Right Ventricular Failure and Pulmonary Hypertension

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KEYWORDS

• Right ventricular failure • Pulmonary hypertension • Cardiogenic shock
• Massive pulmonary embolism

KEY POINTS

- Right ventricular dysfunction plays a central role in high-risk, but relatively rare, conditions such as massive pulmonary embolism and primary pulmonary arterial hypertension; however, it also can be an important component of several disorders routinely encountered in the emergency department (ED) setting, including sepsis, adult respiratory distress syndrome, and chronic heart failure.
- Comorbid conditions frequently present in the ED population–such as COPD, methamphetamine abuse, and morbid obesity–are frequently associated with undiagnosed underlying pulmonary hypertension, and these patients may be particularly susceptible to the development of acute decompensated right ventricular failure when presenting with acute disorders that are independently associated with right ventricular dysfunction.
- Because the pathophysiology of acute decompensated right ventricular failure involves a cascade of superimposed vicious cycles that, once established, can be difficult to extricate from, avoiding diagnostic and management pitfalls in the ED becomes particularly important.
- Frequent diagnostic pitfalls include attributing lactic acidosis to septic rather than cardiogenic shock, ruling out cardiogenic shock based on observation of a hyperdynamic left ventricular function on bedside echo, and inferring the absence of volume overload based on normal-appearing lung fields on chest radiograph.
- Frequent management pitfalls include aggressive intravenous fluid administration, failure to support blood pressure by prompt initiation of appropriate vasopressors, and unnecessary endotracheal intubation.

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INTRODUCTION

It is most useful for emergency providers (EPs) to approach pulmonary hypertension (PH) in the context of a broader understanding of right ventricular failure. Patients with known, chronic PH will constitute a minority of patients with right ventricular dysfunction (RVD) encountered in the emergency department (ED), and EPs will be best served by viewing PH as part of a spectrum of patients presenting with acute decompensated right ventricular failure (ADRVF).

EPs often regard PH and RVD as relatively rare entities that are mainly the province of specialists. In actuality, they are important components of the pathophysiology of several conditions frequently encountered in the ED:

- *Sepsis*: RVD is present in more than one-third of septic patients.[1] Although the presence of left ventricular (LV) systolic dysfunction does not seem to confer an increased risk of mortality, RVD seems to be associated with a 2- to 3-fold increase in mortality in patients with septic shock.[2]
- *Congestive heart failure (CHF)*: RVD is present in greater than 40% of patients with chronic left-sided heart failure and is a predictor of mortality in these patients.[3]
- *Chronic obstructive pulmonary disease (COPD)*: some degree of PH is present in approximately 20% of patients with COPD, and PH may occur in up to 90% of patients with severe COPD.[4]
- *Adult respiratory distress syndrome (ARDS)*: RVD is present in greater than 20% of patients with ARDS and is associated with a significantly increased risk of mortality.[5]
- *COVID*: in a recent meta-analysis, RVD was found to be present in 1 out of 5 patients hospitalized with COVID-19 and was associated with more than a 3-fold increase in mortality.[6]
- *Obesity hypoventilation syndrome*: greater than 50% of patients with obesity hypoventilation syndrome have PH,[7] and PH frequently goes undiagnosed in this population.[8]
- *Methamphetamine abuse*: a recent study of the national Pulmonary Hypertension Association Registry found that methamphetamine-associated PH accounted for greater than 20% of PH cases.[9]
- *Massive pulmonary embolus (PE)*: mortality in patients with massive PE is due to hemodynamic collapse from ADRVF, with most of the deaths occurring in the first 1 to 2 hours after presentation.[10]

Failure to recognize PH and/or RVD can become particularly problematic because routine interventions often performed early in a patient's ED course—such as intravenous fluid (IVF) administration and emergent endotracheal intubation (ETI)—have the potential to precipitate clinical deterioration in these patients. As such, it is important for EPs to become comfortable with early recognition and ED management of ADRVF; this is an area that lacks a robust body of evidence to guide management and instead relies on a solid understanding of the relevant pathophysiology.

PATHOPHYSIOLOGY

Right Ventricular Afterload

The systemic vascular resistance (SVR) constitutes the LV afterload, and the pulmonary vascular resistance (PVR) constitutes the RV afterload (**Fig. 1**). Pressures in the systemic and pulmonary circulations can fluctuate independently; the PVR can be elevated in the absence of SVR elevation and vice vera.

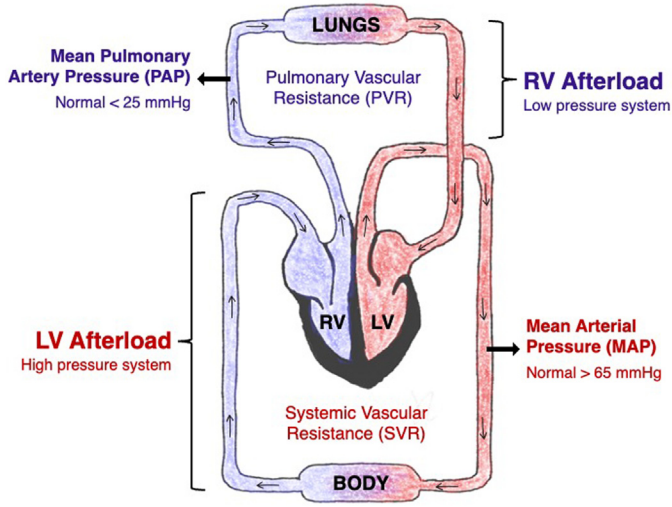

Fig. 1. Comparison of right and left ventricular afterload. The left side of the circulatory system is a high-pressure system, whereas the right side of the circulatory system is normally a low-pressure system. MAP, mean arterial pressure; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

Perhaps the most important thing to understand about the physiology of the RV is how it responds to afterload (Fig. 2).

- The muscular LV tolerates afterload well, with a minimal drop in stroke volume even in response to relatively large increases in SVR.
- The RV, on the other hand, is highly sensitive to increasing afterload, whereby even a small increase in PVR results in a precipitous decline in RV stroke volume.

The major factors driving elevations in RV afterload fall into 2 categories: obstructive and vasoconstrictive.

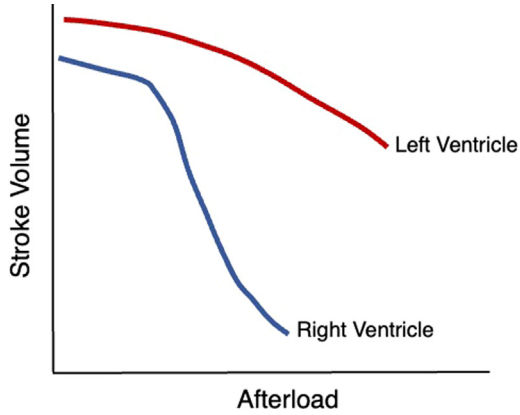

Fig. 2. Comparison of the left and right ventricular stroke volume in response to increasing afterload.

Obstructive: major causes of mechanical obstruction to flow through the pulmonary circulation include the following:

1. *Venous thromboembolic disease (VTE)*: both acute and chronic pulmonary thromboemboli cause mechanical obstruction to flow. The presence of a large volume of smaller emboli—while less visually impressive on computed tomography (CT) scan compared with a saddle embolus—can still cause significant mechanical obstruction.
2. *Pulmonary arterial hypertension (PAH)*: PAH comprises a subset of PH causes arising from primary pulmonary artery (PA) hypertrophy due to endothelial dysfunction and vascular remodeling.
3. *Lung disease*: both acute and chronic pulmonary disease can cause obstruction of forward flow through the lungs due to destruction of lung parenchyma and obliteration of lung vasculature.
4. *Morbid obesity*: elevated intrathoracic pressure from excessive weight compressing the chest wall and diaphragm can cause functional restrictive lung.

Vasoconstrictive: although adrenergic stimulation plays a role in regulation of pulmonary vasoconstriction, there are several additional factors that affect the vasomotor tone of the pulmonary circulation, often in ways that are distinct from the systemic circulation:

1. *Hypoxemia*: hypoxemia triggers pulmonary vasoconstriction in order to optimize ventilation perfusion matching (**Fig. 3**). A "side effect" of this vasoconstrictor response is elevated PVR associated with hypoxemia.
2. *Hypercarbia and acidemia*: pulmonary vasoconstriction is enhanced by both hypercapnia and acidemia (**Fig. 4**).
3. *Inflammation*: in contrast to the systemic circulation—in which the predominant vasomotor response to inflammation is vasodilation—release of inflammatory mediators into the pulmonary circulation triggers pulmonary vasoconstriction. Pulmonary vasoconstriction in response to cytokines released by activated platelets plays a significant role in the pathogenesis of massive PE.

Obstructive and vasoconstrictive mechanisms act synergistically, whereby obstructive causes tend to promote the development of vasoconstrictive causes, which can

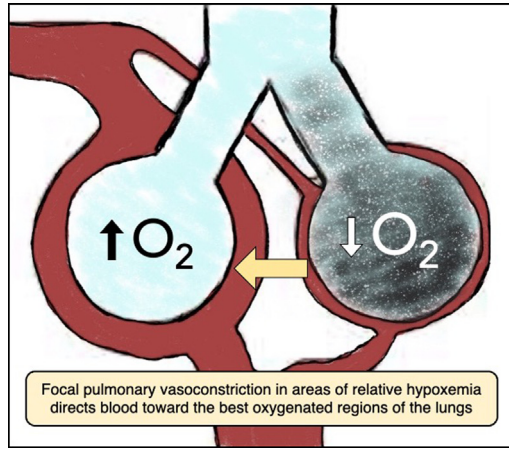

Fig. 3. Hypoxic pulmonary vasoconstriction. As a consequence of this phenomenon, hypoxia causes increases in pulmonary vascular resistance.

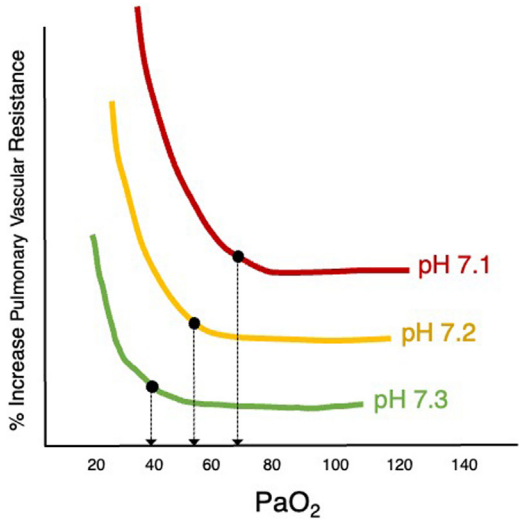

Fig. 4. Pulmonary vasoconstriction in response to hypoxemia and acidemia. Hypoxemia causes a "dose-dependent" increase in pulmonary vascular resistance, which is magnified in the presence of acidemia.

then promote the development of vascular remodeling and thrombosis that subsequently exacerbate obstructive causes.

Right Ventricular Preload

The RV is a significantly more compliant structure than the LV, with large changes in volume resulting in relatively small changes in pressure. Consequently, at the lower end of the volume spectrum, the RV is preload dependent insofar, as it relies on adequate intravascular volume to maintain right-sided filling pressures sufficient to sustain cardiac output (CO). Once, however, volume loading reaches the point at which further increases in RV volume result in significant increases in RV pressure; the RV–by the same token of its relatively high compliance–can rapidly become overdistended.

The point at which this occurs highly depends on whether the RV afterload is normal or elevated. Regardless, once RV overdistension begins to occur, several sequelae arising from RV dilation ensue that, together, can precipitate ADRVF in patients with or without underlying PH or RVD:

1. Impaired ability of the RV to generate contractile force due to the mechanical effect on myocytes of overstretching the RV free wall.
2. Elevated RV wall tension that simultaneously results in a reduction in coronary filling and increased oxygen demand, making the RV more susceptible to ischemic insult.
3. Tricuspid annular dilation that can precipitate or exacerbate existing tricuspid regurgitation, contributing to worsening RV volume overload and overdistention.
4. Reduction of LV preload that arises from interventricular septal shift, as discussed later.

Ventricular Interdependence

The functional interplay between the LV and the RV involves both in-series and in-parallel interactions.

Series interaction: in order of maintain LV CO, the RV CO must match that of the LV. When RV forward flow supplying blood to the LV decreases, LV forward flow to the body must necessarily also decrease.

Parallel interaction: because they share a common septum, volume and pressure changes in one ventricle affect the other (Fig. 5).

- Because the ventricles co-exist within the nondistensible space of the pericardium, ventricular diastolic filling is functionally a zero-sum-game: if the end-diastolic volume of one ventricle is increased, the end-diastolic volume of the other will necessarily decrease.
- Under normal conditions, LV end-diastolic pressure (LVEDP) exceeds RV end-diastolic pressure (RVEDP) with bowing of the interventricular septum into the RV.
- Under conditions that cause RV overdistention, however, the RVEDP begins to increase. At the point at which the RVEDP exceeds the LVEDP, septal bowing toward the LV begins to impair LV diastolic filling with a concomitant drop in LV end-diastolic volume (ie,: LV preload).

Right Ventricular Perfusion

Recall that tissue perfusion is not determined by blood pressure alone, but rather by a pressure *gradient* (Fig. 6).

- LV systolic pressures, by definition, approach systemic systolic blood pressure. Because of the absence of a pressure gradient between the LV and coronary arteries during systole, most of the LV perfusion occurs during diastole.

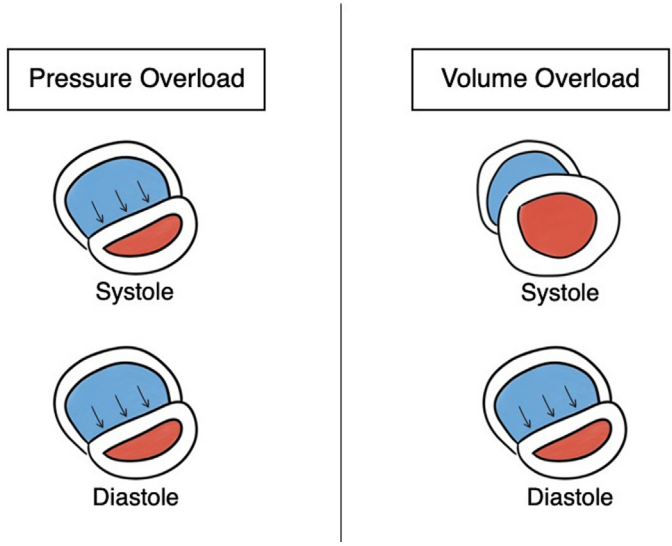

Fig. 5. Comparison of interventricular septal shift under conditions of pressure overload versus isolated volume overload. Echocardiographic appearance on parasternal short view of the RV (*blue*) and the LV (*red*) during systole and diastole under conditions of either right ventricular pressure overload versus right ventricular volume overload. Depending on the severity of volume overload and the degree and chronicity of pressure overload, right ventricular dilation may or may not be observed. A chronic pressure-overloaded RV. LV, left ventricle; RV, right ventricle.

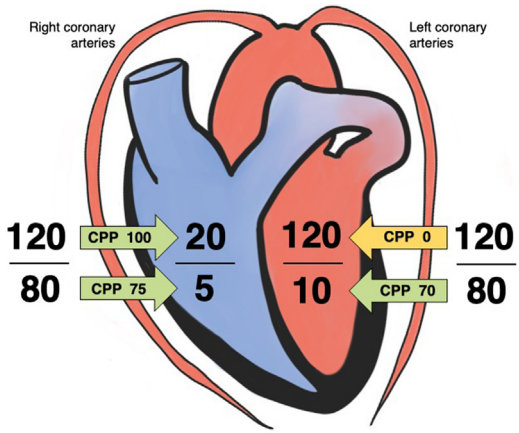

Fig. 6. Comparison of perfusion of the right and left ventricles throughout the cardiac cycle. CPP, coronary perfusion pressure.

- The right heart, in contrast, is a low-pressure system. Consequently, there is a robust gradient between the coronary artery pressure and RV pressure during both diastole *and* systole, providing continuous perfusion to the RV throughout the cardiac cycle with most of the perfusion occurring during systole when the pressure gradient is greatest.

Causes of Right Ventricular Failure

Causes of RV failure in acutely ill patients may be divided into 3 categories (**Table 1**): pressure overload, volume overload, and decreased contractility.

Pressure overload: RV pressure overload can occur acutely or chronically. When exposed to chronic elevations in afterload, RV remodeling occurs such that the RV begins to resemble the more muscular LV and is thereby able to better sustain forward flow even in the context of even significantly increased afterload.

Causes of RV pressure overload are generally broken down into categories using the World Health Organization PH Groups system and detailed in **Table 2**.

Volume overload: RV volume overload can occur in patients both with and without chronic PH and/or RVD.

Patients with chronic disease: patients with chronic PH may be compensated from a pressure loading standpoint; however, they generally require diuretic management to maintain a steady state. In failures to maintain euvolemia–often in the context of worsening renal function and/or medication noncompliance–these patients can present with ADRVF due to volume overload.

Patients without chronic disease: ADRVF due to volume overload in the absence of chronic disease is most often iatrogenic.

- This may occur in the settings such as massive PE, when the clinician either fail to recognize the underlying cause of acute deterioration and/or has misconceptions regarding the utility of fluid administration in patients with ADRVF due to increased afterload.
- Even in the absence of elevated RV afterload, excessive volume loading can precipitate RVD once volume administration reaches the point of cause RV overdistention and progressive dilation, as discussed earlier.

Table 1
Major causes of right ventricular failure

Pressure Overload	Volume Overload	Depressed Contractility
Thromboembolic disease	Excessive fluid administration	Right ventricular myocardial ischemia
Primary pulmonary arterial hypertension	Insufficient diuresis	Myocarditis
Lung disease	—	Sepsis
Morbid obesity	—	—

Depressed contractility: the major acute causes of isolated RV contractile depression are essentially similar to those of the LV:

1. Myocardial ischemia
2. Myocarditis
3. Septic cardiomyopathy

It is notable that the septal component of LV contraction is a significant contributor to the ability of the RV to generate systolic pressures; as such, RV contractile dysfunction that occurs in concert with LV dysfunction can be particularly profound.

Pathophysiology of Acute Decompensated Right Ventricular Failure

The pathophysiology of acute decompensated RV failure is outlined in Fig. 7 and may best be conceptualized as a cascade of superimposed vicious cycles, that, once established, can be difficult to extricate from. Any of the 3 etiologic categories mentioned earlier can act as entry points to the vicious cycle of acute decompensated RV failure. It is also important to note that multiple sequala of ETI—including systemic hypotension, hypoxemia, hypercarbia, and positive pressure ventilation—can act as vicious cycle precipitants, and the potential for simultaneous occurrence of 2 or more of these factors places patients with PH and/or RVD at high risk for dramatic hemodynamic deterioration during ETI. In one study of patients taken to the operating room for pulmonary embolectomy, hemodynamic collapse occurred in nearly 20% of patients during ETI.[11]

CLINICAL PRESENTATION AND EVALUATION

Types of Presentations

Major precipitants of acute RV failure in patients without any prior history of RVD or PH include the following:

- *Massive PE*: although it is a common misconception that “massive” refers to the thrombus size, massive PE is in fact defined by hemodynamic instability due to ADRVF as a consequence of acute VTE.
- *COVID-19*: acute presentations of patients with COVID with abrupt hemodynamic deterioration triggered by ADRVF in the *absence* of massive PE are increasingly being reported.[12]
- *RV myocardial infarction (RVMI)*: isolated RVMI is relatively rare and most often associated with acute MI of the LV inferior wall.
- *Myocarditis*: although biventricular involvement is common, isolated RV myocarditis is exceptionally rare.
- *Left ventricular assist device (LVAD)*: there is a high rate of RV failure in LVAD patients with multifactorial mechanisms consequent to derangements in both the series and parallel interactions between the RV and LV.

Table 2
Classification of pulmonary hypertension

	Group	Pathogenesis	Common Causes
1	Primary pulmonary arterial hypertension	• Increased pulmonary vascular resistance due to intrinsic disease of the pulmonary arterial vasculature • Associated with endothelial dysfunction and hyperplasia similar to that seen with systemic essential hypertension	Connective tissue & autoimmune disease (scleroderma, SLE, RA) Drugs and toxins (methamphetamine, fenfluramine, dasatinib) Portal hypertension Infectious (HIV, schistosomiasis) Idiopathic and heritable
2	PH due to left heart disease	• Chronic elevations in venous back pressure from left heart failure • May develop secondary vascular remodeling that can resemble intrinsic disease	LV systolic dysfunction LV diastolic dysfunction Mitral regurgitation & stenosis Aortic regurgitation & stenosis
3	PH due to chronic lung disease	• Chronic hypoxic pulmonary vasoconstriction • Ultimately results in vascular remodeling	COPD ILD OSA Obesity hypoventilation syndrome
4	PH due to chronic thromboembolic disease	• Mechanical obstruction of the pulmonary arterial vasculature	Chronic thromboembolic disease Intrathoracic tumors
5	Multifactorial PH	• Potpourri of mechanisms	Myeloproliferative disease Sickle cell disease Sarcoidosis Hyperthyroidism (primarily toxic multinodular goiter)

Abbreviations: COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; ILD, interstitial lung disease; LV, left ventricle; OSA, obstructive sleep apnea; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Although patients may present acutely with truly de novo ADRVF, it is more common to see acute or chronic presentations whereby some degree of underlying pulmonary vascular disease is exacerbated by 1 of the 3 main causes of RV failure detailed earlier.

Many patients may have undiagnosed underlying PH and/or RVD, making it more difficult to rapidly identify ADRVF as their primary problem in the acute setting. Specific scenarios that should raise suspicion include the following:

- Morbid obesity, especially when associated with obesity hypoventilation syndrome and/or obstructive sleep apnea
- Severe COPD or interstitial lung disease
- Methamphetamine use

In patients with an established diagnosis of PH and/or RVD, the major clinical question becomes the identification of factors that may have provoked an acute decompensation. Frequent precipitants include the following:

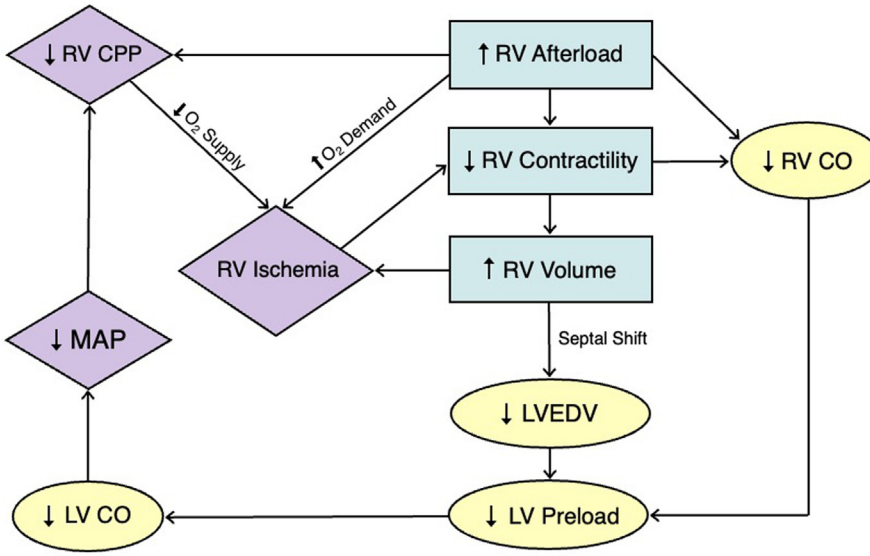

Fig. 7. Vicious cycle pathophysiology of acute decompensated right ventricular failure. Because of the inability of the RV to maintain normal contractility in response to even relatively small increases in afterload (see Fig. 3), a frequent entry point into this vicious cycle is an increase in RV afterload. As RV stroke volume decreases, RV volume begins to increase, as blood backs up into the RV. This increasing RV volume eventually leads to progressively worsening interventricular septal shift, which ultimately compromises LV filling (see Fig. 6). The associated drop in LVEDV in combination with low RV CO due to depressed RV contractility and/or increased RV afterload can dramatically decrease LV preload, at which point LV CO will start to decrease. Systemic hypotension ensues, decreasing RV coronary perfusion. The RV CPP takes a second hit if elevated RV systolic pressures associated with high RV afterload are simultaneously present (see Fig. 1). Depressed RV CPP compromises RV oxygen supply and precipitates the development of worsening ischemia, even in the absence of primary coronary artery pathology; the resultant RV ischemia can be particularly profound if the drop in RV oxygen supply occurs concurrently with increased oxygen demand associated with elevated RV wall tension due to RV volume and/or pressure overload. Global RV ischemia further contributes to worsening RV contractility, perpetuating the vicious cycle. CO, cardiac output; CPP, coronary perfusion pressure; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; MAP, mean arterial pressure; RV, right ventricle.

- Interruption of pulmonary vasodilator medications (eg: sildenafil, Remodulin).
- Volume overload due to noncompliance with diuretic therapy and/or worsening renal function.
- Exacerbation of underlying primary pulmonary disease.
- PH predisposes to the formation of *in situ* PEs due to slow flow through the PA, and patients with underlying RVD may not have the physiologic reserve to tolerate even relatively small thromboemboli.

History and Physical Examination

Signs and symptoms: patients with RV failure do not necessarily present with what are thought of as "classic" symptoms of heart failure.

- The lung examination is generally normal in the absence of concomitant LV failure or chronic lung disease.
- Patients often present with abdominal pain or distention in the context of congestive hepatopathy due to elevated right heart pressures being transmitted to the portal venous system and may even present with mesenteric ischemia secondary to a combination of increased back pressures due to mesenteric venous congestion combined with decreased forward flow from concomitant cardiogenic shock.
- Prominent jugular venous pressure elevations as well as peripheral edema may be present, although it is important to note that absence of these signs does not rule out ADRVF, particularly if acute in onset.

Patients will often present tachypneic, tachycardic and, not infrequently, hypoxemic. Particularly given the significant risks associated with ETI in these patients, it is crucial to understand that their oxygen saturation (SpO_2) may be low due to several possible mechanisms, most of which are likely to be exacerbated rather than alleviated by ETI:

- *Massive PE*: hypoxemia in massive PE is not due to dysfunction of the pulmonary parenchyma (eg: pulmonary edema, pneumonia, and so forth) but rather due to VQ mismatch and global tissue hypoperfusion, neither of which will be improved by ETI.
- *Chronic lung disease*: patients with PH due to chronic lung disease often have a baseline low SpO_2. It can be extremely challenging to assess whether their acute presentation is due primarily to an exacerbation of their chronic lung disease as opposed to the development of ADRVF in the context of chronic PH. Regardless, attempting aggressive treatment that simultaneously address both possibilities is prudent before considering ETI.
- *Falsely low SpO2 reading*: patients presenting in cardiogenic shock not infrequently have spuriously low SpO_2 readings due to decreased peripheral perfusion. In contrast to patients with LV failure, patients with cardiogenic shock due to ADRVF are unlikely to have pulmonary edema, and it is therefore important to identify spurious SpO_2 values early, as that ongoing concern for hypoxemia could trigger an unnecessary ETI, which can precipitate acute hemodynamic collapse in these patients.

Past medical history (PMH): the key details of PMH specific to patients with PH and RVD include the following:

- *Disease history*: establish if the patient has a known PMH of RVD or PH and, if so, whether they are listed for transplant or undergoing a transplant evaluation. The latter may help inform decisions about whether transfer for possible extracorporeal membrane oxygenation may be reasonable in cases of refractory ADRVF.
- *Medication history*: this should focus on 3 different categories:
  1. Pulmonary vasodilators that are associated with rebound PH when acutely discontinued (eg,: sildenafil, Remodulin).
  2. Oral anticoagulant use in the absence of other obvious indications suggests severe enough PH to warrant prophylaxis for in situ PE.
  3. Loop diuretic use and home doses to help guide initial dosing of furosemide and/or bumetanide if diuresis becomes necessary.
- *Diagnostic studies*: some patients will have a prior right heart catheterization with direct measurement of PA pressures; more commonly patients may have a previous echocardiogram documenting a PA systolic pressure. Information on

baseline PA pressures is useful both to help determine disease severity as well as to help guide mean arterial pressure (MAP) goals (see later discussion on systemic blood pressure targets).

Laboratory Findings and Imaging

Laboratory findings: the main challenge in the laboratory workup of patients presenting with ADRVF is to avoid misinterpretation of commonly acquired laboratory findings. Laboratory findings in ADRVF are often misconstrued as consistent with septic or hypovolemic shock rather than cardiogenic shock due to ADRVF, which increase the likelihood of clinically significant errors in management.

- *Lactate*: it is a common misconception that lactic acidosis is synonymous with septic shock. Lactic acidosis in fact can be associated with any shock state, including cardiogenic shock due to ADRVF. Recall that fluid administration will only improve a lactic acidosis if volume administration improves tissue perfusion, which is not the case when the cause of tissue hypoperfusion is cardiogenic shock.
- *Renal function tests*: patients will often present with acute kidney injury (AKI) due to renal hypoperfusion secondary to ADRVF. An elevated BUN/Cr ratio that suggests a prerenal cause can be particularly confusing in this context because prerenal AKI is often misinterpreted as synonymous with hypovolemia. In reality, however, a prerenal AKI simply indicates that the kidneys are receiving insufficient forward flow but does not signify whether the underlying cause of this insufficient forward flow is hypovolemic, distributive, or cardiogenic.
- *Liver function tests (LFTs)*: it is not necessary to obtain LFTs, but, if obtained, patients may have a transaminitis due to congestive hepatopathy, which can be misinterpreted as evidence of an RUQ process causing abdominal sepsis, particularly in patients presenting with abdominal pain.
- *Brain natriuretic peptide (BNP)*: BNP can be spuriously low in patients with morbid obesity; this may be problematic in patients with PH secondary to obesity hypoventilation syndrome insofar, as a false-negative BNP may lead to incorrect conclusions regarding the presence of heart failure and/or volume overload.
- *Troponin*: in the absence of electrocardiogram finding that suggests acute inferior and/or posterior ischemia, a positive troponin likely indicates demand ischemia rather than coronary artery occlusion.
- *Arterial blood gas (ABG)*: an ABG can be particularly useful in these patients, especially if there is any question regarding the accuracy of SpO_2 readings. In addition, CO_2 and pH are useful with regard to identification of potentially modifiable factors that may be contributing to increased pulmonary vasoconstriction.

Imaging: chest radiograph may show an enlarged cardiac silhouette but is often normal in the absence of concomitant LV failure or primary lung disease. In addition to ruling out PE, CT angiography (CTA) of the chest can provide a better assessment of RV size as well as underlying lung disease. Reflux of IV contrast into the interior vena cava and/or hepatic vein on CTA is a specific—although insensitive—sign that suggests ADRVF.

Point-of-care ultrasound (POCUS): a frequent pitfall in patients with ADRVF is that the LV often seems hyperdynamic; this is not due to systemic hypovolemia, but rather due to poor RV CO. As such, an underfilled-appearing LV should always trigger evaluation for the presence of RV dilation and septal flattening that suggests ADRVF (see **Fig. 6**). Visual estimation of RV systolic function is not straightforward and should not be used to draw firm clinical conclusions on POCUS. Observation of an abnormally thick-walled RV may suggest a PH with a chronically pressure-overloaded RV.

EMERGENCY CRITICAL CARE MANAGEMENT

RVD and PH are areas that lack a robust body of evidence to guide management, and instead rely on a thorough understanding of related pathophysiology and knowledge of expert opinion, coupled with meticulous clinical attentiveness at the bedside.

There are 5 key management components (**Table 3**):

1. Optimize volume status
2. Support systemic blood pressure
3. Decrease right ventricular afterload
4. Support right ventricular contractility
5. Caution with ETI

Optimize Volume Status

The RV response to volume loading highly depends on whether RV afterload is normal or elevated.

Normal RV afterload: in the setting of normal RV afterload, ADRVF due to contractile dysfunction may result in a "preload-dependent" RV requiring volume augmentation in order to maintain CO. The clinical relevance of this physiologic principle, however, is unclear:

- Based on this presumptive physiology and a single study of 28 patients conducted in 1989, the American Heart Association guidelines continue to state that nitrates are contraindicated in RVMI.[13] In contrast, more recent studies—collectively comprising greater than 1000 patients—found no increased risk of adverse events associated with nitrate administration in patients with acute RVMI.[13]
- The reported efficacy of volume administration in RVMI is variable.[14] Expert opinion suggests careful volume administration in patients with an RVMI presenting with hypotension via aliquots of 200 to 300 mL of crystalloid with serial reassessment of clinical effect.[15]

Elevated RV afterload: when RV failure occurs in the setting of increased RV afterload, intravascular volume expansion can precipitate rapid clinical deterioration and should be avoided. Volume removal is often a critical part of management in these patients.

- Patients with underlying chronic RVD or PH are often volume overloaded on initial presentation. Even in the case of acute PE—in which there is no expectation that these patients would be necessarily hypervolemic at presentation—a single furosemide bolus on admission seems to produce significant and earlier improvements in RV function compared with IVF administration, without any associated adverse events.[16] Certainly in patients presenting with massive PE who have been administered IVF during their initial ED course and are decompensating hemodynamically, it would be reasonable to initiate diuresis to at least restore euvolemia.

It is critical to understand that diuresis may be required even in the presence of AKI. AKI in the context of cardiogenic shock due to ADRVF is generally due to cardiorenal syndrome and can only be successfully addressed by improving forward flow to optimize renal perfusion, which generally requires volume removal.

- In patients with elevated RV afterload, the combination of septal shift due to elevated RV pressures and decreased volume delivery to the LV due to

Table 3
Critical management components of acute decompensated right ventricular failure

Critical Management Priorities	
Optimize fluid status	• Volume administration can precipitate clinical deterioration in patients with elevated RV afterload • Patients with chronic PH and/or RVD often require diuresis • In patient with depressed RV contractility and normal RV afterload, may consider gentle volume boluses with frequent reassessments
Support systemic blood pressure	• Even transient hypotension can be problematic; low threshold to initiate early vasopressors and invasive blood pressure monitoring • Vasopressin and epinephrine are optimal, norepinephrine is also reasonable • Patients with elevated PA pressures may require higher MAP targets to optimize RV coronary perfusion pressures
Decrease RV afterload	• Correct of hypoxemia, hypercarbia, and acidemia • Initiation of an inhaled pulmonary vasodilator
Support RV contractility	• After correction of systemic hypotension, consider additional inotropic support particularly if failing to respond to diuretic challenge • Epinephrine is a reasonable first-line inotrope, can also consider addition of milrinone vs dobutamine if systemic blood pressures have normalized
Extreme caution with intubation	• High risk of hemodynamic deterioration with ETI • ETI rarely has a role in the management of patients whose acute decompensation is due *primarily* to ADRVF; if ETI is required as appropriate management for an acute condition in a patient with *comorbid* PH and/or RVD, it should be undertaken with careful hemodynamic management

Abbreviations: ADRVF, acute decompensated right ventricular failure; ETI, endotracheal intubation; MAP, mean arterial pressure; PA, pulmonary artery; PH, pulmonary hypertension; RV, right ventricle; RVD, right ventricular dysfunction.

depressed RV CO may lead to near obliteration of the LV at end-systole. In this circumstance additional volume loading has actually been shown to *decrease* LV preload.[17,18] Furthermore, worsening RV dilation precipitated by IVF administration increases RV transmural pressure and oxygen demand, thereby worsening RV ischemia.

- It is also important to note that in the case of ADRVF due to either pressure or volume overload, hypotension is not necessarily a contraindication to volume removal; due to the physiology of ADRVF in the context of elevated pulmonary pressures, volume removal may be expected to actually improve blood pressure by increasing CO, whereas volume administration is in fact likely to worsen hypotension as per the mechanisms outlined earlier.
- It is, however, the case that an initial diuretic challenge may not be successful because the kidneys are unlikely to respond robustly to diuretics in the absence of sufficient renal perfusion. As such, hemodynamic interventions to support systemic blood pressures and optimize RV function are often necessary preconditions to facilitate volume removal. Furthermore, because the RV has a flatter

Starling curve than the LV, a considerable amount of volume unloading may be necessary before any improvement in RV function is seen.[19] Once sufficient hemodynamic optimization occurs with associated improvements in renal perfusion, a "virtuous cycle" of RV volume offloading often begins, at which point significant increases in urine output may occur in a relatively short amount of time.

Approach to volume removal: early placement of a Foley catheter is recommended to monitor hourly urine output in order to guide prompt escalation of diuretic therapy.

- Diuresis may be initiated with a loop-diuretic bolus, followed by rapid dose escalation if an adequate response is not observed. Intravenous administration is preferred, as that severe mesenteric venous congestion may compromise intestinal perfusion in these patients. If there continues to be a suboptimal response to escalating doses of loop-diuretics, then it is reasonable to add chlorothiazide, and initiation of a furosemide or bumetanide drip may also be considered.
- If the patient still fails to respond, then further optimization renal perfusion may be accomplished by adding an inhaled pulmonary vasodilator if not already initiated, and it is also reasonable to consider initiation of additional RV inotropic support at this point.

Support Systemic Blood Pressure

Blood pressure targets: the RV is particularly prone to ischemia when RV coronary perfusion is hit with the dual insult of elevated pulmonary pressures occurring concurrently with systemic hypotension.

- Even relatively transient hypotension can act as a trigger for the vicious cycle of ADRVF; there should be a low threshold for pressor initiation and placement of an arterial line.
- To preserve the pressure gradient between the coronary arteries and the pressure-overloaded RV, it may be necessary to maintain systemic pressures higher than an MAP goal of 65; this is particularly important in patients with chronic PH, in whom RV systolic pressures may approach systemic pressures. Prior documentation of PA pressures can be helpful to guide MAP goals in these patients.

Pressor selection: as discussed earlier, in patients with elevated RH pressures, volume administration is unlikely to improve hypotension, and pressors are the mainstay of treatment. The ideal vasopressor for use in acute RV failure would be an agent that increases systemic blood pressure without increasing pulmonary pressures. In this context, pressor choice may be based on the degree to which a given pressures is associated with favorable effects on the PVR to SVR ratio. See **Fig. 8** for a comparison of vasoactives in the management of ADRVF.[20,21]

Decrease Right Ventricular Afterload

Correct hypoxemia, hypercapnia, and acidemia: these factors act both independently and synergistically to increase pulmonary vasoconstriction such that even if correction of all 3 is not possible, correction of even one of these variables will have disproportionally beneficial effects on pulmonary vasoconstriction (see **Fig. 5**).

Pulmonary vasodilators: pulmonary vasodilators may be administered systemically or via inhalation.

- *Systemic pulmonary vasodilators*: the major side effect of oral or intravenous administration of pulmonary vasodilators is systemic hypotension. Abrupt discontinuation of these medications should be avoided in the ED, if at all possible. If a patient who is taking chronic systemic pulmonary vasodilators presents with hypotension, the MAP should be supported with vasopressors while awaiting more definitive intensive care unit management. Alternatively or in addition, an inhaled pulmonary vasodilator may be initiated as a temporizing measure.
- *Inhaled pulmonary vasodilators*: the advantage of inhaled pulmonary vasodilators is that they rapidly induce pulmonary vasodilation and decrease PVR with relatively minimal effects on systemic blood pressure. Inhaled pulmonary vasodilators may be administered through ETI, high-flow nasal cannula, or—in some cases—venturi mask. At centers where it is not possible to initiate epoprostenol or nitric oxide through specialized continuous inhalational devices, off-label use of inhaled milrinone[22] or nitroglycerin[23] may be considered (**Table 4**).

Inotropic Support

Once RV perfusion has been improved through the correction of systemic hypotension and measures to decrease RV afterload have been undertaken, inotropes to support RV contractility may be initiated (see **Fig. 8**). In cases of PH due to LV failure, inotropes carry the additional benefit of improving LV forward flow, thereby decreasing RV afterload as well as indirectly improving RV contractility through augmentation of the role of the septum. Epinephrine is a reasonable first-line inotrope in patients who continue to have borderline low MAPs and/or escalating vasopressor requirements. In patients whose MAPs have normalized and are on stable vasopressor doses, dobutamine or milrinone may also be considered, particularly in the context of an inadequate response to diuresis due to suboptimal renal perfusion.

Caution with Endotracheal Intubation

The most important consideration regarding ETI is not selection of periintubation medications, but rather the decision of whether a patient truly requires intubation in the first

Drug	PVR	SVR	PVR : SVR	Comments
Vasopressin	↔ ↓	↑↑	↓↓	• Probably ideal first-line vasopressor to support systemic blood pressure for acute decompensated RV failure • Not titratable, so may need to add additional vasoactive medications.
Epinephrine	↓	↑	↓	• Can be useful as a single agent to support both RV contractility and systemic blood pressure • β1 and β2 effects more prominent than α1 effects at doses less than ~20mcg/min • Increasingly prominent α1 effects at higher doses.
Norepinephrine	↔ ↑	↑↑	↔	• Without the β2 to balance out the α1 effects on the pulmonary circulation, higher risk for pulmonary vasoconstriction, particularly at high doses
Phenylephrine	↑↑	↑↑	↑↑	• Suboptimal due to effect on PVR:SVR ratio
Dopamine	↑↑	↑↑	↑↑	• Suboptimal due to effect on PVR:SVR ratio • Risk of tachydysrhythmias
Dobutamine	↓↓	↓	↓↓	• Supports RV contractility and can decrease PVR • Can cause systemic hypotension and so may not be ideal during initial resuscitation • Risk of tachydysrhythmias
Milrinone	↓↓	↓	↓↓	• Supports RV contractility and decreases PVR • Can cause systemic hypotension so may not be ideal during initial resuscitation, particularly given the significantly longer on-off time compared to other vasoactive • Useful addition in patients who continue to have inadequate perfusion once systemic blood pressure has stabilized

Fig. 8. Comparison of vasoactive medications in the management of acute decompensated right ventricular failure.

Table 4
Inhaled pulmonary vasodilators

Drug	Route of Administration	Dose
Epoprostenol (*Brand names: Flolan, Veletri*)	Continuous inhalation via ETT or HFNC	0.05 mcg/kg/min
Nitric oxide	Continuous inhalation via ETT or HFNC	20 ppm
Milrinone	Intermittent inhalation via venturi mask	Concentration: 1 mg/mL Inhale 5 mg over 15–30 min
Nitroglycerin	Intermittent inhalation via venturi mask	Concentration: 1 mg/mL Inhale 5 mg over 15–30 min

place. Although ETI may be required as part of appropriate management of various acute conditions in patients with *comorbid* RVD or PH, ETI rarely has a role in the management of patients who are acutely ill *because* of ADRVF. Making this distinction necessitates both recognition of cases when ADRVF is the primary factor driving a patient's acute presentation, as well as the understanding that ETI is unlikely to be of benefit in this situation and in fact has significant potential to cause precipitous clinical deterioration in patients with ADRVF. The details of periintubation management of patients with comorbid RVD and/or PH requiring ETI has been discussed elsewhere.[24]

SUMMARY

Although RVD plays a central role in high-risk, but relatively rare, conditions such as massive PE and chronic PAH, it is also an important—if frequently unrecognized—component of several disorders routinely encountered in the ED setting such as sepsis, ARDS, and CHF. Comorbid conditions frequently present in the ED population, such as morbid obesity, COPD, and methamphetamine abuse, are not infrequently associated with undiagnosed underlying PH, and these patients may be particularly susceptible to the development of ADRVF when presenting with acute disorders that are independently associated with RVD. ADRFV may be easily mistaken for entities such as abdominal sepsis or septic shock, and a high index of suspicion in the appropriate clinical setting is required to avoid common pitfalls in the recognition of evolving ADRVF.

It is important for emergency physicians to understand the pathophysiology of ADRVF in order to avoid common management pitfalls that can result in significant morbidity and mortality, including aggressive IV fluid administration, failure to support blood pressure by prompt initiation of appropriate vasopressors, and unnecessary ETI.

Early diagnosis and appropriate management of PH and RVD by EPs has the potential to profoundly affect a patient's clinical course and can mean the difference between a routine admission of a hemodynamically stable patient and that same patient going into cardiac arrest in the ED.

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