Chapter 7
The Failing Right Heart from Pulmonary Hypertension

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Case

This is a 42-year-old Caucasian female with a past medical history of asthma who presented with dyspnea on exertion. She was previously active without limitations but 1 year ago noticed progressive dyspnea after a flight of stairs. She was evaluated by her primary care physician (PCP) and diagnosed with asthma. She was prescribed inhalers initially and a trial of steroids but experienced no improvement in her symptoms. She was referred after her PCP found enlarged pulmonary arteries on a Chest X-ray (Fig. 7.1). She denied a history of miscarriages. Her family history is negative for clotting disorders, pulmonary, cardiac or auto-immune disease. She is a lawyer who denies the use of alcohol, tobacco, intravenous drugs, or diet medications. She took no additional medications or supplements.

On exam, she was well appearing with a heart rate of 107 beats per minute (bpm), blood pressure 112/78 mmHg, O2 saturation 93% on room air, and temperature of 37 °C. She had clear breath sounds bilaterally on lung exam.

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Cardiovascular exam revealed jugular venous distension (JVD) of 12 cm H2O, a loud second heart sound (P2) with a faint holosystolic murmur radiating to the lower right sternal border louder with inspiration, and no edema. Her dermatologic and musculoskeletal exams were negative for joint deformities, rashes, clubbing or cyanosis.

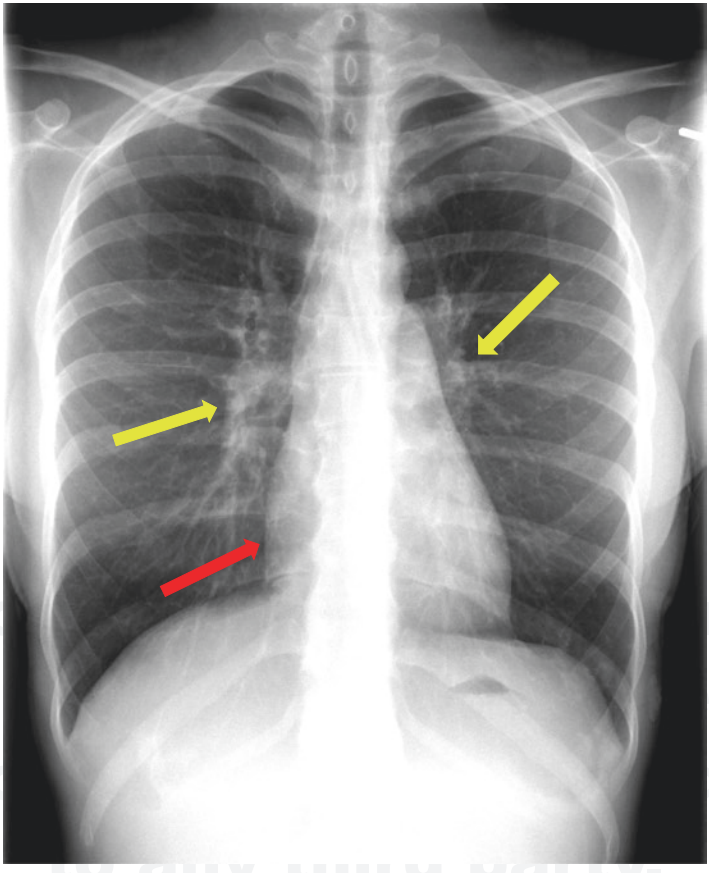

Figure 7.1 Chest X-ray shows a slightly enlarged right atrial silhouette (red arrow), prominent central right and left main pulmonary arteries (yellow arrows), and peripheral hypovascularity

7.1 What Are the Clinical Manifestations of Pulmonary Hypertension?

There are a range of clinical manifestations of pulmonary hypertension (PH), therefore a thorough exam should focus on evaluating for the disease, its severity, and different etiologies. Patients typically present with shortness of breath on exertion, but more severe disease can include weight gain, lower extremity swelling, palpitations from tachyarrhythmias, hemoptysis, and syncope [1]. The cardio-pulmonary exam is particularly important. Key findings on the cardiac exam include an accentuated second heart sound (P2) from increased flow across the pulmonary valve; a right ventricular third heart sound (S3) auscultated at the lower right sternal border due to right ventricle (RV) dysfunction; a palpable RV heave at the lower left sternal border associated with an enlarged RV; a pan-systolic murmur over the lower left sternal border that is more accentuated on inspiration from tricuspid regurgitation; or an early diastolic crescendo murmur from pulmonary regurgitation at the upper left sternal border. If right atrial pressures (RAP) are increased, JVD will be present when evaluating the lateral neck with the head of the bed at a 30° angle. In addition, peripheral edema, hepatomegaly, or ascites may also be seen.

The lungs are typically clear in Group 1 pulmonary arterial hypertension (PAH) patients. However, the lung exam could present with 'dry crackles' in the setting of interstitial lung diseases (ILD) or rales and decreased breath sounds from pleural effusions when PH develops from left sided heart disease. It is also important to evaluate for other systemic illnesses that can cause PH. Telangiectasias, digital ulceration and sclerodactyly can be seen in scleroderma patients. Swan neck deformities and bilateral joint tenderness and swelling may be suggestive of rheumatoid arthritis. Pericardial or pleural rubs and a malar rash are concerning for systemic lupus. Spider nevi, palmar erythema, and ascites may suggest underlying liver disease. Finally, digital clubbing should prompt consideration of ILD, cyanotic congenital heart disease, and pulmonary veno-occlusive disease (PVOD) [1].

Case Continued

She was referred for pulmonary function testing (PFT), a six-minute walk test (6MWT), chest imaging, and laboratory studies to investigate for PAH. Her 6MWT test revealed desaturation to 89% with a Borg score of 3 after 442 m. Her Ventilation Perfusion (VQ) scan was low risk for pulmonary embolism. The computed tomography (CT) scan of her Chest with contrast was negative for acute pulmonary embolism, ILD, nodules, or lymphadenopathy but did show an enlarged main pulmonary artery and RV (Fig. 7.2). Her PFT showed

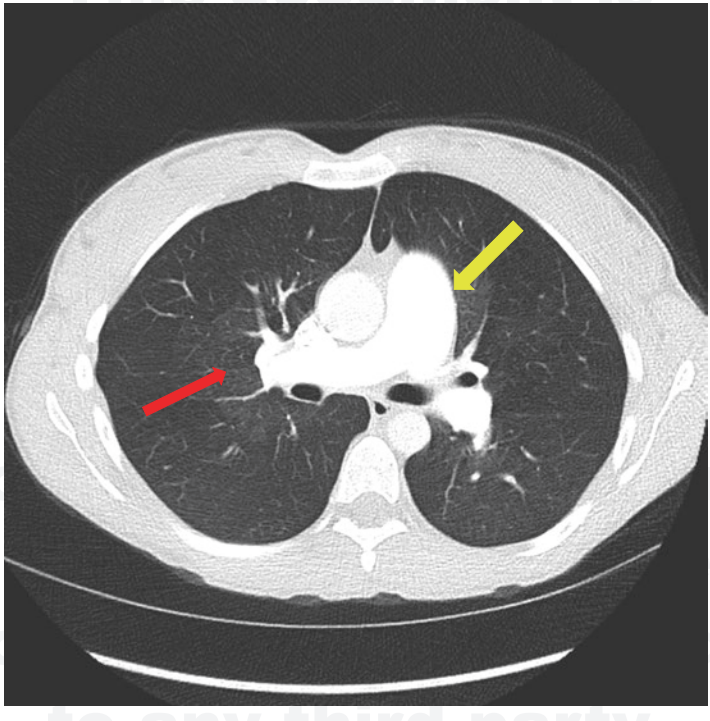

FIGURE 7.2 CT Chest with pulmonary embolism protocol reveals an enlarged pulmonary artery (yellow arrow) compared to the aorta and bilateral peripheral mosaicism (red arrow) which are both seen in pulmonary hypertension

normal spirometry with no significant reversibility with bronchodilators and a DLCO 40% of predicted. An arterial blood gas showed pH 7.42, pCO2 31, PaO2 70. Her complete blood count, complete metabolic profile, HIV test, urine drug screen, thyroid studies and auto-immune panels were negative. Her BNP was elevated at 500 pg/mL (reference <100 pg/mL).

7.2 How Does the Right Ventricle Fail in Pulmonary Hypertension?

Right ventricular failure is the ultimate fatal consequence of pulmonary hypertension. In PH the right heart fails overtime due to increasing afterload which leads to maladaptive changes in the RV. Typically, the pulmonary vascular bed is a high-flow, low resistance, and low-pressure circuit with distensible vessels that dilate and recruit to accommodate increases in flow. However, in PAH, the small arteries undergo remodeling caused by vasoconstriction, in situ thrombosis, and proliferation of smooth muscle and endothelial cells which become resistant to apoptosis [2]. This remodeling causes increased pulmonary vascular resistance (PVR) which directly impacts the pulmonary artery pressure (PAP). PAP = LAP + (CO × PVR)/80, where LAP equals left atrial pressure and CO represents cardiac output. As a result, increasing PVR leads to elevated PAP over time and thus increased afterload, which the RV must pump against.

The RV's geometry is adapted to variations in venous return, but it is not designed to operate against a high resistance and poorly compliant system. The RV's first response to this increasing afterload is enhanced systolic contraction, known as the Anrep effect [3]. To accomplish this, the RV undergoes concentric remodeling with an increase in the number of cardiac sarcomeres [3]. As afterload continues to increase, this adaptive hypertrophy fails as the RV reaches its limit of enhanced contractility. A second maladaptive remodeling begins to occur, right ventricular dilation.

Right ventricular dilation is problematic for several reasons. First, it supersedes the Frank-Starling mechanism and results in a dramatic and irreversible decrease in RV contractile function. Second, it pushes the interventricular septum toward the left ventricle (LV) reducing LV filling. As the RV dilates further, it prolongs its time in systole leading to more compression of the LV as it is trying to fill since both ventricles compete for space within the pericardium [1]. Finally, right ventricular dilation increases wall stress leading to increased oxygen demand and reduced coronary perfusion. As the RV fails to maintain forward flow, cardiac output is reduced which can progress to systemic hypotension, right ventricular ischemia, and a downward spiral of shock leading ultimately to death [4, 5].

Case Continued

Her transthoracic echo (TTE) revealed a normal left atrium and ventricle with intact systolic and diastolic function (LVEF 60%). There was systolic and diastolic flattening of the interventricular septum consistent with right ventricular pressure and volume overload, a dilated right atrium, moderately dilated right ventricular cavity with moderately reduced function, an estimated RV systolic pressure (RVSP) of 63 mmHg, moderate tricuspid regurgitation, and no pericardial effusion (Figs. 7.3 and 7.4). She was referred for right heart catheterization (RHC) which revealed RAP 12 mmHg, RV pressure 53/12 mmHg, pulmonary capillary wedge pressure (PCWP) 10 mmHg, PAP 62/30 mmHg with a mean PAP (mPAP) 40 mmHg, Cardiac output (CO) 4.1 L/min and Cardiac index (CI) 2.5 L/min/m^2, PVR 10 wood units (WU), systemic vascular resistance (SVR) 1100 dynes s cm^{-5}, and a mixed venous saturation (SVO2) 66%. She had no significant change in mPAP with oxygen or inhaled nitric oxide but her PVR did improve to 7 WU and her CO improved to 6 L/min.

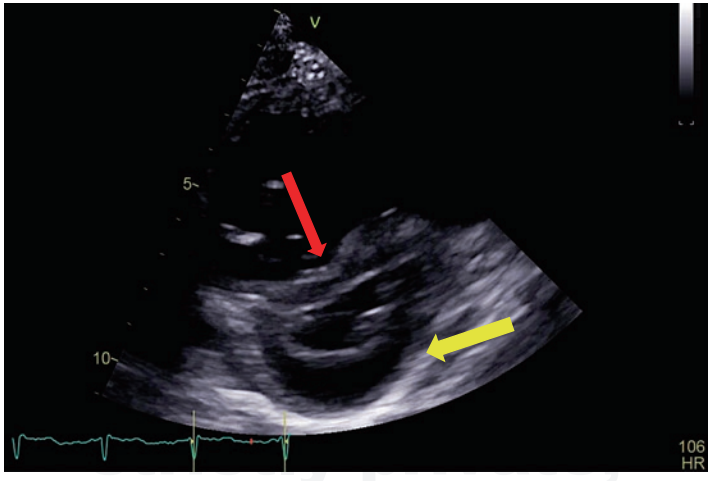

FIGURE 7.3 Parasternal short axis view on TTE showing flattening of the interventricular septum (red arrow) causing a "D" shape of the LV (yellow arrow) due to right ventricular pressure and volume overload

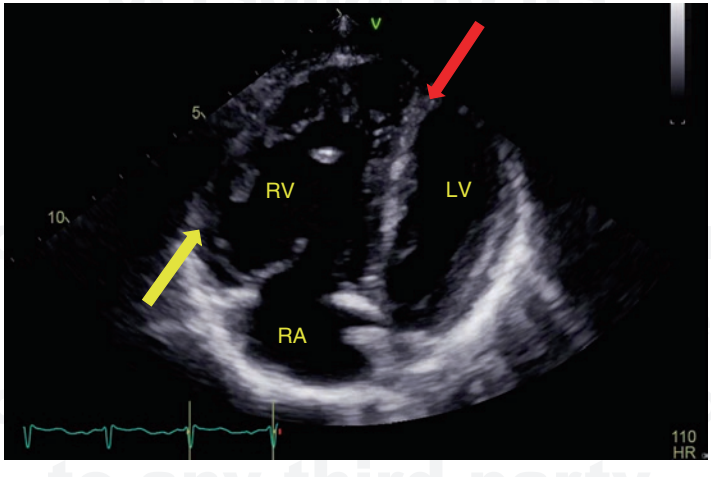

FIGURE 7.4 Four Chamber View on TTE demonstrating RV and RA enlargement, with notable RV hypertrophy (yellow arrow) and bowing of the interventricular septum (red arrow) toward the LV

7.3 What Is the Initial Approach to Evaluate Right Heart Failure?

Initial evaluation for right heart failure (RHF) in PH involves a combination of clinical exam, imaging and hemodynamics. Since the RV fails overtime, the symptoms of dyspnea and decreased exercise tolerance occur before the physical exam signs of RHF develop [4]. A good physical exam as previously mentioned is important to assess for RHF as well as a laboratory assessment for end organ damage of the liver and kidneys. Although not specific to the RV, a brain natriuretic peptide (BNP) is also helpful because it correlates with hemodynamic severity and prognosis in patients with PAH [6].

A TTE is the first non-invasive imaging that is utilized to evaluate the RV's size, shape, and function. Two-dimensional (2-D) TTE can be used to directly visualize RV enlargement, thickening of the right ventricular wall, and reduced systolic function. It is also important to assess the septum for flattening or impinging on the LV, which is a sign of right ventricular pressure overload [7]. Quantitative measurements of RV size can also be made at the basal and middle segments to measure chamber width as well as RV free wall thickness [7]. M-mode and tissue doppler are useful tools to evaluate RV systolic function. Specifically, the tricuspid annulus plane systolic motion (TAPSE) measures the movement of the tricuspid annulus on M-mode to assess systolic function with a value of <1.8 mm considered abnormal [7]. Tissue doppler peak systolic velocity of the tricuspid annulus assesses apical motion of the tricuspid annulus with a value of <10 cm/s considered abnormal [7]. Chapter 3 reviews echocardiographic findings in RHF.

Estimates of RVSP obtained by echocardiogram correlate well with measurements made by RHC, but the variance can be >10 mmHg in up to 50% of cases [8]. Therefore, RHC is the gold standard not only for diagnosing PH but also for assessing the severity of RHF. A mPAP >20 mmHg at rest with a PVR ≥3 wood units and a PCWP ≤15 mmHg is diagnostic for "pre-capillary" PAH. A mean PAP >40 mmHg is

considered severe but clinical outcomes and severity are based on assessing the impact this is having on the RV and not just the mPAP. An RV pressure >17–32/10–12 mmHg suggests RV overload. This leads to elevated RV end diastolic pressure which is transposed onto the right atrium making RA pressures >12 mmHg an important indicator of RHF. As the RV fails to adapt to increased afterload in PH, CO and SVO2 begin to fall signifying failure of the right heart.

7.4 Discuss the Hemodynamic Assessment of Afterload Induced Right Heart Failure?

It is not the PVR and mPAP which dictate clinical outcomes in PH, but instead the interplay between the RV and its ability to adapt to these changes in the pulmonary circulation. As previously described, the RV hypertrophies to increase contractility against this rising afterload. However, there is a point at which afterload overcomes this compensatory contractility, which has been described as "RV-PA uncoupling" [9–11].

To quantify RV-PA coupling, one must first understand how RV contractility and afterload are measured from RV pressure volume loops (Fig. 7.5). Systole begins when there is a rise in pressure caused by actin-myosin cross bridging without a change in volume, known as isovolumic contraction. Pressure rises until it supersedes pulmonary arterial pressure, causing the pulmonic valve to open and the RV to eject blood into the pulmonary circulation. Ultimately the RV empties and diastole begins. Elastance is defined as the pressure divided by volume, so the point in the cardiac cycle at which pressure is the highest and volume is low is considered the point of maximal elastance (E_{max}). This point occurs during systolic ejection and is important because E_{max} is the gold standard for determining RV systolic function [11, 12]. The standard measurement of afterload is labeled arterial elastance (E_a), which is measured from a line that transects the

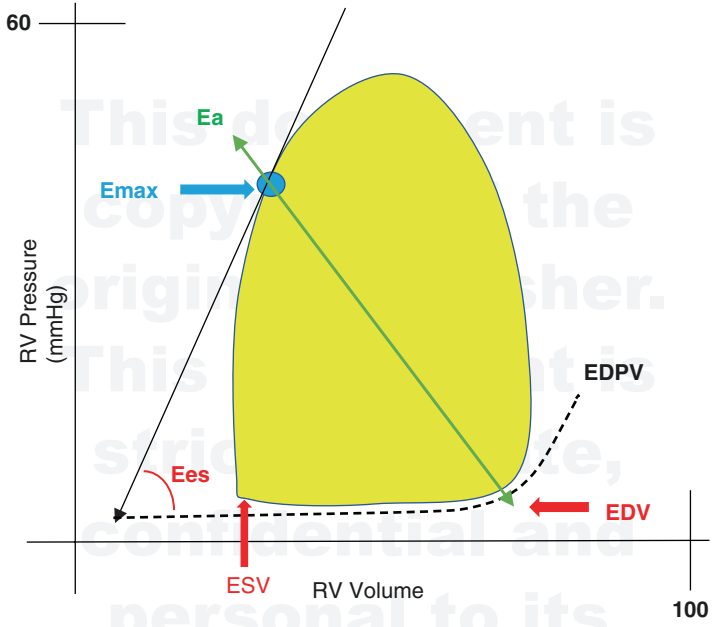

FIGURE 7.5 RV pressure volume loop. RV Afterload (E_a) is measured by drawing a line between the point of end diastolic pressure volume relationship (EDPVR) and the point of maximum elastance (E_{max}). Contractility (E_{es}) is determined using the slope of the line connecting the E_{max} to the end systolic volume (ESV). Ultimately, using the E_{max} we can determine RV contractility (E_{es}) and RV afterload (E_a) and use it to assess RV-PA coupling (E_{es}/E_a)

end diastolic volume and E_{max} [11, 13, 14]. The E_a is more reflective of right ventricular afterload during resistive, pulsatile and passive flow of blood out of the RV compared to static measures of mPAP and PVR [12]. Finally, contractility is determined by the slope of the line connecting the E_{max} to the end systolic volume since a 'stronger' ventricle with increased contractility will generate larger pressures. Contractility is labeled end systolic elastance (E_{es}) [11]. These values are used to assess, RV-PA coupling, which is defined as E_{es}/E_a with the understanding that the RV and PA circulation act together as a unit to maintain cardiac output [3, 5, 11, 14–16].

Although measuring RV pressure and volume loops are considered the gold standard, it requires multiple measurements to be taken while occluding venous return to the heart, making it an impracticable maneuver in human studies. Therefore, Bellofiore et al**.** investigated 'the single beat method', which was first studied in the LV and applied it to the RV in both animal and human models [9, 10]. This method measures RV pressure during isovolumic contraction and relaxation and determines RV contractility without relying upon measuring RV volume [5, 9]. Graphing these pressures enables calculation of a maximum-pressure (*Piso*) which is used to calculate E_{es} and E_a [9, 11] (Fig. 7.6). This method was

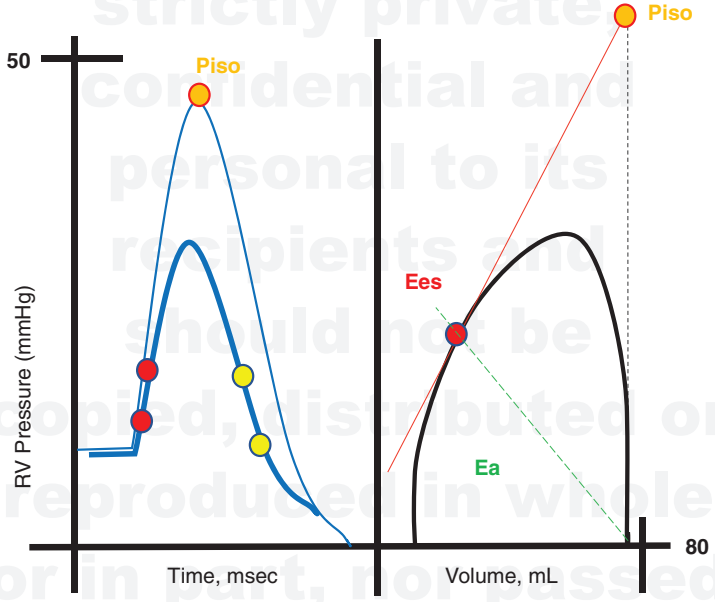

FIGURE 7.6 Single Beat Method. Pressures measured in the early and late portions of the RV pressure curve during isovolumic contraction (red dots) and relaxation (yellow dots) are used to determine the maximum pressure that can be reached by an isovolumic contraction (Piso). Piso is then used to defined the end systolic pressure volume relationship and ultimately to calculate E_{es} and E_a

validated and ultimately used to assess PH patients during RHC [10, 13–15, 17]. Vanderpool et al. demonstrated that in a mix of pre-capillary PH patients, RV-PA coupling based on this method was the only independent predictor of transplant-free survival [17]. The optimal coupling occurs at an E_{es}/E_a ratio between 1.5 and 2 and studies have found that a ratio <0.805 was associated with onset of RV failure [15, 16].

In addition, RV-PA coupling has been found to be an earlier marker of disease even in patients with normal RHC data at rest. In studies of patients with chronic thromboembolic disease and normal RHC, they evaluated RV-PA coupling and found a ratio of <0.68 demonstrated a lack of RV reserve during exercise [18]. Exercise studies measuring RV-PA coupling in PH have shown that progressive exercise intolerance is due to a decline in the efficiency of the hemodynamic interaction between the RV and pulmonary vasculature, rather than either ventricular or vascular impairment alone [10]. Sing et al. demonstrated that even in exercise PH, an early form of PH, RV-PA uncoupling is seen during incremental increases in load during exercise suggesting that this phenomenon is present early in the disease state [13, 14]. One major mechanism for this uncoupling appears to be a loss of pulmonary artery distensibility. In patients with exercise PH and PAH there was an increased RV-PA uncoupling with exercise which correlated with decreased measured pulmonary distensibility [14]. It appears that vascular remodeling in PH leads to a loss of pulmonary distensibility which becomes evident during exercise when increased volume and flow are delivered to the pulmonary circulation.

Case Continued

She was considered an NYHA Functional Class II and initiated on dual therapy with an oral PDE5 inhibitor (tadalafil) and an endothelin receptor antagonist (ambrisentan) with good clinical response. On a repeat 6MWT 3 months later she could complete 492 m with a Borg Score of 2. Her repeat TTE showed RVSP 45 mmHg and RV with improved function to mildly reduced function. Repeat RHC showed RAP 6 mmHg,

RV pressure 43/6 mmHg, PAP 44/24 mmHg, mPAP 30 mmHg, PCWP 13 mmHg, CO 7 L/min, CI 5 L/min/m^2, PVR 3 WU, SVR 900 dyne s/cm^{-5}, SVO2 70%.

7.5 How Do You Prognosticate RV Failure Induced Pulmonary Hypertension?

RV function is one of the major factors determining morbidity and mortality in PH patients. In addition to RV-PA coupling discussed above, a combination of tools is used to prognosticate mortality in these patients and guide medical management. The 2015 ERC/ERS guidelines have divided PH patients into three categories based on one-year mortality: Low risk is defined as <5%; intermediate risk 5–10%; and high risk is >10% [1].

The low risk patients lack clinical signs of right heart failure, progressive symptoms, or syncope. They are NYHA Class I or II and have a 6MWD of >440 m [1,19]. If cardiopulmonary exercise testing is done, testing shows peak VO2 > 15 mL/min/kg and VE/VCO2 slope <36. TTE assessment would show right atrium area <18 cm^2 on imaging. Laboratory studies show a BNP <300 pg/mL. Finally, RHC shows RAP <8 mmHg, CI >2.5 L/min/m^2 and a SVO2 > 65% [1]. Since our patient fit into this category, she was initiated on dual oral therapy.

Comparatively, high-risk patients have signs of RHF with rapid progressive symptoms or syncope. These patients are defined as NYHA functional Class IV with a 6MWD of <165 m. However, it is important to note that response to treatment on follow up has more valuable prognostic information. Patient with a good baseline functional class who progress on treatment to a functional class of III or IV have worse survivals than those who started at NYHA Class III or IV but improved with therapy [20]. A peak VO2 < 11 mL/min/kg and VE/VCO2 slope > 45 on cardiopulmonary exercise testing correlates with poor prognosis. Laboratory studies show a BNP >300. TTE reveals an right atrium area

>26 cm^2 on imaging and the presence of a pericardial effusion, which is an independent predictor of morality [19, 21]. Finally, a RHC with RAP >14 mmHg, CI <2 L/min/m^2, and an SVO2 <60% are consistently associated with worse survival in PAH patients [1, 7, 22]. This patient group requires evaluation for IV drug therapy [1, 23].

Case Continued

One year later she presented to clinic with worsening shortness of breath on exertion and pre-syncope. She was afebrile with a new 6–8 L O_2 requirement to keep her O_2 saturation >90%. Her heart rate was 124 bpm with a blood pressure of 95/62. Exam revealed JVD to 15 cm H2O, an RV heave, a loud P2, and peripheral edema with cool extremities. She denied fever, chills, cough, hemoptysis, chest pain, or palpitations but has been light-headed with exertion and noted new ankle swelling. She was sent to the emergency department. Her initial labs revealed a BNP 4000 pg/mL, Arterial blood gas pH 7.28/25/70 with an elevated lactate, new acute kidney injury, and elevated transaminases. An EKG revealed new atrial flutter with 2:1 block with rapid ventricular rate of 124 with no ischemic changes. A computed tomography pulmonary embolism protocol was unremarkable. A TTE with bubble study was negative for intracardiac shunt or left ventricular systolic heart failure (LVEF 60%) but there was new systolic and diastolic flattening of the interventricular septum consistent with RV pressure and volume overload. The ventricle was severely dilated with severely reduced function; TAPSE 1.10 cm. Right atrium was also moderately dilated, RSVP 80 mmHg, severe tricuspid regurgitation, and a small pericardial effusion. She was admitted to the intensive care unit and a Swan-Ganz Catheter was placed. Initial measurements revealed RAP 20 mmHg, RV 80/20 mmHg, PCWP 12 mmHg, PAP 90/35 with a mPAP 65 mmHg, CO 3.1 L/min and CI 1.5 L/min/m^2, PVR 13 WU, SVR 1800 dynes s/cm^{-5}, SVO2 40%. A central line, arterial line, and foley catheter were placed and she was initiated on furosemide drip. However, her heart rate increased to 140 bpm and blood

pressure dropped to 72/50 mmHg, prompting initiation of norepinephrine to maintain mean arterial pressure >65 mmHg. She was then started on IV dobutamine and inhaled Epoprostenol (iPGI2) through a high-flow nasal cannula. An amiodarone drip was also started for atrial flutter with rapid ventricular rate.

7.6 Discuss the Management of the Failing Right Heart from Pulmonary Hypertension?

Progressive PH leads to RHF and end organ damage from decreased cardiac output and venous congestion making it a challenging disease to manage with a high mortality rate. As with any patient in shock, it is important to evaluate for other causes of shock and treat factors that may contribute to worsening RHF. Arrhythmias, common in RHF, reduce effective coronary filling in diastole and should be treated aggressively with consideration of amiodarone or electrical cardioversion [24]. Acidosis, hypoxemia, and hypercapnia can worsen pulmonary vasoconstriction therefore it is important to keep O2 saturation >92% and aim for a normal pH and pCO_2. Although it is preferable to avoid intubation since anesthetics and positive pressure ventilation can cause hypotension and reduce preload to an already pre-load dependent LV, intubation is sometimes necessary. Avoiding high tidal volumes and excess positive end-expiratory pressure (PEEP) may help reduce the risk of significantly worsening PVR in this setting [25].

Treatment should focus on improving RV contractility, reducing excess preload, and preventing RV ischemia. The placement of a Swan-Ganz Catheter can be useful to understand the hemodynamics and assess the impact of each medical intervention. One of the first steps to improving RV contractility in PH is to reduce excess preload. Unlike other forms of RHF where fluid administration may enhance right ventricular output, in PH the RV is already dilated and fluid administration will further displace the interventricular

septum, impair LV diastolic filling, and reduce cardiac output. Since the RV has a flatter Frank-Starling curve than the LV, a considerable amount of volume unloading may be necessary before any improvement in RV function is seen [24]. This unloading can be accomplished with diuretics or dialysis to keep the CVP 8–12 mmHg with adjustments to optimize RV function and cardiac output [24].

A failed response to diuretics and especially hypotension warrants initiation of vasopressors and ionotropic agents. Stabilizing systemic blood pressure with vasopressors above the RVSP is critical to provide a pressure gradient for right coronary artery perfusion. Current recommendations include the use of norepinephrine to accomplish the goal as it has α1 agonism to improve SVR, β1 stimulation to enhance contractility, and has been shown to improve RV-PA coupling in animal models [26, 27]. Additional vasopressors which can be used include epinephrine and vasopressin, which can induce pulmonary vasodilatation by stimulating endothelial nitric oxide at doses ≥0.04 units/min [28–30]. Phenylephrine and dopamine should be avoided as the former increases PVR without improving RV contractility and the latter causes excess tachycardia that reduces LV filling and worsens demand ischemia [24, 26, 27, 31, 32]. Inotropic agents such as dobutamine and milrinone are also helpful in the setting of acute RV failure especially in conjunction with vasopressors since they can cause vasodilation. Animal studies have shown that dobutamine and milrinone are effective at improving CO and even RV-PA coupling [33, 34]. In general, norepinephrine, vasopressin, and epinephrine can be used in combination with dobutamine or milrinone in PH with right ventricular failure as long as the focus remains on titrating medications based on hemodynamic monitoring.

In addition to improving RV contractility and preventing ischemia, it is important to treat afterload with pulmonary vasodilator therapy. IV prostacyclin (Epoprostenol and Treprostinil) is the drug of choice for any patient considered to be NYHA Class III or IV since it has been shown to improve not only CO, PVR, and RV-PA coupling but also

functional status and survival [23, 35, 36]. Although studies are limited in acute RHF, the short half-life makes IV therapy a titratable option in the ICU with close monitoring for side effects of hypotension, gastrointestinal symptoms, and headaches [5]. In acute and chronic PH, the combination of dobutamine and inhaled nitric oxide (iNO) improved CO, decreased PVR, and increased the PaO_2/FiO_2 ratio in animal studies [37]. As a result, inhaled prostacyclin (iPGI) and iNO have been utilized in ICUs to treat RV failure since they are effective at improving CO, oxygenation, and PVR in cardiothoracic surgery patients with elevated PAP. They have the theoretical advantage of reduced risk of VQ mismatch and hypotension compared to IV therapy [38–42]. Although promising, neither of these inhaled drugs has been studied extensively in PAH patients with acute RHF. Other classes of PH medications have not been tested at length, but it is currently recommended to avoid endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, and guanylate cyclase stimulators given the long half-life and risk of hypotension [24].

Case Continued

Initially the transplant and ECMO teams were consulted. After several hours on iPGI2, dobutamine, and norepinephrine, her urine output began to improve and her lactate normalized. A furosemide drip was re-initiated. After 48 h, norepinephrine was weaned down to 2 μg/min and the decision was made to trial IV treprostinil starting at 2 ng/kg/min with careful up-titration.

7.7 What Are the Surgical and Interventional Alternatives for Pulmonary Hypertension?

Given the complexity of decompensated RV failure from PH, other advanced interventional and surgical options may be investigated in select patients. These options are intended for

patients that have potentially reversible RV failure or who fail maximal medical therapy. Right ventricular assist devices (RVADs) have been designed for use in RV failure, but in patients with RHF due to increased afterload, there is limited data and potential harm with their use [5]. As a result, current options are limited to extracorporeal membrane oxygenation (ECMO) and transplant.

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) should be considered in certain patients who fail medical therapy. Since it relies on an intact RV to pump blood to the LV, Veno-venous ECMO (VV-ECMO) is generally reserved for patients with preserved RV function who have intractable hypoxemia. VA-ECMO, however, oxygenates venous blood and delivers it directly to the arterial circuit. The data for VA-ECMO in PAH patients is based on case reports where it has been utilized as a bridge for patients undergoing pulmonary endarterectomy in chronic thromboembolic pulmonary hypertension (CTEPH) and for a treatment naïve PH requiring hemodynamic support until clinical recovery with PH therapy [5, 24, 43–45]. More studies are needed to fully evaluate its role in the management of decompensated PH with RV failure.

Finally, transplant should be a consideration in patients with RHF who have failed medical therapy. As noted before, PH patients with high RA pressures and low cardiac output have worse outcomes, therefore a transplant referral is appropriate for those with a RAP >15 mmHg and a cardiac index <2.0 L/min/m^2 [5, 24, 46]. Despite the fact that PH leads to RHF, these patients do not necessarily need a dual heart-lung transplant [22]. In fact, most PH patients with lung transplant alone have a rapid decrease in their PA pressures immediately post-op with significant improvement in their RV function a year after transplant [22]. The data suggests that a dual lung transplant is more effective than single lung transplant [22]. Overall, although post-transplant PAH patients had a higher early mortality, after 5 years they had similar outcomes compared to other matched lung transplant patients and a dramatic improvement in their quality of life [22, 47].

Case Conclusion

After 3 weeks in the hospital, she was weaned off dobutamine and norepinephrine, her treprostinil dosing was titrated to 24 ng/kg/min, and her oxygenation improved to 2 L nasal cannula. Transplant was delayed given her recovery. She was discharged to cardiopulmonary rehab with close follow-up.

Clinical Pearls

1. The RV in PH fails due to rising afterload from increased resistance and reduced distensibility in the pulmonary vasculature.
2. Outcomes in PH patients are based on the RV's ability to adapt to rising afterload and maintain contractility.
3. Assessments of RV-PA coupling have demonstrated that dysfunction occurs early in PH and impacts exercise tolerance and transplant free survival.
4. The focus of treating RV failure in PH is to reduce excess preload, improve RV contractility, prevent RV ischemia, and decrease afterload in the pulmonary vasculature.
5. In patients with severe RHF who have failed medical therapy or are bridging to therapy, transplant and VA-ECMO should be considered at an expert center.

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