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# ACUTE RIGHT HEART FAILURE IN MEDICAL INTENSIVE CARE UNITS, A CRITICAL CARE PERSPECTIVE

Pulmonary Medicine

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## ABSTRACT

Acute right heart failure in patients admitted to the intensive care unit with acute or chronic pulmonary disease is common, occasionally unrecognized, and difficult to manage. Right ventricular function is a major determinant of survival in patients with pulmonary diseases and this has been recently highlighted with critically ill patients infected with Covid. Basic understanding of the physiology of the right heart as related to pulmonary disorders and approach to management is required. Right heart failure can be classified as acute or chronic based on acuity and pathophysiology. Right heart failure is associated with poor clinical outcomes independent of the etiology; early identification and management can potentially improve outcomes. Shareholders for right heart failure include cardiologists, physicians and intensivists managing right heart failure in critical care. The focus of this review is on acute heart failure in the setting of Medical Intensive Care units.

## KEYWORDS

Right Heart Failure, Pulmonary Hypertension, Acute Pulmonary Embolism, ARDS

## INTRODUCTION:

Right heart failure (RHF) is a clinical syndrome where the cardiac output is insufficient for tissue perfusion in association with elevated central venous pressure. Is usually happens due to right ventricular (RV) limitation and associated with clinical evidence of hypoperfusion [1, 2]. Advances in our understanding of the role of RHF in the clinical outcomes of critically ill patients have led to better diagnosis and management and hopefully better outcomes.

Acute right heart failure and worsening of chronic RHF are not uncommon in the Medical Intensive Care units (MICU). Covid pandemic was associated with acute RHF syndromes. It was quite common for trainees rotating in MICU to be perplexed with this syndrome and management options. There are many excellent reviews that have been published on this topic. The focus of this review is to highlight and summarize current knowledge regarding the relationship between acute pulmonary conditions and RHF in the critical care setting and management implications for trainees and non-intensivists working in the MICU.

### Physiology And Uniqueness Of The Right Ventricle

The RV has been regarded as a forgotten and neglected chamber and it has been overshadowed by the left ventricle (LV) academically and clinically. The right heart is structurally and functionally distinct from the left side. Contrary to the LV, the RV is a thin-walled crescent-shaped structure that is the most anterior of the four heart chambers, it is composed of the inlet, the trabeculated apical myocardium and the conus which constitute the outlet region.

Normal RV function is determined by systemic venous return, RV afterload, pericardial compliance and native contractibility of RV free wall and interventricular septum. The normal RV wall thickness is 3±1 mm, with a basal diameter of 33±4 mm, mid-diameter of 27±4 mm compared to the left ventricular septal, and a posterior wall thickness of 6–10 mm [3]. This is due to differences in pressures in the pulmonary and systemic circulation between ventricles. The RV receives blood from the right atrium and pumps blood out to the pulmonary trunk and is highly sensitive to changes in afterload. The primary function of the RV is to optimize venous return pressure gradient by maintaining low right atrial pressure and perfusion through the low pressure and low resistance pulmonary vascular bed. This is made possible by two different cavities termed sinus and the cone. The sinus and conus are anatomically and functionally different. The former is a flow generator, and the latter is a pressure regulator [4].

As the RV is distinct from the LV, we cannot use the mechanics of the LV to determine the functional qualities of the RV. Since the pressure in pulmonary circulation is generally much lower than that in systemic circulation, less muscle power is needed. Consequently, right ventricular stroke work is approximately one fourth of the left ventricular stroke work. The venous return to the right atrium is dependent on intrathoracic pressures, varying between respiratory cycles. Therefore, the RV is slightly larger and more complaint than the LV. Right coronary artery perfusion is different from left coronary artery perfusion. It occurs during both systole and diastole.

### Interventricular Septal Dependence

The interventricular septum interacts with both ventricles during contraction, inducing ventricular interdependence. In 1910, Bernheim conceptualized the "Bernheim effect" [5]. The Bernheim effect occurs when left heart failure (LHF) and left ventricular hypertrophy causes the interventricular septum to bulge towards the RV, causing RHF, which sometimes precedes LHF.

The reverse Bernheim phenomenon refers to a leftward shift of the interventricular septum in patients with right ventricular pressure or volume overload. This induces smaller left ventricular cavity and less left ventricular end diastolic volume, resulting in impaired stroke volume and hypotension.

In RHF, there is a dysfunction of any of the component of the right heart circulatory system composed by the systemic veins up to the pulmonary capillaries. RHF has been defined as a clinical syndrome due to structural or functional alteration of the right heart circulatory system that results in changes in the delivery of blood flow to the pulmonary circulation and/or elevated venous pressures [6].

### Pathophysiology Of Right Heart Failure

Right ventricular response to disease states depends on the trigger and whether the injury is acute or chronic. Pathophysiological mechanisms of RHF in patients with underlying pulmonary hypertension (PH) include: a) increased RV afterload, b) altered RV preload, c) decreased RV contractility, d) abnormal ventricular interdependence, and e) arrhythmias [7].

Normally the RV is thinner and has a different shape than the LV, allowing it to act as a low pressure system and quickly adapt to changes in preload. In patients with chronically elevated pulmonary pressures and elevated afterload, the RV wall hypertrophy as a compensatory mechanism and eventually the right side cardiac contractility decreases, leading to decreased RV perfusion and increased myocardial oxygen demand. This is associated with increased pulmonary vascular resistance (PVR) and right atrial (RA) pressure. Increasing RV dilation will lead to compression of LV cavity and decreased LV filling [8, 9] .

### Case Presentation:

62-year-old male patient with no prior medical history presented with shortness of breath for few days. He did not report any orthopnea or paroxysmal nocturnal dyspnea. On admission, he had a heart rate of 110, respiratory rate of 26, $SpO_2$ of 90 on ambient air, blood pressure of 92/62mmHg. Bilateral pedal edema was noted, and cardiovascular exam revealed systolic murmur at right sternal border and S3. The lung exam was normal.

Chest-x-ray was normal and the echocardiogram was reported as right ventricular volume and pressure overload. Systolic LV function was normal.

Our patient was admitted to MICU for suspected right heart failure.

**What are the clinical presentation and diagnosis of right heart failure?**

In acute RHF, dyspnea is the most common symptom. In patients with chronic PH presenting with RHF, symptoms are usually progressive; chronic exertional dyspnea due to increased dead space ventilation and cardiac output limitation, syncope, and chest pain can be seen. The diagnosis of RHF among patients with acute or chronic lung diseases requires a high index of suspicion as symptoms and signs can be subtle and non-specific. A detailed history and physical exam and basics laboratory and biomarker could suggest the diagnosis. Common signs of RHF include elevated jugular venous distension and peripheral edema with clear lungs. Examination can reveal a right parasternal heave, the second heart sound can be widely split, and a right-sided S3 and murmur of tricuspid regurgitation can be heard. Hypotension indicates systemic hypoperfusion. Other signs of RHF and hypoperfusion like hepatomegaly, ascites, cool and clammy skin can be found.

**Laboratory:** Plasma brain natriuretic peptide or cardiac troponins levels are not specific for RHF, but in the absence of LHF this should prompt evaluation of RV dysfunction.

In patients with chronic pulmonary or vascular diseases, a low diffusion capacity for carbon monoxide ($D_{LCO}$) and a restrictive ventilatory defect on the pulmonary function test, worsening hypoxemia, abnormal findings in chest computed tomogram (CT), and elevated brain natriuretic peptide are suggestive of PH. These tests are neither very sensitive nor specific. See table 1 for RHF diagnosis.

**What are Echocardiographic features of RHF?**

Echocardiogram findings play a significant role in the diagnosis of RHF, findings suggesting RV dysfunction or failure includes:

1. RV/LV ratio: measured at end diastole, a ratio of >0.6 suggests moderate RV dilation, whereas a ratio of >1.0 indicates severe RV dilation. RV enlargement may be caused by states of acute or chronic pressure overload, chronic volume overload, or intrinsic myocardial pathology, often indicating severe and/or advanced disease with a relatively poor prognosis.
2. RV wall thickness: increased wall thickness suggests chronic RV failure. Normal width is ≤5 mm, an RV thickness of >10mm is considered to indicate chronic process.
3. Interventricular septum: in patients with RV pressure overload, the interventricular septum is pushed to the left (flattened interventricular septum) and the normally circular LV becomes D-shaped. A D-shaped left ventricular cavity in diastole suggests RV volume overload.
4. Tricuspid annular plane systolic excursion (TAPSE) measures the longitudinal excursion of the tricuspid annulus in one dimension. TAPSE is measured in M mode. The normal range for TAPSE is greater than 22–24 mm, and decreased RV systolic function is defined as a TAPSE less than 17 mm.
5. Pulmonary artery pressure: if the tricuspid regurgitation jet can be identified by color Doppler imaging, pulmonary artery systolic pressure (PASP) can be estimated using the equation PASP = 4Vsquare + right atrial pressure estimation from the IVC diameter. Moderate to severely increased PASP generally indicate chronic RV pressure overload.
6. In patients with acute pulmonary emboli (PE), the echocardiogram can show the 60/60 and McConnell's sign. The 60/60 sign refers to the coexistence of a truncated right ventricular outflow tract acceleration time (AT <60 ms) with a PASP of more than 30 but less than 60 mmHg and it has been reported in 71% of patients with PE with a poor sensitivity [10].The diffuse hypokinesis of the RV with apical sparing is referred as McConnell sign with a sensitivity of 22%-52% and a specificity of 97% for acute PE [11, 12].

**Caveats:**

1. The accuracy of echocardiography can be limited in patients with pulmonary diseases due to lung artifacts [13-15].
2. Up to one-third of patients with PH will not have a detectable tricuspid regurgitation required to estimate PASP [16]

Cardiac MRI has a role in the initial evaluation and follows up of patient with chronic right heart dysfunction, advantages of the MRI is that in addition of estimating right ventricular volumes and ejection fraction, it can assess myocardial tissue.

The role of right heart catheter (RHC) in patients with acute RHF of pulmonary causes is not well defined; RHC is considered gold standard for the diagnosis of PH in group 3, but its use is limited. Current guidelines suggest RHC for diagnosis of patients considered for surgical treatment or have suspected pulmonary arterial hypertension or CTEPH, episodes of RV failure, and an inconclusive echocardiogram where diagnosis may lead to a change in management [17].

**Table 1 Diagnostic approach to right heart failure**

| Tools | Findings |
|---|---|
| History and exam | Family history of cardiac disease<br>Social history mainly tobacco and illicit drugs and medications<br>Comorbid conditions including cardiopulmonary diseases, sleep disorders, systemic diseases<br>Symptoms and signs of right heart failure |
| Serum biomarker | Brain natriuretic peptide levels |
| Electrocardiogram | Signs of right atrial or right ventricular enlargement or right axis deviation |
| Echocardiogram | Evidence of right or left side and valvular abnormalities (see text for details ) |
| Cardiac MRI | Main use in patients with chronic right heart dysfunction |
| Right heart catheter | Obtain direct measures of intracardiac and pulmonary pressures and cardiac output |

The most common causes for RHF syndrome can be seen in Table 2. Acute RHF can present after a sudden increase in RV afterload or decreased RV contractility. Chronic RHF usually is due to gradual increase in RV afterload caused by pulmonary hypertension (PH) and the most common etiology is LHF.

**Table 2- Causes of acute and chronic right heart failure**

| Pathophysiology | Acute Right Heart failure | Chronic Right Heart failure |
|---|---|---|
| RV pressure overload (Elevated afterload) | Acute pulmonary emboli<br>Acute respiratory distress syndrome<br>Acidosis<br>Hypoxia<br>Positive pressure ventilation | Chronic obstructive airway disease<br>Chronic thromboembolic pulmonary hypertension<br>Sleep disorder breathing disorders<br>Pericardial diseases<br>Chronic hypoxic interstitial lung diseases<br>Pulmonary arterial hypertension<br>Pulmonary stenosis<br>Left sided valvular disease<br>Restrictive cardiomyopathy<br>Left heart disease |
| RV Volume overload (Elevated Preload) | Excessive transfusion<br>Sepsis<br>Left ventricular assist device support<br>Valvular insufficiency /intra-extra cardiac shunts | Left heart disease<br>Pulmonary or Tricuspid regurgitation<br>Ebstein anomaly<br>Valvular insufficiency /intra-extra cardiac shunts |
| Decreased RV Contractility | Sepsis<br>Left ventricular assist device support<br>Right ventricular myocardial infarct<br>Myocarditis<br>Arrhythmia<br>Peri-operative injury/ ischemia / cardiac contusion | Ebstein anomaly<br>Right ventricle cardiomyopathy / arrhythmias |

**What are the common causes of right heart failure encountered in MICU?**

1. Pulmonary Embolism
2. Acute Respiratory Distress Syndrome

3. Covid-19-associated acute respiratory failure
4. Sepsis
5. Right heart failure in setting of chronic lung diseases

**1- Pulmonary Emboli**

Right ventricular failure has been described in up to 45% of patients with acute PE with a mortality of 25 to 65% depending of hemodynamic stability[18].

Massive PE is defined as presence of hemodynamic compromise with either a systolic blood pressure of ≤ 90 mmHg for 15 min, need for inotropic support, and pulseless or profound bradycardia [19, 20]. Massive PE is seen in less than 5% of all diagnosed cases of PE [21, 22].

Submassive PE refers to patients presenting without systemic hypotension but with evidence of RV dysfunction or myocardial necrosis.

The european guidelines define massive PE as a high-risk PE in which the patient is in shock and submassive PE as an intermediate-risk PE that is further stratified as intermediate low and intermediate high based in the presence of either or both, RV dysfunction or increase in serum biomarker levels respectively [23].

*Pathophysiology:* Acute massive or submassive PE obstructs the right ventricular outflow tract, which is the most important determinant of acute pressure overload. In addition to the release of vasoconstrictors, reflex pulmonary vasoconstriction and hypoxia may add to the increase in PVR and RV afterload [24]. As the RV pressure overload worsens, the interventricular septum shifts to the left decreasing LV cavity volume, and a consequent decrease in LV preload and cardiac output.

This increase in right ventricular wall stress due to acute pressure overload can induce impaired right coronary perfusion, worsening the function of the RV. The sum of these events induces hypotension and could lead to cardiac arrest.

A critical step in the management of acute PE is rapid risk stratification to identify patients at high or intermediate risk. As therapeutic options increases and continues to evolve, the concept and role of having a pulmonary emboli response team available is increasing. Improved outcomes have been reported with use of a multidisciplinary team especially in the high or intermediate risk PE [25].

The management of submassive and massive PE is guided by hemodynamic stability of the patient and available therapies; ranges from anticoagulation and thrombolysis to interventional approaches. The PEITHO trial in patients with submassive PE demonstrated that use of tenecteplase was associated with a significant decrease in the primary endpoint of all-cause mortality or hemodynamic decompensation, and associated with increased rates of major extra cranial bleeding and strokes at 7 days [26]. Chatterjee et al study supported those conclusions [27].

In patients with massive PE, standard anticoagulation is associated with high mortality rates; options for those patients include thrombolysis and surgical or mechanical embolectomy. Good patient outcomes have been reported with use of systemic thrombolysis in patient without contraindications [28-30]. This is currently recommended by the European Society of Cardiology (ERS), American Society of Hematology and American College of Chest Physicians.[23, 31, 32]

Catheter directed therapies (CDT) can decrease thrombus burden by delivering thrombolysis to affected pulmonary artery branches at a lower dose that systemically administered thrombolytic. The use of interventional radiology clot removal or surgical embolectomy can be a valuable intervention for patients with massive (high-risk) PE with contraindications to or failed systemic thrombolysis or shock likely to cause death before thrombolysis can take effect (e.g., within hours. In centers with appropriate expertise and resources, CDT is suggested [32].

*Outcomes:* Acute massive PE accounts for up to 5% of hospitalized cases and carry a mortality of approximately 30% [33-35]. The mortality rate of massive PE has been reported to be over 30%–40% in patients who require cardiopulmonary resuscitation [36-39]. The mortality rate of submassive PE varies from 1.2%–16% [37, 40-42]. Early interventions in patients with hemodynamic instability could explain the lower mortality in some studies.

**2-Acute respiratory distress syndrome (ARDS)** is defined as a) the onset of respiratory symptoms within a week of known clinical insult, b) bilateral opacities in chest radiography not fully explained by pleural effusions, lobar collapse, or nodules and not due to cardiac failure or fluid overload, c) impairment of oxygenation characterized by a ratio of arterial oxygen tension to fraction of inspired oxygen ($PaO_2/FiO_2$) of less than 300. The severity of ARDS is based on the $PaO_2/FiO_2$ ratios [43], and an incidence of 10%–18% of all patients on mechanical ventilation in the ICU [44, 45]. ARDS is frequently complicated by pulmonary hypertension and acute RHF.

The pathophysiology of ARDS is characterized by acute diffuse, inflammatory lung injury, leading to increased pulmonary vascular permeability, increased lung weight, and loss of aerated lung tissue [46]. In addition to alveolar damage, ARDS induces injury to pulmonary circulation by other mechanisms involving endothelial dysfunction, pulmonary microvascular occlusion, microvascular cell sequestration, pulmonary vasoconstriction, extrinsic vessel compression, occlusion by alveoli distension, and pulmonary vascular remodeling and neomuscularization [47]. In addition of the intrinsic reasons for RHF in patients with ARDS, ventilator management can affect right heart function. Factors associated with acute RHF in those patients include increased driving pressure ≥18 $cmH_2O$, $PaCO_2$ ≥48 mmHg and $PaO_2/FiO_2$ <150 mmHg

*Management:* The mainstay in the management of ARDS is treatment of the precipitating conditions and use of mechanical ventilation (MV) with lung protecting strategies with low tidal volume and high positive end expiratory pressure (PEEP). A large cohort of patients with ARDS showed that pulmonary hypertension is a common complication. Mechanical ventilation with increased trans-pulmonary pressure induces increased RV afterload and the use of PEEP, especially higher than 8–10 $cmH_2O$, further increases RV afterload [48-50]. With a severe increase in PVR and septal shift, RV coronary perfusion begins to fall due to systemic hypotension, which can lead to RV contractile failure. Hypoxia and hypercarbia increase PVR further.. Hypoxic pulmonary hypertension also plays a role in the pathophysiology [51]. Additional factors include microvascular thrombi. In a post mortem study of 22 patients with ARDS, 19 exhibited macro- and micro-thromboembolism [52].

*Right ventricular protection* A driving pressure of >18 mmHg, $PaCO_2$ of >48 mmHg, $PaO_2/FiO_2$ of <150 mmHg, and pneumonia as a cause of ARDS are risk factors for acute RHF. Ventilator strategies for those patients with acute RHF should take the aforementioned aspects into consideration in addition of minimizing hypoxia and hypercapnia and patient self-inflected lung injury. Plateau pressure and driving pressure should be limited to lower than 30 mmHg, and less than 15 mmHg respectively [53]. PEEP must be individualized based on oxygenation, RV preload, and afterload. Prone positioning should be considered if no contraindications; this will augments recruitment, prevents alveolar over inflation, improve oxygenation and hypercarbia [54]. Prone positioning is an efficient way to unload the RV and control RV volume overload [55].

Extracorporeal membrane oxygenation (ECMO) is another management options in a subset of patients with very severe ARDS. ECMO may decrease PVR by controlling oxygenation, hypercarbia and acidosis, and may decrease driving pressure by allowing very low tidal volumes. There are no studies evaluating the use of ECMO and outcomes in patients with ARDS and acute RHF.

*Outcomes* ARDS carries a high mortality rate, with an in-hospital mortality of 40% [45]. Studies looking at mortality in patients with RV failure and ARDS are unequivocal and contradictory [56-58]. A meta-analysis of 9 studies concluded that the presence of RV injury was significantly associated with increased overall and short-term mortality [59].

**3. Covid-19-associated acute respiratory failure**

The pooled incidence of RV dysfunction in patients with Covid-19 is 20.4% [60]. The incidence of acute RHF among patients with Covid-19 is uncertain and could vary for different waves [61]. Right heart dysfunction among patients with Covid-19 with acute heart failure is multifactorial and some of the mechanisms include the following: a)

ARDS: Covid-19 related ARDS caused by direct alveolar injury; b) thromboembolism, reported in approximately 24% of patients with Covid-19 pneumonia and in 50% of those patients in the ICU [62]. A recent meta-analysis reported that PE and deep vein thrombosis (DVT) occurred in 16.5% and 14.8% of patients with Covid-19 respectively, and more than half of patients with PE had no DVT [63]; c) myocardial injury usually manifested by an elevation in cardiac troponins and associated with poor outcomes [64-66]. The most common mechanism of elevated troponins levels in those patients is acute RV damage, rather than LV functional impairment [67]. Myocarditis can occur before pulmonary symptoms. Diffuse myocardial damage caused by viral toxicity and the host immune response can weaken RV function. Virus-induced endothelial shedding and microvascular damage may lead to thrombosis and myocardial infarction [68]. Additional mechanisms of RV dysfunction include increased vascular inflammatory infiltrate and endothelial dysfunction secondary to an infection of SARS Cov virus on the endothelium [69, 70].

The association between RV dysfunction and poor outcomes in patients with Covid-19 has been reported [60, 61]. Li et al. observed that the right ventricular longitudinal strain in those patients is a powerful predictor of mortality [71]. In patients with Covid-19 and ARDS, RV dilatation with systolic impairment was independently associated with increased mortality [72].

Therapy is directed against the etiology for RV failure. Lung protective strategies and steroid use in ARDS associated with COVID 19 is helpful. Therapeutic anticoagulation in patients with thromboembolic disease is recommended, but prophylactic use of anticoagulation is not. Cytokine storm partly accounts for RV dysfunction but there is no data that use of immunomodulators such as Tocilizumab, Baricitinib or Anakirna or convalescent plasma in patients with RHF associated with Covid 19 infection.

**4. Sepsis**

Right ventricular dysfunction in patients with sepsis and septic shock can be seen; Lanspa et al. reported RV dysfunction in 48% of patients with sepsis or septic shock [73]. The RV dysfunction in sepsis is multifactorial and attributed to direct myocardial depression and increased PVR. Causes of sepsis-induced cardiac dysfunction include myocardial ischemia due to micro circulatory dysfunction, endothelial dysfunction, and ventricular-arterial uncoupling; direct myocardial suppression is due to the downregulation of beta adrenoreceptors, myocardial depressants, apoptosis, and mitochondrial dysfunction [74]. Volume replacement is the key to maintain perfusion; however, excessive hydration can induce RV dilatation.PVR is often increased in patients with sepsis, especially in the presence of acute lung injury. The decreased production of nitric oxide contributes to an increase in PVR. Other causes include an increase in RV afterload due to hypoxemia, hypercapnia, and the application of mechanical ventilation in patients with acute respiratory failure [75, 76].

The management is focused of control of infection and adequate management of ventilation and fluids.

RV dysfunction in patients with sepsis is associated with increased mortality. Vincent et al. reported that RV dysfunction is common among patients with septic shock and directly related to severity and increased mortality [77]. RV dysfunction is associated with an over three-fold higher 28-day mortality [73].

**5. Right heart failure in patients with chronic lung disease**

Patients with chronic pulmonary conditions complicated with acute or worsening of chronic RHF are frequently managed in the ICU. The classic pulmonary diseases associated with PH and right heart failure decompensation seen in the ICU include chronic obstructive pulmonary disease (COPD), interstitial lung diseases (ILD), chronic thromboembolic pulmonary hypertension (CTEPH) and breathing-related sleep disorders such as obstructive sleep apnea (OSA), obesity hypoventilation syndrome. Details for each condition are out of the scope of this review, however worsening RHF and decompensation of those patients can be catastrophic if not identified and treated promptly.

Survival among patients in group 3 PH ranges from 16%–90%, with an overall 3 year survival of 44%, with the best survival reported in patients with OSA and the worst in patients with ILD-PH [78, 79]. The outcomes of patients with PH due to any of the conditions associated with groups 3, 4 and 5 depend on underlying diseases, severity of PH-associated RHF, and systemic complications of PH. Cardiac arrhythmias, left-side HF, neurohumoral overactivation, congestive hepatopathy, and renal and skeletal muscle dysfunction are some of the systemic complications of PH [80].

Pathophysiological reasons for worsening of RHF in patients with chronic pulmonary conditions are diverse; the most important are hypoxemia, acid base imbalance with acidosis and hypercapnia like in patients with COPD, ILD or sleep disorders. Vascular obstruction predominates in CTEPH. In addition, systolic or diastolic left heart failure can be a contributing factor [81].

**What is the general management of critically ill patients with right heart failure?**

The general management of patients with chronic pulmonary conditions and worsening RHF includes:

- General medical management of underlying condition with a focus on relieving bronchoconstriction and hypoxemia, targeting a $SatPO_2$ of 90%, and identifying and treating precipitating conditions including associated venous thromboembolism, higher risk in patients with COPD and ILD [82].
- Evaluation for the presence of left side heart failure, where use of diuretics could be beneficial. Patients with OHS have an increased risk of cardiovascular complications and increased mortality than patients with OSA [79, 83].
- Correction of hypoxemia and use of noninvasive ventilation remains the cornerstone of therapy in patients with sleep disorders

Management of acute RHF either due to acute factors precipitating it or in the setting of chronic pulmonary conditions with associated PH and RHF follows the same basics principles. In general, there is no specific therapy for patients with lung disease-associated PH [17]. The management is mainly supportive and tailored to the optimization of the underlying condition and the identification and treatment of precipitating factors [7]. In complicated patients or in those with inconclusive clinical data, RHC could be useful but not routinely recommended. Table 3 summarizes management strategies.

**Table 3- Management of acute right heart failure**

| Variable | Recommendations |
|---|---|
| RV preload optimization (volume management) | 1- SBP>90 mmHg and volume overload: diuretics-furosemide, torsemide and close monitor of urine output and fluid balance. Continuous renal replacement therapy as indicated<br>2- SBP <90 mmHg and volume depleted: careful fluid loading with isotonic fluids |
| RV afterload reduction | 1- General: correction anemia, acid base imbalance, avoid hypoxia and hypercapnia<br>2- Mechanical ventilation: avoid high PEEP, hyperinflation, pSILI<br>3- SBP >90 mmHg - vasodilators – Nitroglycerin or nitroprusside<br>4- Inhaled nitric oxide in selected cases |
| RV contractility and coronary perfusion support | 1- SBP<90 mmHg: vasoactive drugs – vasopressors, inotropes, or both<br>a) Vasopressors<br>-Norepinephrine- first choice<br>-In refractory hypotension consider arginine vasopressin, phenylephrine , adrenaline<br>b) Inotropes<br>-Dobutamine, levosimendan, phosphodiesterase III inhibitors (risk arrhythmias and hypotension). They can be combined with vasopressors<br>c) Mechanical circulatory support (ECMO or ECLS) in severely impaired RV function. |

ECMO: extracorporeal membrane oxygenation; ECLS: extracorporeal life support; RV= right ventricle; SBP= systolic blood pressure; pSILI: patient self-inflicted lung injury

Knowledge on the physiology of the right heart is essential, as common therapies used in the critically ill interact with RV dysfunction, including fluid management, vasopressors, and MV.

**Mainstay of treatment of RV failure:**

**a) Optimizing RV preload.**

The primary goal is to establish adequate filling pressures with the aim

of avoiding RV overloading. Clinical exam showing edema and jugular venous pulsations may suggest volume overload. Confounders include a systolic V wave due to tricuspid incompetence. Central venous pressure measurement is a static marker, it does not predict fluid responsiveness and it is no longer recommended as an isolate tool to asses RV preload [84-86].

Measures of volume responsiveness include:

a. Passive leg raise.
b. Pulse pressure variation and stroke volume variation.
c. Sonographic assessment of the right atrial area and diameter as well as the septal shift to the left and inferior vena cava size and collapsibility index. Sonographic assessments are operator-dependent, do not give continuous data and requires serial measurements. Evaluation of IVC has technical limitations and confounding factors.

Use of RHC for management is limited due several randomized trials showing lack of survival benefit in patients with cardiogenic and septic shock or ARDS and needs of additional expertise and training [87-90]. There are technical challenges regarding interpretation of data and insertion of catheter which could lead to wrong interpretation [91, 92]. Pulmonary artery pulsatility index (PAPi) is useful in management of advanced heart failure, cardiogenic shock and left ventricular assist therapy; it was initially reported as a predictor of RV failure in patients with acute MI [93, 94]. The utility of this measure in RHF due to pulmonary diseases remains to be established.

**Can we give IV fluids in patients with right heart failure?**

Fluid administration in patients with RHF and shock requires close hemodynamic monitoring as this can lead to septal deviation, decreasing LV and RV function and overall hypoperfusion. In patients considered to be volume overloaded, the use of diuretics or continuous renal replacement therapy could improve hemodynamic [95]. The use of dynamic fluid responsiveness can be faulty and invalid in patients with RV dysfunction as these predictors assume a normal RV function. Serial clinical examination is required to detect the presence or absence of significant overload.

**b) Decreasing RV afterload.**

The main goal is to decrease PVR. General principles include evaluations of acid base and metabolic abnormalities that potentially can worsen RHF and adjustment of MV [7, 96].

*Mechanical ventilation:* Passive ventilation decreases preload and increases RV afterload. Changes in RV preload depend on the increase in juxtacardiac pressure, which depends on tidal volume, PEEP, and chest and lung compliance. The use of high levels of PEEP or tidal volumes potentially increases PVR due to the compression of the vascular bed [95]. Use of lung protective strategies in ARDS has to be balanced with the impact in acid base, acidosis which potentially worsens the PH.

*Medication:* The use of medications to decrease PVR and consequently RV afterload and increase cardiac output may be challenging. Inhalation medications have the advantage of a short half-life and less pronounced effect on SVR, avoiding unnecessary hypotension. Inhaled nitric oxide is the most commonly used drug, followed by inhaled iloprost Inhaled nitric oxide results in transient improvement in oxygenation with no survival advantage and a potential increase in renal impairment [97]. Intravenous short acting vasodilators are also recommended with avoidance of hypotension and tachycardia.

**c) Increasing RV contractibility and adequate coronary perfusion pressure**

The coronary perfusion of the right coronary artery (RCA) occurs during both systole and diastole. In patients with RV pressure and volume overload, both RV systolic and end diastolic pressures are elevated. Coronary perfusion pressures will decrease with systemic hypotension, compromising RCA flow and inducing risk of RV ischemia. It is imperative to keep the systolic blood pressure higher than the pulmonary pressure to maintain RCA perfusion.

The main goal of vasoactive drugs it to maintain adequate perfusion and ideally lower the ratio of PVR to that of SVR. These medications have different effects on vascular tone. *Vasopressors:* norepinephrine is the preferred vasopressor due to its safety profile. It increases RV function and SVR as PVR increases, likely at high doses [98]. Epinephrine and low-dose vasopressin could be used as well. Avoiding drugs that induce pulmonary vasoconstriction is advised [95, 99].

*Inotropes:* Low-medium doses of dopamine or dobutamine (≤ 10 ug/kg/min) and milrinone have been used in patients with RHF; all had a safety concern for arrhythmia and hypotension. The control of tachyarrhythmia is needed to improve RV contractibility [7, 95]. In hypovolemic patients, dobutamine due to alpha1 and beta1&2 effects could trigger hypotension due to systemic vasodilatation. Vasopressor support may be necessary to counter vasoplegia. Dobutamine increases oxygen consumption, and prolonged use may worsen the supply/demand of oxygen consumption for the cardiac muscle.

Phosphodiesterase inhibitors such as milrinone have a positive inotropic response and decrease both SVR and PVR to a greater extent than dobutamine and unlike dobutamine, decrease oxygen consumption. They can trigger hypotension, risking right coronary perfusion. Vasopressor support may be necessary and may limit its use.

**Back To Our Patient:**

Investigation in our patient revealed elevated troponins and pro-BNP. Chest angiogram showed pulmonary emboli and his PESI score revealed Class IV. He was classified as having a sub-massive PE or PESI high risk; he received systemic thrombolysis, preload optimization, and inotropes with low doses dobutamine. He improved and he was later started on anticoagulation and successfully discharged.

**Are there any other management options in right heart failure when nothing works?**

Extra Corporeal Membrane Oxygenation (ECMO) should be considered in selected critically ill patients not improving with medical therapy either as a bridge to recovery or transplant if indicated. It is a viable alternative when heart failure is a consequence of hypoxic pulmonary disease. Indications for ECMO can be divided into three categories according to the supported organ, cardiac and respiratory support, or a combination of the two. Carefully selection of patients and the right type of ECMO is needed.

## CONCLUSION

The management of RHF, either acute or worsening of chronic RHF continues to evolve as new technological and medical advances are incorporated to patient care and this is especially true in the critical care environment. Right ventricular function is a major determinant of survival in patients with pulmonary diseases and basic understanding of the physiology is the key for skillful management. The critical care management of those complex patients needs to focus in identification of presence of RHF, treating precipitating factors, hemodynamic optimization and a multidisciplinary approach to offer advanced treatment as needed.

**Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Author Contributions**

Both of the authors Drs Gilda Diaz-Fuentes (GDF) and Sindhaghatta K Venkatram (SKV) contributed equally.

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