Acute Right Heart Failure

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Abstract

Heart failure is defined as a life-threatening complex clinical syndrome with exacerbation of symptoms signifying decompensation and requires emergent treatment. In its acute state it presents within 24 hours with symptoms such as shortness of breath, volume overload including pulmonary edema, sometimes forward failure and even cardiogenic shock. Two forms of acute heart failure exist: newly diagnosed "de novo" or acutely decompensated chronic heart failure. This chapter summarizes the clinical and prognostic classification of acute right heart failure, epidemiology, diagnostic work-up and the principles behind treatment and management options that focus on preload optimization, afterload reduction and improvement of contractility.

Keywords

Right heart failure · Cardiomyopathy · Acute heart failure · Congestive heart failure

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10.1 Introduction

Research efforts have disproportionately concentrated on the left ventricle in heart failure, however recent efforts recognize the need to achieve a comprehensive understanding of the right ventricle. In the past, the general laws regarding cardiac mechanics and treatment modalities to improve cardiac performance have been similar in both the right ventricle (RV) and left ventricle (LV). However, the RV is distinct from the LV in regards to structure, geometry, and mechanics [1]. During the past two decades, with the help of imaging modalities, RV function has proved to be an important contributor in the prognosis of heart failure regardless of underlying etiology [2].

Heart failure (HF) is generally a chronic medical condition with exacerbation of symptoms signifying decompensation and requires medical attention. It is a complex syndrome that is caused by structural or functional cardiac disorders leading to impairment of either ventricle to fill or eject blood. It can, however, present as an acute condition within 24 h as seen in pulmonary edema or cardiogenic shock [3]. Right HF is now more frequently identified in current clinical practice due to the increase in the prevalence of predisposing conditions in the population such as LV failure and myocardial infarction [2]. The clinical syndrome presents predominantly as systemic congestion leading to jugular venous regurgitation and ankle swelling [3].

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10.2 Epidemiology

The prevalence of HF is estimated at 1–2% in Western countries and the incidence is about 5–10 per 1000 persons per year [3]. It is estimated that five million Americans are diagnosed with heart failure. The majority of HF patients are hospitalized for acute heart failure. The median length of stay in hospital is 3 days [4]. HF is one of the most common diseases affecting adults in Europe today. In Germany, for example, HF is reported to be the most common diagnosis leading to hospitalization. In persons aged 20–40 years, the prevalence is under 0.5%, however in persons over age 60 years, the prevalence reaches as high as 10% in men and 8% in women [5]. The high prevalence is attributed to the aging population, advances in medicine in primary and secondary prevention of coronary events, as well as in available treatment options. In developed countries, the mean age of patients with HF is 75 years [3].

10.3 Prognosis

Due to recent advancements in medicine such as drug therapy providing beneficial long-term effects, implantable defibrillators and cardiac resynchronization systems, the five-year mortality rate of patients with chronic HF has decreased. A study using enalapril as treatment for HF patients demonstrated significant reduction in cardiac death (hazard ratio was 0.90 for treatment group) and extension of median survival by 9.4 months [6]. Implantable cardioverter-defibrillator (ICD) could reduce mortality rate by 23% among patients with HF [7]. However, minimal improvement in the prognosis among patients with acute HF has been demonstrated. The in-patient mortality rate is reportedly 7% according to the Euro Heart Failure Survey, with a one-year mortality rate at 20–30%. Cardiogenic shock notably has the highest mortality rate, followed by pulmonary edema, and then followed closely by de novo acute HF and right HF [5].

10.4 Etiology and Pathophysiology

Two forms of acute HF exist: (1) newly arisen or "de novo" and (2) acutely decompensated chronic heart failure (ADCHF). Two thirds of all patients with acute HF have a previous history of HF [5].

Common causes of de novo HF include coronary heart disease, mainly acute coronary syndrome and its mechanical complications (e.g. ventricular septal defect, acute mitral insufficiency, right heart infarct), valvular diseases, myocarditis, hypertensive crisis, arrhythmias, circulatory failure (e.g. acute pulmonary embolism, pericardial tamponade, aortic dissection), and surgical intervention and associated perioperative complications [5].

ADCHF is associated with delayed clinical deterioration, such as infections (endocarditis), acute exacerbation of chronic obstructive pulmonary disease and asthma, anemia, worsening renal failure, inadequate fluid and salt intake, non-compliance with medication, adverse drug reaction and interaction (e.g. non-steroidal anti-inflammatory drugs, corticosteroids), uncontrolled arterial hypertension, hypo- or hyperthyroidism, and substance abuse [5].

10.4.1 Acute Right Ventricular Failure

RV dysfunction is a result of pressure overload or volume overload, or a combination of both [2]. Notably, the thin-walled chambers and lesser elasticity of the RV structure accommodate changes in volume overload better than the LV, making the RV more afterload-dependent [1]. Additionally primary loss of myocardium leads to right HF, however it is a rare cause and not confined to the right heart [2].

The RV systolic function remains well-preserved despite long-standing volume-overload secondary to atrial septal defect (ASD) or tricuspid regurgitation (TR). However, due to ventricular interdependence, shift of the interventricular septum, and increased pericardial constraint, these valvular abnormalities lead to

decreased LV cardiac output and LV elasticity. The over circulation of the pulmonary vasculature causes fixed pulmonary hypertension and increased RV afterload [1].

In adults, the RV cannot tolerate acute increases in afterload. An increase in pulmonary artery pressure of 20 mmHg results in a 30% decline in RV stroke volume. Pulmonary hypertension thereby leads to RV dilation and subsequent failure, as seen in acute pulmonary embolism with a sudden drop in RV systolic volume [1].

There are several causes of right HF [2]. The most common cause of RV dysfunction is LV dysfunction and failure resulting in pressure overload and pulmonary venous hypertension [8]. The causes of right heart failure and their corresponding mechanisms are listed in Table 10.1.

Table 10.1 Causes and corresponding mechanisms of right heart failure [2]

Causes of right heart failure	
Left ventricle failure or arrhythmia	
Right ventricle ischemia or injury	RV infarction secondary to pressure overload
Increased afterload	Acute pulmonary embolism
	Pulmonary microthrombi (sepsis)
	Pulmonary arterial hypertension (PAH)
	Hypoxic vasoconstriction
	Mechanical ventilation
	Post CABG
Decreased preload	Hypovolemia
	Capillary leak
	Sepsis
	Superior vena cava (SVC) syndrome
	Right ventricle outflow tract (RVOT) obstruction
	Mechanical ventilation
	Tamponade
Myocardial disease	Left ventricle cardiomyopathies
	Arrhythmogenic right ventricular dysplasia (ARVD)
	Cytokines (sepsis)
Congenital/Valvular	Mitral valve disease
	Ebstein anomaly
	Tetralogy of Fallot
	Transposition of great vessels (TOGV)
	Atrial septal defect (ASD)
	Tricuspid regurgitation (TR)
	Pulmonic regurgitation (PR)
Pericardial	Constrictive pericarditis

10.4.2 Acute Pressure Overload

As a response to increased pressure, the RV compensates via the Frank-Starling mechanism by increasing its contractile state. An increase in ventricular inotropy as a result of a sudden increase in afterload, known as the Anrep effect, is mediated through changes in calcium dynamics and occurs by maintaining the adrenergic state. Catecholamines also contribute to the increase in RV pressure by increasing the inotropy. With a further increase in the afterload, the subsequent dilated RV relies on the Frank-Starling mechanism to function. However, when all of the adaptive mechanisms in response to pressure overload are exhausted, the systemic pressure begins to fall, with a sudden, dramatic, and irreversible decrease in the contractile function of the RV. This concept was first demonstrated in 1954 by Guyton et al. in which it was established that a steady rise in the pressure of the RV secondary to the progressive constriction of the main pulmonary artery to the point where the RV can no longer compensate would lead to a sudden decrease in systemic pressure and cardiac output [9].

Acute pulmonary embolism serves as the prototype of RV failure due to acute pressure overload. Pre-existing cardiac or pulmonary disease and anatomic severity of the obstruction influence the cascading events seen in pulmonary thromboembolism. As vasoconstrictive factors are released from the thrombus and in response to hypoxia, the pulmonary vascular resistance increases, with subsequent increase in pulmonary artery pressure. The result is a dilated and hypokinetic RV. The myocardial oxygen demand increase and eventually leads to myocardial ischemia or infarction [2]. Ischemia or infarc-

tion then causes both a decrease in RV ejection and a septal shift, thereby reducing the LV preload. Ultimately, the heart is unable to maintain cardiac index and arterial pressure, leading to cardiogenic shock [2].

10.4.3 Chronic Pressure Overload

Chronic pressure overload leads to multiple episodes of decompensation, as seen in PAH. The adaptive response of the RV to pressure overload is myocardial hypertrophy and a change in shape from the normal conformation to a spherical geometry. This is a result of increased protein synthesis and increase in cell size. Paracrine, autocrine, and neurohormonal signals such as the renin-angiotensin-aldosterone system (RAAS) and enhanced sympathetic activity, as well as stretch, induce protein synthesis. The long term effect causes the pressure overload to eventually decrease the cardiac contractile force. The accompanying extracellular matrix synthesis impacts the RV function and morphology, thus leading to electrical instability [2]. The adaptive mechanism of the RV in chronic pressure overload due to congenital heart disease, where the RV shape is concentric with preserved function, is attributed to persistent expression of fetal genes [8].

The RV adequately adapts to chronic pressure overload in contrast to acute pressure overload. It is reported that 55% of incident patients with PAH and chronic pressure overload average a survival rate of 3 years. However, some patients with severe PAH remain highly functional (New York Heart Association Functional Class I) for years without developing RV failure [10].

In maladaptive cardiac remodeling, the alpha to beta isotype switching of the myosin heavy chains (MCH) causes a reduction of the alpha-MCH isotype, which represents one third of the total MCH in adults. This type of remodeling is seen in PAH-associated right heart failure. Since beta-MCH has lower adenosine triphosphate (ATP) activity than alpha-MCH, a reduction in systolic function is seen. Additionally, the phosphorylation of troponin T by protein kinase C inhibits the binding of troponin T to tropomyosin, resulting in inhibition of maximal myofibrillar ATP and contraction. Maladaptive remodeling also demonstrates abnormalities in enzymes and ion channels, mitochondrial effects, depletion of myocardial ATP and changes in myocardial substrate use (from fatty acids to glucose) [2].

10.4.4 Right Heart Failure Secondary to Left Heart Failure

Multiple mechanisms contribute to RV failure secondary to LV dysfunction: (1) LV failure increases the afterload by increasing pulmonary arterial pressure, (2) cardiomyopathy in the LV may simultaneously affect the RV, (3) MI that may involve both ventricles, (4) LV dysfunction affecting the systolic driving pressure of the RV coronary perfusion, (5) through ventricular interdependence due to septal dysfunction, and (6) RV diastolic function could be restricted in the setting of LV dilation with a limited pericardial compartment [11].

In the setting of an inferior MI, acute RV failure is a result of LV dysfunction and elevated LV filling pressure. The increase in LV and left atrial pressure leads to a corresponding increase in mean pulmonary artery pressure to maintain the same cardiac output at the same pulmonary resistance. These events lead to a simultaneous decrease in RV contractile function [9].

In left HF, although RV dysfunction appears to be more common in non-ischemic cardiomyopathy, it is also seen in ischemic cardiomyopathy. RV dysfunction in this setting more closely parallels LV dysfunction. RV ejection fraction is a strong and independent predictor for mortality in left HF [12].

The RV may be unable to maintain the flow volume required to keep adequate left ventricular preload in LV failure. The RV status serves as a common final pathway in the progression of congestive HF due to the multiple factors that influence RV function in LV failure. Thus, this is a sensitive indicator of poor prognosis or impending decompensation [11].

10.4.5 Ischemic RV Failure and RV Infarction

Coronary artery disease (CAD) represents the main preceding event (around 70%) in heart failure. The high prevalence of reduced flow reserved

in patients with HF and non-significant stenosis in the main coronary arteries suggests that microvascular impairment contributes to myocardial dysfunction [3].

In acute myocardial infarction (MI), the death of myocytes in one or more ventricular segments results in scarring resulting in inadequate relaxation in diastole and impaired contraction in systole. The lack of synchronicity in the movement connected to the infarcted area reduces the efficiency of pump function [3].

Coronary ischemia leads to a decrease in the contractile function of the RV. It is commonly a consequence of acute coronary syndrome; however, other causes include severe pulmonary hypertension and/or decreased systemic pressure. The blood supply of the RV originates from the right coronary artery, and supplies the inferior wall of the heart in about 90% of the population [9].

The RV is more adept at tolerating ischemia in comparison to the LV due to lower oxygen demand and the presence of coronary collateral flow. RV failure due to RV infarct may improve simultaneously overtime. However, if the RV infarct is hemodynamically significant, mortality is high [9].

RV infarction occurs in the setting of an inferior MI. This is often unrecognized, as an isolated decrease in the RV contractile function with preserved RV outflow pressure is a clinically silent phenomena. In this setting, normal right atrial function is crucial to prevent a loss of atrioventricular synchronicity contributing to cardiogenic shock [9].

Infarction of the RV could cause sufficient myocardial damage resulting in heart failure, shock, arrhythmias, and death in the absence of any superimposed volume or pressure overload, and unrelated to the extent of LV damage. The enlarged hypocontractile right ventricle plays an important role in compromising the overall circulatory status. Patients with right HF and defective RV are found to be more susceptible to deterioration [11].

Tachyarrhythmias, such as nonsustained ventricular tachycardia (NSVT) and atrial fibrillation and flutter (AF), impact right atrial function. In AF, atrial contraction is reduced leading to a decrease in ventricular filling and stroke volume. In NSVT, the systolic volume is diminished due to atrioventricular dissociation and the consequent preload drop. Further decreasing the filling and cardiac output is the shortened diastolic time. Persistent tachyarrhythmias lead to tachycardia-induced myopathy (tachycardiomyopathy) [3].

10.4.6 Congenital Heart Disease and RV failure

RV failure is a common consequence of congenital heart disease (CHD). In patients with large atrial septal defect (ASD), left-to-right shunting and volume overload is seen in the RV. The long-standing volume overload is associated with increased mortality and morbidity, such as HF, decreased exercise tolerance, and arrhythmias. Incomplete RV and right atrial remodeling, and increased risk of arrhythmias are correlated with older patients (>40 years of age) with delayed repair or closure. In comparison to ventricular septal defects, only a small percentage of patients with ASD develop Eisenmenger syndrome presenting later in life. This is attributed to two factors: (1) the timing of the shunting, which is delayed until RV hypertrophy regresses and maturation of pulmonary vasculature occurs, and (2) the absence of high-pressure shear forces as seen in VSD [12].

Ebstein's anomaly is a congenital heart defect in which there is apical displacement of the septal and posterior tricuspid leaflet exceeding 8 or 20 mm/m^2 in the adult. The result is an atrialized portion of the RV and moderate to severe tricuspid regurgitation. Associated congenital defects include ASD with bi-directional shunt, pulmonary stenosis, and accessory pathways. Due to the volume overload of the RV and the inability of the hypoplastic RV chamber to adequately handle systemic venous return, RV failure ensues. Surgical management depends on the valve morphology (attachment, commissures, surface) and the size of the functional RV before repair can be considered [12].

A number of congenital abnormalities such as pulmonary valve stenosis, double-chambered RV, infundibular hypertrophy, or dynamic obstruction of the RV lead to RV outflow tract obstruction. When pulmonary valve stenosis is severe, the RV maintains the ability to adapt. Symptoms rarely manifest during childhood and adolescence; however, long-standing, untreated severe

obstruction lead to RV failure and tricuspid regurgitation. Adults present with symptoms of fatigue and dyspnea which reflect the inability to increase cardiac output during exercise [12].

A common surgical complication of Tetralogy of Fallot is severe pulmonic regurgitation (PR) associated with RV dysfunction, decreased exercise capacity, atrial and ventricular arrhythmias, and sudden death. Timely replacement of the pulmonic valve protects patients from post-surgical complications [13].

In patients with D-transposition of the great arteries who underwent atrial switch surgery and patients with congenitally corrected L-transposition of the great arteries, the anatomic RV supports systemic circulation. These patients present with late-onset RV failure since the RV properties and mechanics are not designed to support the systemic circulation. A progressive decline in RV function due to myocardial perfusion defects, uncoordinated myocardial contraction, and systemic atrioventricular valve (tricuspid valve) regurgitation is seen in patients who have undergone atrial switch surgery. Congenital correction of the L-transposition of the great arteries is associated with moderate to severe systemic atrioventricular (tricuspid valve) regurgitation and increased mortality. Replacement of the tricuspid valve slows the progression of the RV failure [12].

10.5 Clinical Presentation

In the emergency setting, the most common presentation in patients with acute right HF is dyspnea. However, dyspnea is a non-specific symptom that includes pulmonary etiologies, such as asthma and COPD exacerbation, and various cardiac etiologies, such as myocardial infarction [14]. Dyspnea has a high sensitivity of 84–100%, but a poor specificity (17–34%). Paroxysmal nocturnal dyspnea is more specific at 80–84%, but it has low sensitivity at 39–41% [15]. Other clinical presentations include orthopnea, fatigue, weakness and lethargy, as well as peripheral edema and abdominal distention. Orthopnea has a specificity of 77% and a sensitivity of 50% [14]. Right hypochondrial pain is mostly likely due to right sided heart failure, with a specificity of 80% and sensitivity of 23% [15].

Furthermore patients with right HF present with jugular venous distention, lower extremity edema and parasternal holosystolic murmur that is compatible with tricuspid regurgitation [16]. On physical examination, the presence of a third heart sound has the highest specificity of 99%, but has a very low sensitivity of 13%. Jugular venous distention and presence of murmurs have specificities of 90% but they also have low sensitivities of around 30% [14]. In critically ill patients, the most recognizable signs are elevated right-sided filling pressures, such as jugular venous distention and peripheral edema. A parasternal heave may also be felt over the right sternal border [17]. Rales and lower extremity edema both have specificity of 78% but their sensitivity is at 60% and 50%, respectively. Wheezing has low sensitivity and specificity, at 22% and 58%, respectively [14]. Hepatojugular reflux and ascites are not frequently found in HF but they both have a high specificity of more than 96%, but their sensitivity is only at 24% and 1%, respectively [15]. In patients with right to left shunting or severely low cardiac output, cyanosis can also be present [16].

10.6 Diagnostic Work Up

Since most symptoms of acute right HF have either low sensitivity or specificity, it is essential to complete a thorough medical history and physical examination. Recommended investigations for each patient include: (1) 12-lead electrocardiogram, (2) laboratory evaluation, (3) chest radiograph, and (4) echocardiogram [14].

10.6.1 Electrocardiography (EKG)

Obtaining an EKG is routinely done to assess the cardiac rhythm, QRS duration, and presence of atrioventricular conduction block [16]. Although specific, EKG lacks sensitivity [18].

10.6.2 Echocardiography

Echocardiography plays a significant role in the diagnosis of right heart failure. RV enlargement, RV systolic dysfunction, tricuspid regurgitation, pulmonary hypertension, congenital heart defects, valvular heart disease, or left heart disease are consistent in patients with RHF [16].

In the parasternal short-axis view, changes in the RV associated with hemodynamic overload could be seen. The crescent-shaped RV is lost while the septum becomes flat. The LV becomes non-spherical (D shape) resulting in impaired LV filling and decreased cardiac output [2].

Because of the complex structure of the RV, only diameters and areas are used in echocardiographic assessment of RV size. The normal free wall thickness is at 5 mm, and measurements above 5 mm are considered hypertrophy. Using the apical 4-chamber view, the long- and short-axis views can be measured and the end-systolic and end-diastolic area are determined. Normally, the RV area and mid-cavity diameter are smaller than the LV. Visual echocardiographic assessment is inaccurate for identification of functional abnormalities [2].

Three-dimensional echocardiography can be used determine volumes and ejection fraction without geometrical assumptions. This has been proven to be accurate and reproducible compared to cardiac MRI [2].

Measurement of right atrial pressure and cardiac index are the strongest prognosticators in PAH and a more accurate reflection of RV function than PAP. A right atrial pressure of ≥15 mmHg or a cardiac index ≤2 l/min/m^2 is an indication for transplantation referral in PAH [18].

10.6.3 Magnetic Resonance Imaging (MRI) and Computerized Tomography Scan (CT scan)

MRI is the gold standard for quantifying the RV chamber, right heart structure and function [2]. This is especially useful in patients with complex congenital heart defects such as Ebstein's anomaly and hypoplastic RV, precise quantification of valvular regurgitation, and planning of complex surgeries. Recent studies have also shown the prognostic value of RV end-diastolic volumes and pulmonary compliance as assessed by MRI in PAH [16].

Tricuspid annular plane systolic excursion (TAPSE) is most commonly used in clinical practice to evaluate global RV function. It is easily measured by using an M-mode cursor that is passed through the tricuspid lateral annulus in a 4-chamber view. The extent of systolic motion of the lateral portion of the tricuspid ring towards the apex is then measured. This exhibits a good correlation with isotope-derived RV ejection fraction [2]. It has an established prognostic value in patients with PAH and values of <1.8 cm indicates significantly decreased survival [18].

Cardiac CT can provide accurate assessment of structure and function, including the coronary arteries. However, in patients with tachycardia, the cardiac CT and MRI has lower accuracy [15].

10.6.4 Right Heart Catheterization

Cardiac catheterization remains the gold standard for assessing hemodynamics of the pulmonary circulation. It measures the pressures directly and estimates the flow indirectly. Right heart catheterization is useful in confirming the presence of pulmonary hypertension (mean pulmonary arterial pressure at ≥25 mmHg at rest), defining the underlying causes and providing prognostic information [2].

Indications for right heart catheterization include assessment of pulmonary vascular resistance or impedance, pulmonary pressures, cardiac output shunt fraction, and pulmonary vasoreactivity [16].

10.6.5 Exercise Stress Testing

Exercise stress testing is very useful is objective assessment of clinical deterioration in patients with PAH or congenital heart disease. However, this is contraindicated in patients with severe pulmonary vascular disease [16].

10.6.6 Brain Natriuretic Peptide (BNP)

HF-specific tests include brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP). A neuro-hormone, BNP is the activated form of proBNP, and is stored in secretory granules in both ventricles and lesser in the atria. ProBNP is secreted into the ventricles and is broken down into its two cleaved form—the inert N-terminal fragment (NT-proBNP) and its biologically active hormone BNP as a response to volume expansion and pressure overload. If measured in patients with acute dyspnea, BNP levels of less than 100 pg/ml have a negative predictive value (NPV) of 90%, while values of more than 500 pg/ml have a positive predictive value (PPV) of 81%. Its level is a strong predictor of risk of death and cardiovascular events in patients who are previously diagnosed with heart failure or cardiac dysfunction [15]. BNP could predict survival in patients with acute RVH in PAH. Increased levels are associated with increased mortality (1415 pg/ml vs 628 pg/ml) [18].

NT-proBNP has a longer half-life of 72 h compared to 4 h of BNP. They have no clinically significant difference, aside from NT-BNP levels are less affected by obesity. Elevated levels have been associated with renal failure, pulmonary embolism, pulmonary hypertension, and chronic hypoxia. Obese and overweight individuals are found to have relatively low BNP levels [15].

10.6.7 Other Tests

Chest radiography can be used to evaluate cardiac size, pulmonary congestion, and to detect other cardio-pulmonary diseases that are contributory to the patient's symptoms [15]. Once the chest radiograph shows signs of RV dysfunction, RVF is usually advanced and is associated with high mortality [18].

Baseline renal and liver function tests, albumin, uric acid levels and B-type natriuretic peptide could help in determining the prognosis of right heart disease [16]. Sodium levels ≤136 mml/l could predict RVF and increased risk of death in patients with PAH. Creatinine could also predict survival as increased levels suggest increased mortality. Elevated levels of C-reactive protein are associated with increased mortality. Liver transaminases, though its prognostic value has not been established, could reflect hepatic congestion and/or hypoperfusion due to compromised LV function and forward failure [18].

In patients with PAH, the following tests are also obtained: ventilation perfusion scan, pulmonary function tests, overnight oximetry, and serology for human immunodeficiency virus (HIV) and connective tissue diseases. To determine protein-losing enteropathy, stool alpha-1 antitrypsin is also obtained [16].

10.7 Treatment and Management

Treatment of acute right heart failure focuses on three targets: (1) preload optimization, (2) afterload reduction, and (3) improvement of contractility [18]. The primary goal in the setting of acute RHF is to avoid systemic hypotension in order to prevent sequela events such as myocardial ischemia and further hypotension [16].

In etiology-specific management, the treatment options include early revascularization for RV infarction, thrombolysis for pulmonary embolism, antibiotics for endocarditis, and surgical repair. In ST-elevation myocardial infarction (STEMI) involving the right ventricle, early reperfusion has been shown to improve RV ejection fraction and decrease the incidence of complete heart block [16].

In critically ill patients admitted to the intensive care unit (ICU), acute RV failure is mostly a combination of established pulmonary vascular disease complicated by acute derangements in one or all of the following: (1) RV preload, (2) RV afterload, and (3) RV contractility. For example, in an ICU patient who develops cor pulmonale from emphysema and subsequent severe pneumonia, management is directed at optimizing RV function. In patients with acute RV failure secondary to a massive pulmonary embolism, the targeted treatment is to reduce the increased afterload [17].

10.7.1 Optimizing the Preload

Most of the clinical conditions that lead to RHF are associated with increased RV afterload. Diuretics or hemofiltration reduce the excessive RV preload, and thereby reduce RV dilatation and free wall tension. This minimizes ischemia and improves contractility [19]. Progressive diuresis of 500–1000 ml daily is the target goal in patients with volume overload. In patients with hypovolemia, a bolus of 500 ml is given [16].

Generally maintaining moderately high RV diastolic filling pressure of 8–12 mmHg is optimal in RHF [19]. It is then adjusted to optimize RV function and cardiac output. In ICU patients, a central venous catheter is used to monitor superior vena cava oxygen saturation (Sv_{O2}) and central venous pressure, which help in assessing right-sided filling pressures and oxygen delivery. The normal range for Sv_{O2} and lower values suggest reduced cardiac output [17]. In conditions like acute RV infarction (further discussed below) where the RV output is impaired due to contractile dysfunction but the afterload is normal, a higher preload is needed to keep the forward flow [19].

10.7.2 Reducing the Afterload

Pulmonary vasodilators are used in conditions with high pulmonary vascular resistance (PVR). Increased PVR is seen in critically ill patients with acidosis, hypoxia, and hypercapnia. Using lung protective ventilation (using lower effective plateau pressure, tidal volume, and positive end-expiratory pressure) while avoiding hypoxemia and hypercarbia, helps improve RV preload and afterload [19]. The Sa_{O2} is ideally kept above 92% and ventilator settings are adjusted to achieve a lung volume near functional residual capacity and a P_{CO_2} and pH that are near normal as possible [17].

The pulmonary vasodilator agent of choice in critically ill patients is inhaled nitric oxide (iNO), used off-label. Its pharmacologic properties of rapid onset of action and short-half-life have been shown to improve pulmonary hemodynamics in RHF [19]. It improves oxygenation by diverting blood flow away from areas of very low ventilation-perfusion ratio or shunt. In patients with acute respiratory distress syndrome (ARDS), iNO does not improve the outcome but has been shown to improve the RV ejection fraction and end-diastolic volume and improve mixed venous oxygenation saturation in patients with acute RV failure. It must be noted that systemic administration of pulmonary vasodilators can worsen gas exchange and impair ventilation-perfusion matching [17].

Prostanoids are used in patients with PAH and RV infarction [16]. Similar to iNO, three prostacyclin derivatives are currently available in the United States for the treatment of pulmonary arterial hypertension: (1) epoprostenol, (2) treprostinil and (3) iloprost. These agents act as potent pulmonary vasodilators with rapid onset of action and short half-lives. They function to increase the intracellular cAMP level, and provide inotropic effects. These agents are administered via inhalation, thus minimizing the systemic effects [17].

Phosphodiesterase-5 (PDE5) inhibitors are alternate therapeutic agents used to manage patients with acute RHF and underlying chronic pulmonary hypertension. They act by decreasing the pulmonary arterial pressure and increasing the cardiac output in both acute and chronic pulmonary hypertension. However, the potential adverse effect of causing systemic hypotension and blunting hypoxic pulmonary vasoconstriction must be taken into consideration [19].

Other pulmonary vasodilator agents such as the endothelin receptor antagonists and the soluble guanylate cyclase stimulator, riociguat, should also be used with caution in management of acute RV failure. Endothelin receptor antagonists have reportedly been associated with increased mortality in left heart failure. Riociguat has significant systemic vasodilator effects, especially in conditions like sepsis wherein the endogenous nitric oxide production may be increased. Calcium channel blockers should also be avoided because of associated negative inotropic effects and the potential to increase RV stroke work index [17].

10.7.3 Improving Contractility

Supraventricular tachyarrhythmias (SVTs) can further compromise cardiac function. In the setting of chronotropic incompetence, atrial or atrioventricular sequential pacing may improve cardiac output in RHF. Electrical cardioversion is performed on patients with tachyarrhythmias, while pacemaker implantation is performed in patients with high grade AV block [16].

The therapeutic goal in patients who are hypotensive with severely elevated pulmonary artery pressure is to maintain the systemic arterial pressure higher than the pulmonary arterial pressure. Vasopressin, which binds to vasopressin-1 (V1) receptors on vascular smooth muscles, can cause pulmonary vasodilation at low doses (0.01–0.03 U/min). However, at higher doses, it causes coronary vasoconstriction by increasing catecholamine responsiveness [19].

In patients with acute RHF and signs of low cardiac output, inotropic therapy is indicated. Dobutamine acts to increase cardiac index and stroke volume while maintaining preload. At doses of 2–5 mcg/kg/min, dobutamine increases cardiac output while decreasing pulmonary vascular resistance in PAH. Its combination with iNO in pulmonary hypertension has shown to increase cardiac index, decrease pulmonary vascular resistance, and significantly increase PaO2/FiO2 ratio. In hypotensive patients, the preferred agent is dopamine, whereas milrinone is preferred in patients with tachyarrhythimas [16].

If the patient remains hemodynamically unstable after preload optimization, in which dobutamine is primarily used, mechanical support options such as extra corporeal membrane oxygenation (ECMO) and right ventricular assistive device (RVAD) are considered, as well as urgent transplantation and surgery in selected cases [16].

Levosimendan, a calcium sensitizer with inotropic properties, improves RV function or pulmonary hemodynamics in patients with biventricular failure or ARDS [16]. It functions to increase contractility without increasing oxygen consumption. This effect is achieved by sensitizing cardiac troponin C to the effects of intracellular calcium. However, its use is limited by adverse effects, such as hypotension and arrhythmias, especially with bolus dosing [18]. Future studies are needed to determine its role in managing patients with acute RHF [16]. It is currently approved in Europe, but not in the U.S. [18].

10.7.4 Treatment of RV Ischemia and Infarction

RV ischemia presents with both systolic and diastolic dysfunction which causes a serious deficit in LV preload and a resultant drop in cardiac output, leading to systemic hypotension. Adequate filling (preload) of the RV is crucial to maintain sufficient RV output volume and LV function. Initial therapy includes administration of adequate volume and avoidance of therapeutic agents that cause venodilation and decreased RV filling, such as diuretics and nitrates. Initial recommendation is a volume challenge of 300–600 ml of normal saline over 10–15 min via a central line or through a large-bore peripheral intravenous site. Invasive hemodynamic monitoring is preferred since further infusion is damaging when additional increases in the RV volume prevent sufficient LV filling, due to interventricular interactions and intra-pericardial pressure equalization [20].

Although conventional management of RV infarction is initially volume replacement, recent studies have cautioned against excessive volume loading. Traditionally, the initial therapy in hypotensive patients with severe RV infarction without pulmonary congestion is volume expansion when the central venous pressure is <15 mmHg. The accepted regimen is administration of normal saline (40 ml/min, up to 2 L) while maintaining the right atrial pressure at <18 mmHg to prevent volume overload. However, recent clinical studies show that volume loading further elevates the right-sided filling pressure without improving cardiac output. Berisha et al. conducted a study demonstrating that the mean optimal pulmonary wedge pressure (PWP), which reflected maximum LV stroke work index in each patient, was 16 mmHg [21].

Early and complete revascularization of the affected vessels, including the major RV branch, is significant in the recovery of RV

function. Adequate heart rate and maintenance of atrioventricular synchrony by electrical stabilization are key factors in preserving cardiac output in RV infarction. Extracorporeal support devices have been used to support RV failure due to infarction which improve RV shock [21].

References

1. Walker L, Buttrick P. The right ventricle: biologic insights and response to disease: updated. Curr Cardiol Rev. 2013;9(1):73–81. https://doi.org/10.2174/157340313805076296.
2. Apostolakis S, Konstantinides S. The right ventricle in health and disease: insights into physiology, pathophysiology and diagnostic management. Cardiology. 2012;121:263–73. https://doi.org/10.1159/000338705.
3. Pazos-Lopez P, Peteiro-Vazquez J, Carcia-Campos A, Garcia-Bueno L, Abugattas de Torres J, Castro-Beiras A. The causes, consequences, and treatment of left or right heart failure. Vasc Health Risk Manag. 2011;7:237–54. https://doi.org/10.2147/VHRM.S10669.
4. Storrow A, Jenkins C, Self W, Aexander P, Barrett T, Han J, McNaughton C, Heavrin B, Gheorghiade M, Collins S. The burden of acute heart failure on U.S. emergency departments. JACC Heart Fail. 2014;2(3):269–77. https://doi.org/10.1016/j.jchf.2014.01.006.
5. Hummel A, Empen K, Dorr M, Felix S. De novo acute heart failure and acutely decompensated chronic heart failure. Dtsch Arztebl Int. 2015;112(17):298–310. https://doi.org/10.3238/arztebl.2015.0298.
6. Jong P, Yusuf S, Rousseau M, Ahn S, Bangdiwala S. Effect of enalapril on 12-year survival and life expectancy in patients with left ventricular systolic dysfunction: a follow up study. Lancet. 2003;361(9372):1843–8. https://www.ncbi.nlm.nih.gov/pubmed/12788569/.
7. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH, Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-debrillator for congestive heart failure. N Engl J Med. 2005;352(3):225–37. https://www.ncbi.nlm.nih.gov/pubmed/15659722/.
8. Farha S, Lundrgrin E, Erzurum S. Novel therapeutic approaches to preserve the right ventricle. Curr Heart Fail Rep. 2013;10(1):12–7. https://doi.org/10.1007/s11897-012-0119-3.
9. Guyton AC, Lindsey AW, Gilluly JJ. The limits of right ventricular compensation following acute increase in pulmonary circulatory resistance. Circ Res. 1954;4:326–32.
10. Voelkel N, Gomez-Arroyo J, Abbate A, Bogaard H. Mechanisms of right heart failure – a work in progress and a plea for failure prevention. Pulm Circ. 2013;3(1):137–43. https://doi.org/10.4103/2045-8932.109957.
11. Voelkel N, Quaife R, Leinwand L, Barst R, McGoon M, Meldrum D, Dupuis J, Long C, Rubin L, Smart F, Suzuki Y, Gladwin M, Denholm E, Gail D. Right ventricular function and failure: report of a national heart, lung, and blood institute working group on cellular mechanisms of right heart failure. Circulation. 2006;114:1883–91. https://doi.org/10.1161/CIRCULATIONAHA.106.632208.
12. Haddad F, Doyle R, Murphy D, Hunt S. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. Circulation. 2008;117(13):1717–31. https://doi.org/10.1161/CIRCULATIONAHA.107.653584.
13. Davlouros P, Niwa K, Webb G, et al. The right ventricle in congenital heart disease. Heart. 2006;92:i27–38. http://heart.bmj.com/content/92/suppl_1/i27.
14. Teichman S, Maisel A, Alan S. Challenges in acute heart failure critical management: optimizing care despite incomplete evidence and imperfect drugs. Crit Pathw Cardiol. 2015;14(1):12–24. https://doi.org/10.1097/HPC.0000000000000031.
15. Inamdar AA, Inamdar AC. Heart failure: diagnosis, management and utilization. J Clin Med. 2016;5(7):62. https://doi.org/10.3390/jcm5070062.
16. Skhiri M, Hunt S, Denault A, Haddad F. Evidence-based management of right heart failure: a systematic review of an empiric field. Rev Esp Cardiol. 2010;63:451–71. https://doi.org/10.1016/S1885-5857(10)70094-3.
17. Ventetuolo C, Klinger J. Management of acute right ventricular failure in the intensive care unit. Ann Am Thorac Soc. 2014;11(5):811–22. https://doi.org/10.1513/AnnalsATS.201312-446FR.
18. Lahm T, McCaslin C, Wozniak T, Ghumman W, Fadl Y, Obeidat O, Schwab K, Meldrum D. Medical and surgical treatment of acute right ventricular failure. J Am Coll Cardiol. 2010;56(18):1435–46. https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0735109710034996?returnurl=http:%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0735109710034996%3Fshowall%3Dtrue&referrer=https:%2F%2Fwww.ncbi.nlm.nih.gov%2F.
19. Mehmood M, Frank T. Treatment of right heart failure: Is there a solution to the problem? EJ Cardiol Pract. 2016;14(33). https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Treatment-of-right-heart-failure-is-there-a-solution-to-the-problem.
20. Ondrus T, Kanovsky J, Novotny T, Anderson I, Spinar J, Kala P. Right ventricular myocardial infarction: from pathophysiology to prognosis. Exp Clin Cardiol. 2013;18(1):27–30. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3716484/.
21. Inohara T, Kohsaka S, Fukuda K, Venu M. The challenges in the management of right ventricular infarction. Eur Heart J Acute Cardiovasc Care. 2013;2(3):226–34. https://doi.org/10.1177/2048872613490122.