ccTGA, complete TGA after atrial switch, and Fontan patients, whereas AV block is most typically encountered in ccTGA and AVSD patients (most often patients with Down syndrome).

Ischemia (serial ECG and high-sensitive troponin)

Cardiac strangulation is a rare complication of epicardial pacemaker lead implantation, but has been reported [69]. Malignant coronary anomalies encompass left coronary artery from the right sinus and a dominant right coronary artery from the left sinus with high-risk anatomic features pose an equally high risk. Adverse features include a slit-like orifice, a longer intraarterial segment, and a high takeoff [70, 71]. Coronary fistulae, if large enough, may cause coronary arterial steal leading to ischemia [56]. Arterial switch operation, which is nowadays the treatment of choice in patients with complete TGA, has 5% late coronary complications [72]. However, as the CHD population ages and traditional risk factors for coronary artery disease (CAD) are accumulated, it is clear that myocardial ischemia due to atherosclerosis-related coronary artery disease will increase in the CHD population [4, 73].

Structure and function (echocardiography)

Echocardiography should be performed in the initial evaluation of all patients with CHD admitted due to (sub)acute

cardiovascular failure. It has the advantage of being low-cost, readily available and allows for serial comparison with echocardiographic examinations performed in the outpatient clinic setting. Depending on the underlying congenital heart defect, attention should be paid to the Achilles' heel of the circulation as stated above. The evolution of residual/persistent lesions as well as the development of new abnormalities should be evaluated. The examination should not focus solely on the subaortic ventricle but on the circulation as a whole. Specific attention should be paid to the subpulmonary ventricle, conduits if present, and valvular function. In patients with Fontan circulation, attention should be paid to the possibility of a thrombus in the Fontan connection, especially the right atrium in patients with an RA-PA Fontan.

Further diagnostic evaluation: magnetic resonance imaging, computed tomography, catheterization

Advanced imaging techniques such as *cardiac magnetic resonance imaging (CMR)* and *computed tomography (CT)* are powerful diagnostic tools [74]. CMR provides a superior view on the RV, allows for shunt fraction and regurgitation fraction calculation, and can identify fibrosis using late gadolinium enhancement. In case of implanted pacemakers, CT is an alternative to evaluate cardiac structure and function. Cardiac CT is extremely useful in detecting the presence of thrombus in patients with a Fontan circulation (Fontan circuit and/or pulmonary embolism) or Eisenmenger physiology (laminated pulmonary artery thrombus).

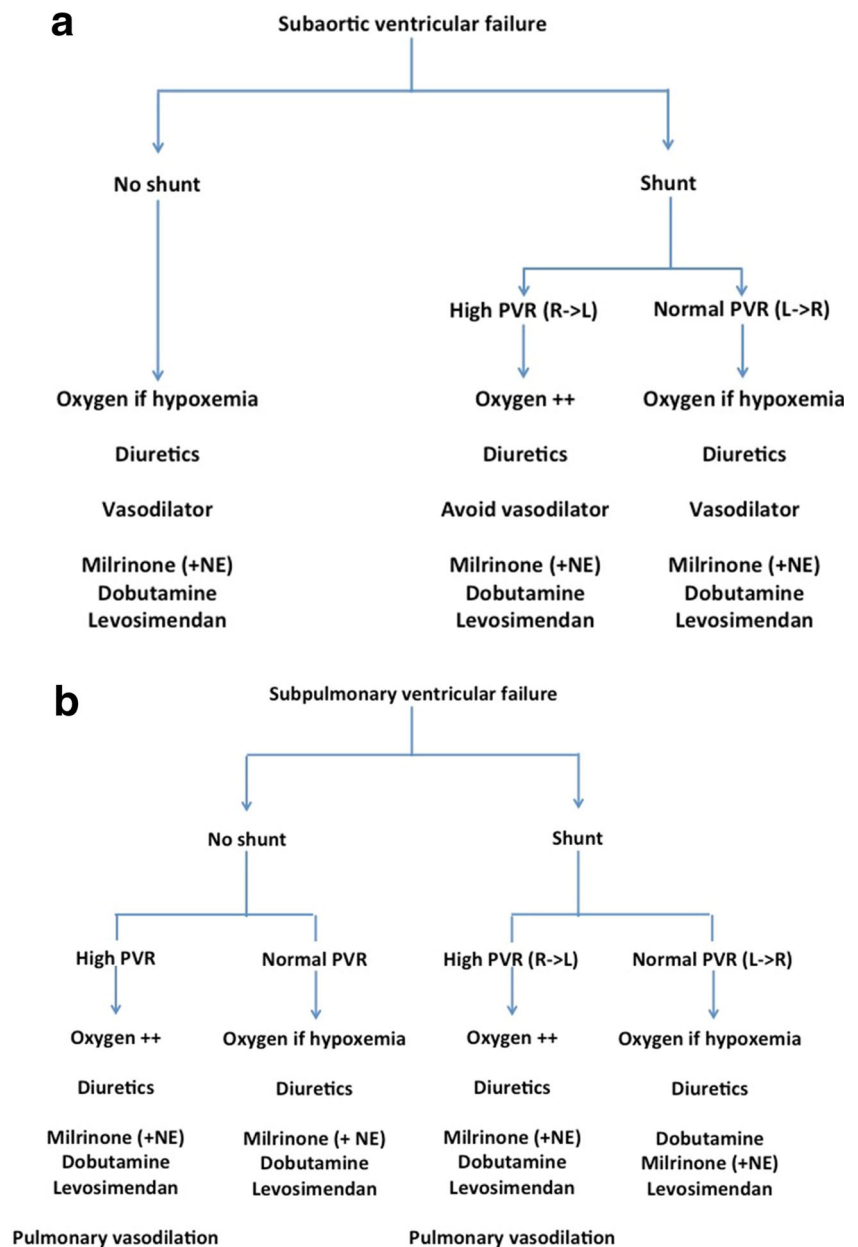
Cardiac catheterization could provide additional information on pulmonary vascular resistance, RV and LV filling pressures, pressure gradients, aorta-pulmonary, arteriovenous or venovenous collaterals, and shunt fraction in selected patients with CHD [74].

Initial management

Treatment will be initiated in parallel with diagnostic work-up. When evaluating the patient with CHD admitted with cardiovascular failure, treatment will be different in patients with subpulmonary failure when compared to subaortic ventricular failure. Patients with persistent intra- or extracardiac shunts require additional attention as medical therapy may increase or decrease shunt fraction.

In patients with subpulmonary failure and/or persistent shunts, pulmonary vascular resistance (PVR) treatment should focus on (1) optimization of preload, (2) optimization of subpulmonary systolic ventricular function (if applicable), (3) decrease afterload by reducing PVR or increased systemic ventricular filling pressures, and (4) maintenance of adequate SVR [75] Fig. 2.

Fig. 2 **a** Treatment algorithm in case of systemic ventricular failure. **b** Treatment algorithm in case of subpulmonary ventricular failure



Oxygen

Oxygen is given to treat hypoxemia. In patients with HFrEF, it is not recommended to treat non-hypoxemic patients as it may decrease cardiac output through an increase in systemic vascular resistance or may increase myocardial ischemia [12, 76, 77]. However, in patients with subpulmonary failure and/or right-to-left shunt, hypoxemia should be avoided as it may increase PVR.

Diuretics

Diuretics remain the cornerstone for symptomatic relief of patients presenting with fluid overload due to immediate

venodilator action and fluid removal. Careful assessment of volume status in patients with subpulmonary failure (preload dependent circulation) is required as both hypo- and hypervolemia will decrease cardiac output [75]. Limited volume loading with evaluation of fluid responsiveness may be useful, but may worsen subpulmonary function in patients with pulmonary hypertension [78].

Vasodilators

Intravenous vasodilators, such as nitroglycerine, isosorbide dinitrate, and nitroprusside, are a cornerstone in the treatment of systemic ventricular failure as they reduce afterload (thereby increasing stroke volume and cardiac output) and preload

(thereby reducing congestion) [79]. Patients with isolated subpulmonary failure are unlikely to benefit from vasodilator therapy. The presence of a right-to-left shunt is a relative contraindication, as it will increase right-to-left shunting and cyanosis in these patients (i.e., decreased SVR/PVR ratio).

Vasopressors

Norepinephrine causes peripheral arterial vasoconstriction through α -1 agonism, and mild positive inotropic effect through β -1 receptor agonism. It may be indicated in subaortic ventricular failure in case of severe hypotension to redistribute blood from the extremities to the vital organs at the expense of increased afterload [12]. In patients with subpulmonary failure and right-to-left shunts, it is important to keep SVR well above PVR to preserve right coronary artery blood flow and avoid myocardial ischemia and increased cyanosis, respectively [75]. Interestingly, in patients with acute or chronic subpulmonary RV pressure load, increased LV afterload (induced by norepinephrine) also resulted in improved RV function and even remodeling [80, 81]. It should be noted that norepinephrine may also increase PVR at higher doses [75].

Inotropes

Milrinone is a phosphodiesterase-3 inhibitor that reduces afterload by vasodilation and has inotropic properties. If subpulmonary RV failure due to volume load (pulmonary regurgitation), milrinone increases contractility of the failing RV and reduces PVR and SVR while maintaining mean arterial blood pressure [82]. It has become the main inotrope in pediatric intensive care after cardiac surgery, independent of subpulmonary, or subaortic ventricular failure [83]. Special caution and monitoring is required as milrinone use has been associated with increased frequency of ventricular arrhythmias [84].

Dobutamine is a β -1 agonist that increases myocardial contractility, reduces SVR and PVR at doses up to 5 μ g/kg/min [75, 85]. Although it improves RV contractility and RV-pulmonary artery coupling [85], doses exceeding 10 μ g/kg/min may cause pulmonary vasoconstriction, which should be avoided in patients with subpulmonary failure.

Levosimendan is a calcium sensitizer with positive inotropic effect by increasing calcium sensitivity of myocytes without increasing oxygen demand. By opening adenosine triphosphate (ATP)-sensitive potassium channels, it also has vasodilatory effects. In patients with severe, low-output heart failure, levosimendan improved haemodynamic performance more effectively than dobutamine [86]. By not affecting intracellular calcium levels, it may also have less pro-arrhythmogenic effects. Levosimendan infused in neonates undergoing congenital cardiac surgery has a potential benefit on post-operative hemodynamic and metabolic parameters [87].

Pulmonary vasodilators

Pulmonary vasodilation in case of increased PVR may be provided by inhaled NO [88] or the inhaled prostacyclin analogue iloprost [89], thereby increasing cardiac output in patients with subpulmonary failure and increased PVR. Inhaled agents, if possible, are preferred over intravenous agents, as these may cause hypotension [75, 90]. Important is to be aware of rebound pulmonary hypertension when admission is interrupted. If the patient was on pulmonary vasodilators prior to admission, it is important to continue those and consider upgrading to dual or triple therapy after the event.

Ventilation

Primary systemic ventricular disease will benefit from positive pressure ventilation (PPV) as it decreases systemic ventricular afterload [91]. In contrast, patients with subpulmonary failure (subpulmonary RV failure, right-sided AV valve regurgitation, and Fontan circulation), PPV decreases cardiac output due to a decrease in subpulmonary preload. Ventilation can be used to decrease PVR and increase blood flow. Hypoxia, hypercapnia, and compression of the pulmonary vasculature at the extremes of lung volumes should be avoided [75].

Congenital heart disease is a systemic disease

Pulmonary function

CHD patients often have diminished pulmonary reserve due to hypoplasia of a part of the lungs, scoliosis, diaphragmatic paralysis, and restrictive lung disease due to previous surgeries [91].

Renal function

Renal dysfunction is frequent in patients with CHD, especially in patients with cyanotic CHD [92]. If a patient is admitted to the intensive care unit, specific attention should be given to deterioration in renal function. Patients with subpulmonary failure, such as patients with Ebstein's anomaly, tetralogy of Fallot, and CHD patients with univentricular heart physiology, may have elevated central venous pressures, decreasing the renal perfusion pressure gradient (difference between mean arterial pressure and central venous pressure) with deteriorating renal function. The same patients may present with increased intraabdominal pressures (in case of ascites), which will adversely influence renal function [92, 93]. Invasive hemodynamic monitoring and measurements of bladder pressures may be useful.

Hematologic consideration and coagulation

CHD patients often present with hematological changes that may increase the risk of clotting and/or bleeding. Patients with cyanotic CHD have secondary erythrocytosis, which is related to increased blood viscosity, a deficiency in platelet numbers and function, and an increased risk for iron deficiency [54, 94–96]. Patients with Fontan circulation have an increased risk for thrombosis due to venous stasis with low flow and inherent prothrombotic state [97].

Cirrhosis and protein-losing enteropathy

Due to chronically elevated systemic venous pressures, hepatic fibrosis with sinusoidal fibrosis and dilatation is present in all adult patients and the degree of fibrosis is increasing over time [98]. Cirrhosis has been associated with greater degrees of desaturation, less related to synthetic liver function and unrelated to the presence of protein-losing enteropathy (PLE) [99]. Hypoalbuminemia, due to PLE, may complicate heart failure treatment in patients with Fontan and is caused by combination of decreased intestinal perfusion pressure (low arterial pressure, high venous pressure) and chronic inflammation [100]. After excluding precipitating factors, various therapies such as diuretics, high-dose aldosterone-receptor antagonists, heparin, steroids, or sildenafil are described being useful in treating PLE in these patients [101]. Even transcatheter fenestration could be considered at the expense of cyanosis [102].

Advanced therapies

In order to identify ACHD patients admitted with acute cardiovascular failure who fail optimal medical treatment, the

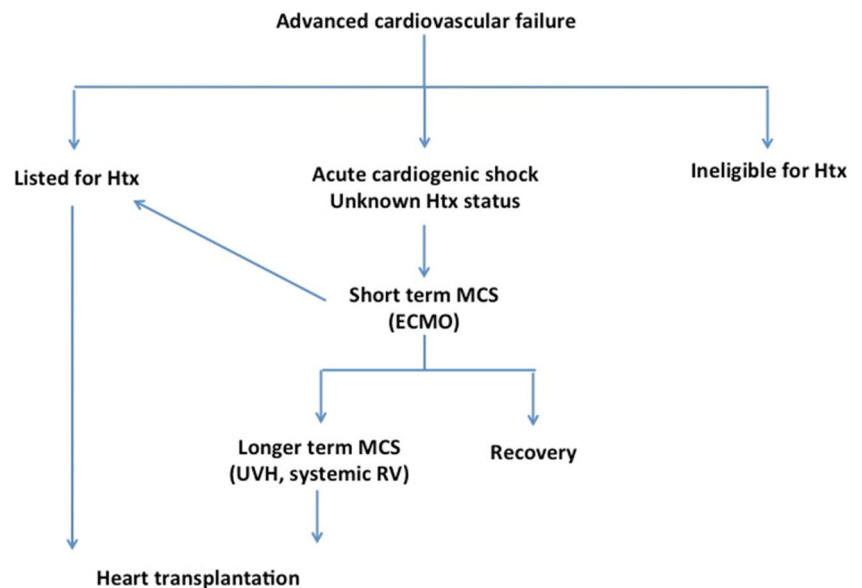
Table 1 INTERMACS profiles [103]

Profile	Description
1	Critical cardiogenic shock
2	Progressive decline on inotropic support
3	Stable but inotrope dependent
4	Resting symptoms home on oral therapy
5	Exertion intolerant
6	Exertion limited
7	Advanced NYHA class III symptoms

INTERMACS profiles could be used to clearly identify risk and patients that may benefit from device therapy (Table 1) [103]. A flowchart for patients with advanced cardiovascular failure is proposed in Fig. 3. INTERMACS 1 and 2 patients should be considered for short-term temporary circulatory support such as veno-arterial extracorporeal bypass with membrane oxygenator (ECMO) [104] either as a bridge to recovery or to transplantation. Veno-arterial ECMO provides full hemodynamic support, but is limited by its complexity and need for perfusion expertise [104]. Moreover, it does not significantly reduce ventricular wall stress [105].

If recovery does not ensue and the patient is listed for heart transplantation, waiting times for a heart transplant often exceed the time that patients can be supported by ECMO. A subset of patients with ACHD may benefit from a mechanical circulatory support (MCS) device as a bridge to transplantation. Main problem with MCS devices in patients with ACHD is related to complex anatomy, biventricular heart failure, and problems related to multiple surgical procedures [106]. Case reports and small series have reported on the use of left ventricular assist devices (LVAD) in patients with a systemic right ventricle [106–110]. Main concerns include anatomical access

Fig. 3 Flowchart for patients with advanced cardiovascular failure in critical cardiogenic shock or deteriorating under inotropic support (INTERMACS 1 and 2). Htx heart transplantation, ECMO extracorporeal bypass with membrane oxygenator, MCS mechanical circulatory support, UVH univentricular heart, RV right ventricle



and cannulation of the systemic right ventricle which has denser trabeculations predisposing to suction events [111]. There has also been an interest in using MCS as a bridge to transplantation in patients with Fontan circulation. Crucially important is identifying the exact cause of Fontan failure. Distinguishing between primary systolic ventricular dysfunction, diastolic ventricular dysfunction, and increased pulmonary vascular resistance is important as it will determine the success of MCS implantation [111]. VAD implantation in Fontan patients is technically challenging due to previous sternotomies. Moreover, aortic cannulation can be difficult in the presence of previous Damus-Kaye-Stansel shunt repair [111]. In patients with a biventricular circulation and RV failure (Tetralogy of Fallot, Ebstein anomaly), there is little evidence for either RVAD or LVAD + RVAD.

When conventional medical and surgical reparative or palliative interventions have failed, heart transplantation is the treatment of choice to improve survival and quality of life. In the international society of heart and lung transplantation database, CHD is a risk factor for 1-year mortality after transplantation with the risk being higher for single ventricle lesions when compared to ACHD patients with a biventricular circulation [112]. There are some specific challenges when considering heart transplantation for these patients.

HLA sensitization is detrimental to transplant outcome and is a specific concern in patients with ACHD who already underwent several surgical procedures, blood transfusion, and/or pregnancies in the past. Even more in the setting of ECMO or VAD, depending on the device used, new or increased sensitization is noted in 20–45% of patients [113, 114]. An increased number of previous sternotomies has been related to worse outcome after transplantation [115]. One of the barriers in listing patients with ACHD is the lack of predictive models for mortality after transplantation, especially for high risk groups such as Fontan patients. A recent study evaluated risk factors in Fontan for mortality after transplantation. It indicates high post-operative mortality specifically in the presence of risk factors [116]. This should be considered when there is doubt whether to list the patient for alternate palliative cardiac surgery or directly for transplantation [115].

Conclusion

In the care of CHD admitted with (sub)acute cardiovascular failure, knowledge of the underlying anatomy and physiology in combination with understanding the effect of medical interventions is crucial. A better definition of a clear treatment algorithm based on the underlying congenital heart defect may help to standardize and improve care for our CHD patients. Avoiding HLA sensitization and additional surgical incisions is important in order to optimize patient chances in case of heart transplantation.

Funding Alexander Van De Bruaene is supported by a grant of the Frans van de Werf Fund for Clinical Cardiovascular Research and the Research Foundation Flanders (FWO).

Compliance with ethical standards

Conflict of interest Alexander Van De Bruaene is supported by a grant of the Frans van de Werf Fund for Clinical Cardiovascular Research and the Research Foundation Flanders (FWO).

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