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Review

Acute Right Ventricle Failure in the Intensive Care Unit: Assessment and Management

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ABSTRACT

Caring for the critically ill patient with acute right ventricle (RV) failure is a diagnostic and management challenge. A thorough understanding of normal RV anatomy and physiology is essential to manage RV failure. Despite the fact that the RV is essentially a volume chamber that ejects into a low-pressure system, the left ventricle contributes significantly to RV function through maintenance of the transseptal gradient (TSG). Preserving systemic mean arterial pressure maintains the TSG and RV perfusion. Various pathological states cause acute RV failure by decreasing the TSG and RV perfusion and/or increasing pulmonary vascular resistance. Early diagnosis prevents rapid progression of RV failure due to the "double hit phenomenon," which is acute intra-abdominal multiple organ system failure as a result of a reduced blood pressure and elevated central venous pressure. Management includes hemodynamic support and reversal of the

RÉSUMÉ

La prise en charge d'un patient dans un état critique en raison d'une insuffisance ventriculaire droite (VD) aiguë constitue un véritable défi diagnostique et thérapeutique. Une connaissance approfondie de l'anatomie et de la physiologie normales du ventricule droit est essentielle à la prise en charge appropriée d'un tel cas. Même si le ventricule droit constitue essentiellement un compartiment de retenue qui permet d'éjecter le sang dans un système à faible pression, le ventricule gauche contribue de manière significative à la fonction du ventricule droit par le maintien du gradient de pression transseptal (GPTS). Pour préserver le GPTS et la perfusion VD, il faut maintenir la pression artérielle générale moyenne dans des valeurs acceptables. Divers états pathologiques entraînent une insuffisance VD aiguë en diminuant le GPTS et la perfusion VD et/ou en augmentant la résistance vasculaire pulmonaire. Un diagnostic précoce permet

Right ventricle (RV) failure is less well understood than left ventricle (LV) failure, and requires an in-depth understanding of RV pathophysiology. In this review pathophysiology, assessment, and management of RV failure in the intensive care unit are summarized.

Normal RV Anatomy/Physiology

The RV differs greatly from the muscular and ellipsoidal LV. It is triangular from the side, crescent-shaped in cross-section, and wraps around the LV.[1] The RV shape is dependent on the position of the interventricular septum (IVS), which normally bulges into the RV (Fig. 1).[1] The RV has a dual embryonic origin and consists of an inflow (sinus) and outflow (infundibulum and conus). The RV sinus extends from the tricuspid valve to the trabeculated, apical part of the RV. Three muscular bands divide the RV: the parietal, the septal, and the moderator bands. The moderator band is the largest and extends from the base of the anterior papillary muscle to the septum. The LV does not have a moderator band. The RV conus is usually free of muscular trabeculations and extends from the moderator band to the pulmonary valve. The volume of the RV is greater than the LV, and hence its ejection fraction (45%-60%) is less than that of the LV (50%-70%). However, the mass is one-sixth of the LV with thin walls measuring 2-5 mm.[1-3]

The RV works against low impedance; pulmonary pressures are one-sixth systemic.[2] The RV free wall contraction occurs with peristalsis-like movement, beginning at the base and ending at the outflow tract.[2] The most important movements are the inward movement of the free wall, contraction of the longitudinal fibres moving the tricuspid

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precipitating cause through optimizing RV rate and rhythm, determining ideal RV filling pressure, reducing RV afterload through nonpharmacologic and pharmacological means, and selecting the appropriate RV inotrope or mechanical support.

d'éviter l'évolution rapide de l'insuffisance VD attribuable au « double phénomène délétère », soit une insuffisance pluriorganique intra-abdominale aiguë causée par une baisse de la pression artérielle et une hausse de la pression veineuse centrale. La prise en charge comprend le soutien hémodynamique et l'élimination de la cause sous-jacente par l'optimisation du rythme et du débit VD, la détermination de la pression de remplissage idéale du ventricule droit, la réduction de la postcharge VD par des interventions pharmacologiques ou non pharmacologiques et la sélection de l'agent inotrope ou du dispositif de soutien mécanique approprié.

annulus toward the apex, and LV free wall contraction.[4] RV afterload is low enough that forward flow into the pulmonary circulation occurs in systole and in early diastole.[4] Coronary perfusion to the RV occurs in systole and diastole, compared with primarily diastolic flow in the LV, making the RV dependent on systolic blood pressure (BP; Fig. 2).[2]

Forces transmitted from one ventricle to the other through the myocardium and pericardium are termed ventricular interdependence.[5] Because of the pericardium, the higher LV pressures are transmitted to the RV through the IVS. This pressure difference, or transseptal gradient (TSG), is present in systole and diastole and accounts for the normal left-to-right bulge of the septum and creates a "scaffold" against which the RV free wall contracts.[6] Although 4%-10% of LV systolic function depends on the RV through ventricular interdependence, 20%-40% of RV systolic function depends on the LV.[5] RV function is therefore dependent on high LV cavity pressure (Fig. 3).[7,8]

RV Failure Physiology

Acute RV failure results in reduced forward flow through the pulmonary circulation. Causes of RV failure are listed in Table 1.

RV volume overload

Increased preload can occur with tricuspid regurgitation (TR), atrial septal defect, pulmonic regurgitation, or anomalous pulmonary venous return. Volume overload of the RV causes IVS flattening. When volume overload is the predominant factor and RV systolic function is still normal, then IVS flattening will abate during systole. The bowing of the septum back toward the normal position into the RV helps preserve RV ejection fraction in RV fluid overload, but there can be a reduction in LV ejection fraction.[5] RV diastolic dysfunction impairs RV filling and increases RV and right atrium (RA) pressures.[9] RV diastolic dysfunction and TR can cause right-to-left shunting across a patent foramen ovale, resulting in hypoxemia.[9]

Increased afterload

It is important to note that pulmonary flow is possible in some situations in which there is no RV function. In Fontan physiology, flow occurs passively if pulmonary vascular resistance (PVR) is low, and the driving pressure is the mean systemic filling pressure (as defined by Guytonian models).[10-12] Similarly, a patient with a left ventricular assist device (LVAD) who has ventricular fibrillation can remain stable if PVR is low, because mean systemic filling pressure will drive flow.

There are many conditions that increase PVR and are important contributors to RV failure. Increased afterload can be due to pulmonary hypertension (PH), pulmonary embolism (PE), RV outflow tract obstruction, hypoxic pulmonary vasoconstriction, or pulmonary stenosis. Table 1 shows the World Health Organization classification of PH.[13] PVR is commonly affected by reversible factors during critical illness, and these are often the precipitants of RV failure. Functional residual capacity is one of these crucial factors (Fig. 4). A decrease in lung volume (atelectasis, endobronchial intubation, effusions, insufficient positive end expiratory pressure [PEEP], pneumothorax, and pneumonia) will increase PVR, as will excessive lung volume (excessive PEEP or tidal volume, air trapping).

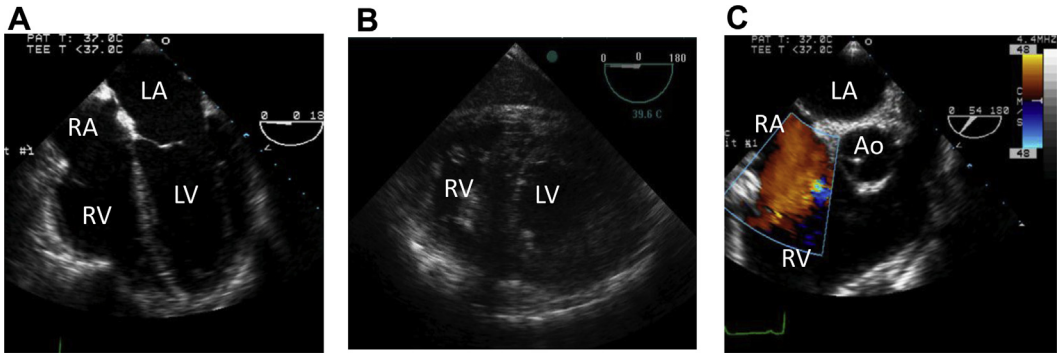

Figure 1. Right ventricle (RV) anatomy on transesophageal echocardiography. (**A**) Midesophageal 4-chamber view; (**B**) transgastric mid short axis; (**C**) midesophageal RV inflow-outflow. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium.

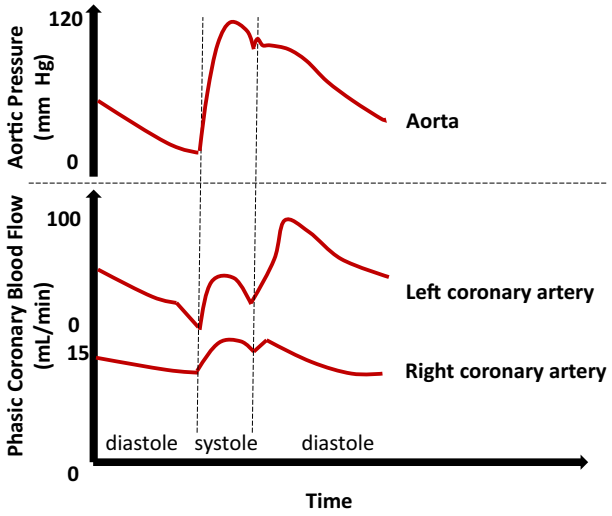

Figure 2. Relationship of coronary blood flow and aortic pressure. Coronary blood flow in the right coronary artery occurs in systole and diastole, whereas left coronary artery perfusion occurs in diastole only.

Other reversible causes of PH include ventilator dyssynchrony, hypoxia, hypercarbia, acidosis, hypothermia, shivering, and α-agonists.[6] In addition to causing elevated systemic vascular resistance (SVR), α-agonists also increase PVR.

Normal hemodynamic values are shown in Table 2. When pulmonary artery (PA) pressure (PAP) is elevated, TPG helps determine the site of the elevated PAP (Table 3). When left atrial pressure (LAP) is normal, the transpulmonary gradient (TPG) is normally low. If the TPG is elevated, there is a precapillary contribution to the PH. If the TPG is normal, then high PAP is due to high LAP or high flow. "Mixed" PH, with increased LAP and TPG, occurs when postcapillary and precapillary changes are present.[14]

Possible causes of increased PAP can be inferred from the following formula:

$$\text{Mean PAP} = \text{LAP} + \text{CO} \times \text{PVR}$$

where CO indicates cardiac output.

(1) Increased LAP
(2) Increased CO (eg, increased flow due to left-to-right intracardiac shunt, fluid overload, hyperdynamic circulation)
(3) Increased PVR (eg, lung disease, thromboembolic disease, idiopathic pulmonary arterial hypertension).[6] Pulmonary vascular remodelling in states of chronic pressure overload due to increased LAP or increased CO lead to secondary increased PVR.[6]

When there has been a chronic increase in PVR, RV hypertrophy occurs. The increased thickness reduces wall stress through Laplace's law[3]:

$$\text{Wall stress} = (\text{pressure} \times \text{internal radius})/(2 \times \text{wall thickness})$$

In acute RV pressure overload, RV systolic pressure increases to a point where there is no further increase and function begins to decline. This corresponds with decreased CO and decreased BP.[5] In RV pressure overload, the TSG is decreased (Fig. 3). Therefore, unlike volume overload, the

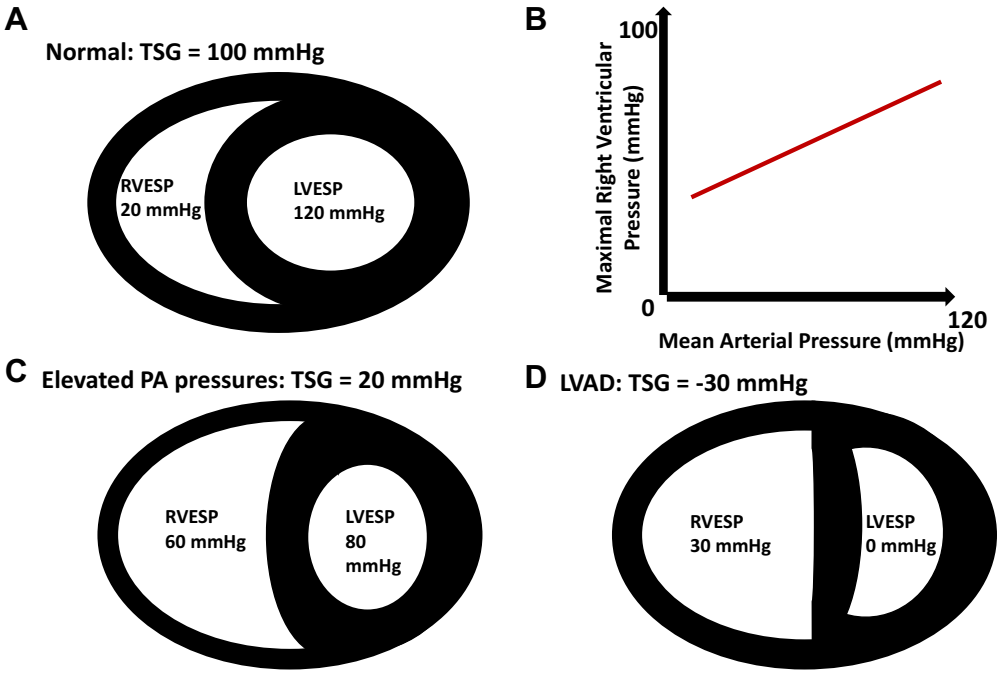

Figure 3. Relationship between transseptal gradient (TSG) and right ventricle (RV) function. (**A**) Normal: TSG = 100 mm Hg (normal range: 80 mm Hg-120 mm Hg). The shape and position of interventricular septum is maintained. (**B**) Normal physiology: RV pressure development is dependent on left ventricle (LV) pressure. (**C**) Patient with elevated pulmonary artery (PA) pressure: TSG = 20 mm Hg. The septum is flattened toward the LV and the RV is dilated. (**D**) Patient with a left ventricular assist device (LVAD): TSG = −30 mm Hg. There is potential for septum to bulge into the LV or to have a "suction event." LVESP, left ventricular end-systolic pressure; RVESP, right ventricular end-systolic pressure.

Table 1. Causes of RV failure

Type of failure	Examples
Increased preload	• Tricuspid regurgitation • ASD • Pulmonic regurgitation • Anomalous pulmonary venous return
Increased afterload	• PH as defined by WHO: Group 1: pulmonary arterial hypertension Group 2: PH due to left heart disease Grade 3: PH due to lung disease Grade 4: chronic thromboembolic PH Grade 5: PH with unclear multifactorial mechanisms • Acute pulmonary embolism • RV outflow tract obstruction • Systemic RV • Pulmonary stenosis
Decreased contractility	• RV infarction • Arrhythmia • Cardiomyopathy • Sepsis
Other/mixed	• Congenital heart disease

ASD, atrial septal defect; PH, pulmonary hypertension; RV, right ventricular; WHO, World Health Organization.

septum does not return to its original shape during systole. When the RV is dilated, the normal helical orientation of myofibrils is reduced and mechanical cardiac function is deleteriously affected. This will occur in most conditions that cause an acute change in the TSG. These changes are notable in patients with an LVAD; the TSG is negative and is aggravated by hypovolemia and too high pump speed, leading to further RV dilatation ("suction events").

Reduced contractility

Decreased contractility occurs with RV infarction, arrhythmias, cardiomyopathy, RV dilatation, acute respiratory distress syndrome (ARDS), and sepsis.[15] As the RV dilates, the septum shifts toward the LV (ventricular interdependence), asynchrony occurs, and RV ejection fraction decreases.[4]

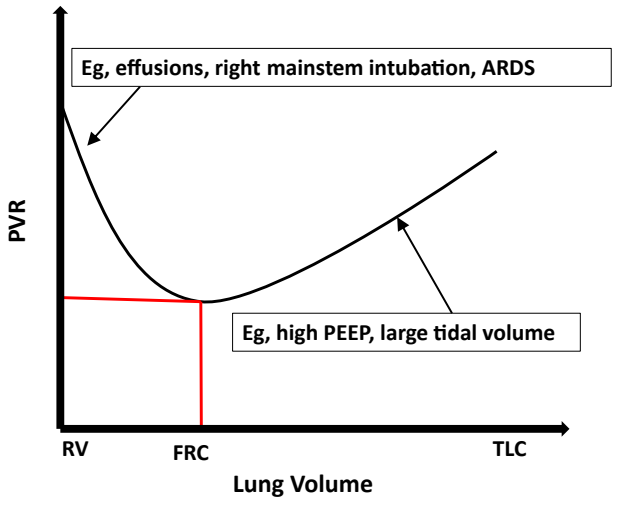

Figure 4. The relationship between pulmonary vascular resistance (PVR) and lung volume. PVR is optimal at functional residual capacity (FRC). ARDS, acute respiratory distress syndrome; PEEP, positive end expiratory pressure; RV, right ventricle; TLC, total lung capacity. Reproduced from Strumpher et al.[6]

Table 2. Normal hemodynamic values

Left atrial pressure	8 mm Hg
Systolic pulmonary artery pressure	25 mm Hg
Diastolic pulmonary artery pressure	10 mm Hg
Mean pulmonary artery pressure	15 mm Hg
Transpulmonary gradient	7 mm Hg
Pulmonary vascular resistance	0.9-1.4 Wood units or 90-120 dynes × s × cm^5

The TSG

The TSG is reduced either through increased RV pressure or decreased LV systolic pressure (or an LVAD). In the former scenario, reduced RV CO leads to reduced systemic pressure and a downward cycle ensues: RV function decreases further due to its globular shape and change in myofibril configuration. This decreases CO, decreases BP, and further increases RV ischemia and dysfunction. In a patient with an LVAD, the TSG can become negative as a result of LVAD inflow, severely affecting RV geometry and function. The RV will become globular, especially if inherent RV contractility is reduced and PVR is increased. This exacerbates RV dilatation and bulging of the septum into the LV. To optimize the TSG in both of the aforementioned situations, PVR must be reduced and LV pressure must be increased.[6] In RV cardiogenic shock, immediate management centres on re-establishing the TSG by increasing LV pressure (Fig. 3). Vasopressin is the ideal vasopressor agent because it increases BP and has minimal effect on PVR.[16-18]

The "double hit" phenomenon

Hypotension causes rapid deterioration of acute RV failure due to reduced TSG and coronary perfusion. Because of high central venous pressure (CVP), vital organ perfusion pressure is reduced in RV shock to a greater degree than LV shock for the same mean arterial pressure and cardiac index (Fig. 5).[6,19,20] Hypotension, coupled with increased CVP, leads to rapid development of abdominal multiple organ failure. Renal failure, hepatic failure, and ischemic bowel are complications of this "double-hit."[6,21,22] Without a rapid

Table 3. Hemodynamic classification of pulmonary hypertension and the importance of TPG

Pulmonary hypertension	Expected measurement
Precapillary PH (↑ TPG: > 12 mm Hg, normal LAP)	↑ mPAP ≥ 25, PCWP < 15, PVR > 3 Wood units (240 dynes × s × cm^5), normal or ↓ CO
Postcapillary PH (Normal TPG: ≤ 12 mm Hg, ↑ LAP)	mPAP ≥ 25, PAWP ≥ 15, PVR ≤ 3 Wood units (240 dynes × s × cm^5), normal or ↓ CO
Mixed precapillary and postcapillary PH (↑ TPG: ≥ 12 mm Hg, and ↑ LAP)	mPAP ≥ 25, PAWP ≥ 15, PVR ≥ 3 Wood units (240 dynes × s × cm^5), normal or ↓ CO

CO, cardiac output; LAP, left atrial pressure; mPAP, mean pulmonary artery pressure; PAWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; TPG, transpulmonary gradient.

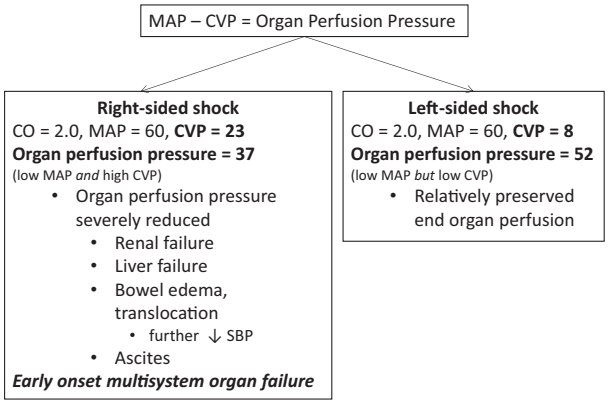

Figure 5. The "double hit phenomenon" in right ventricular cardiogenic shock vs left ventricular cardiogenic shock. Organ perfusion is maintained in left ventricular shock to a greater extent because the central venous pressure (CVP) is low, whereas in right ventricular shock organ perfusion is severely reduced because of the high CVP and low blood pressure. CO, cardiac output; CVP, central venous pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

reduction in CVP and increase in BP, a lethal spiral of RV failure ensues (Fig. 6).

Clinical Assessment

The clinical assessment should focus on evaluating signs of RV failure and establishing the precipitating event. Findings include increased jugular venous pressure and Kussmaul sign (increase in jugular venous pressure with inspiration), prominent V wave, palpable RV heave, TR murmur, a pulsatile liver, and other generic signs of reduced systemic hypotension. Hypoxemia might occur because of right-to-left intracardiac shunting through a patent foramen ovale.

Investigations

Laboratory

Initial investigations should include blood count, creatinine, urea, glucose, sodium, potassium, lactate and liver enzymes, and troponin.[23] Elevated lactate level will have multiple possible etiologies, including decreased oxygen delivery, bowel congestion, and in severe RV failure, reduced hepatic clearance.

Chest x-ray

The RA forms the right heart border on chest x-ray. When enlarged, the RA projects further than 1-2 cm from the right of the spine and the arch between the superior vena cava and RA increases. Normally, the RV is best seen on the lateral chest where increased size will fill the retrosternal space to occupy more than 50% of the retrosternal area between the diaphragm and sternal angle. With RV enlargement, there will also be displacement of the LV backward and counterclockwise, eventually resulting in cardiomegaly on a PA film.[2] Typically, the lung fields are clear in RV shock. Etiology of acute RV deterioration might be identified (eg, atelectasis, endobronchial intubation, pneumothorax, pleural effusion, ARDS, etc).

Electrocardiogram

Electrocardiogram changes are varied and depend on the cause of the RV failure. This might include the signs of chronic RV strain/enlargement, elevated P waves in lead II, signs of right axis deviation, and the signs of acute RV infarction.[2]

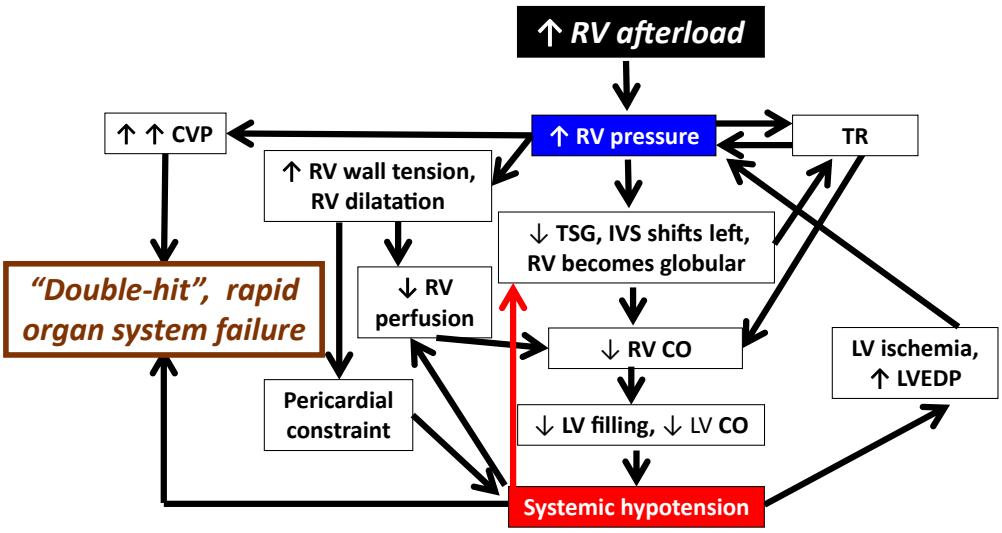

Figure 6. The rapid cycle of deterioration in right ventricle (RV) cardiogenic shock. The "double-hit" consists of hypotension and elevated central venous pressure (CVP). Acute increase in RV afterload or volume results in increased wall tension, septal shift due to transseptal gradient (TSG) reduction, and TR. TR further exacerbates RV volume loading. Increased wall tension decreases right coronary artery (RCA) perfusion and produces ischemia. TSG reduction reduces left ventricle (LV) compliance, decreases preload, and results in hypotension. CO, cardiac output; IVS, interventricular septum; LVEDP, left ventricular end diastolic pressure; TR, tricuspid regurgitation.

Table 4. Echocardiographic assessment of the RV

Echocardiographic findings in RV failure
• Increased RA size
• Increased RV: basal width > 42 mm; midcavity width > 35 mm; length > 86 mm
• Septal flattening
• TR
• RV wall motion: grade 1 = normal; grade 2 = hypokinetic; grade 3 = akinetic; grade 4 = dyskinetic, grade 5 = aneurysmal
• Eccentricity index of LV*: normal = 1; pressure overload > 1 during systole and diastole; pure volume overload > 1 in diastole only
• RV > LV in apical 4-chamber view
• Dilated IVC
• RV wall thickness: > 5 mm is hypertrophy; > 10 mm suggests PA pressures near systemic
• McConnell sign in PE (akinesis of mid free wall, normal apical motion)
• Visible clot (PE)
• TAPSE < 16 mm
• RVSP elevated: Bernoulli method using TR velocity using RA pressure
• S' of tricuspid annulus
• RV myocardial performance index
• RVFAC [(EDA−ESA)/EDA]: normal 35%-60%
• Pulmonic flow signal morphology: PH from left heart disease shows normal morphology; late systolic notching indicative of increased PVR; early systolic notching suggests severe PH and RV dysfunction

EDA, end-diastolic area; ESA, end systolic area; IVC, inferior vena cava; LV, left ventricle; PA, pulmonary artery; PE, pulmonary embolus; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; RVSP, right ventricular systolic pressure; RVFAC, RV fractional area change; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

*Anteroposterior LV diameter/septum-lateral wall diameter in short axis midcavity views.

Echocardiography

Bedside echocardiography is now a basic critical care skill.[24] Focused bedside echocardiography can easily assess enlarged RV, dilated inferior vena cava, and obvious TR.

More advanced findings using complete transthoracic echocardiographic study are beyond the scope of the bedside assessment but are a more important part of longitudinal assessment of chronic RV dysfunction.[25-27] Basic and more advanced echocardiographic findings of RV failure are listed in Table 4.

Monitoring

In RV shock, invasive monitoring is helpful to guide management (Fig. 7). If the CVP is low, RV cardiogenic shock is unlikely. However, excessively high CVP (venous congestion) contributes to decreased vital organ perfusion. Temporal trends and response of CVP to fluids and inotropes is a seminal part of managing RV shock. Efforts should be made to decrease CVP to < 20 mm Hg. The PA catheter is useful in patients with RV shock. PAP response to therapy can be monitored; an increasing or decreasing PAP can be signs of worsening RV failure. An increasing PAP and decreasing CVP might indicate an improved CO through the high PVR system. A decreasing PAP and increasing CVP is indicative of a very low CO. Mixed venous saturation is a valuable surrogate for CO, but will be misleading in presence of intracardiac shunting. PH and RV distention are invariably associated with TR. Acute TR underestimates thermodilution CO (tdCO) when the CO is high, and overestimates when CO is low. Mild TR has minimal effect, but severe TR underestimates tdCO. Consequently, tdCO should be used with caution in RV cardiogenic shock.

The RV port of the PA catheter should be monitored in patients with RV shock.[28] The normal RV is distensible, with low end diastolic pressure; there is a gradient between the PA and RV end diastolic pressure. In RV dysfunction, compliance of the RV is reduced and the slope of the RV diastolic pressure becomes steeper.[28] In severe RV dysfunction the diastolic pressures equalize, and the pressure tracing become sin wave-like (Fig. 8).[28] These patterns are easy to recognize on the bedside monitor.

Frequent monitoring of RV volume and contractility with echocardiography is crucial. Other techniques of noninvasive CO monitoring are not well studied in RV shock.

Management

General treatment principles

Emergency hemodynamic stabilization requires rapid correction of systemic hypotension to improve the TSG and RV perfusion.

Optimizing rate and rhythm. A dysfunctional RV should be maintained in sinus rhythm. Atrial fibrillation and heart blocks are not tolerated.[1,9] Early cardioversion is indicated. Because acute RV failure is associated with TR, higher heart rates (> 80 bpm) are generally indicated; this might reduce RV distention and TR, and might increase CO. Atrial pacing should be considered. In RV shock due to infarction, there is often associated bradyarrythmias, and the clinician should balance optimal heart rate and myocardial oxygen consumption.

Determining the optimum RV filling. Optimal filling of the RV is essential (Fig. 9). The failing RV will not tolerate over- or underfilling. The commonly held belief that the

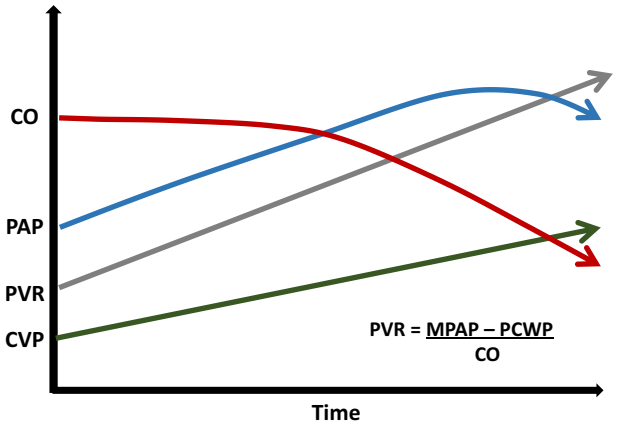

Figure 7. Right ventricular shock. Relationship between cardiac output (CO), pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR), and central venous pressure (CVP). As pulmonary pressures increase, CO will decrease. MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure. Reproduced from Haddad et al.[9] with permission from Wolters Kluwer Health, Inc.

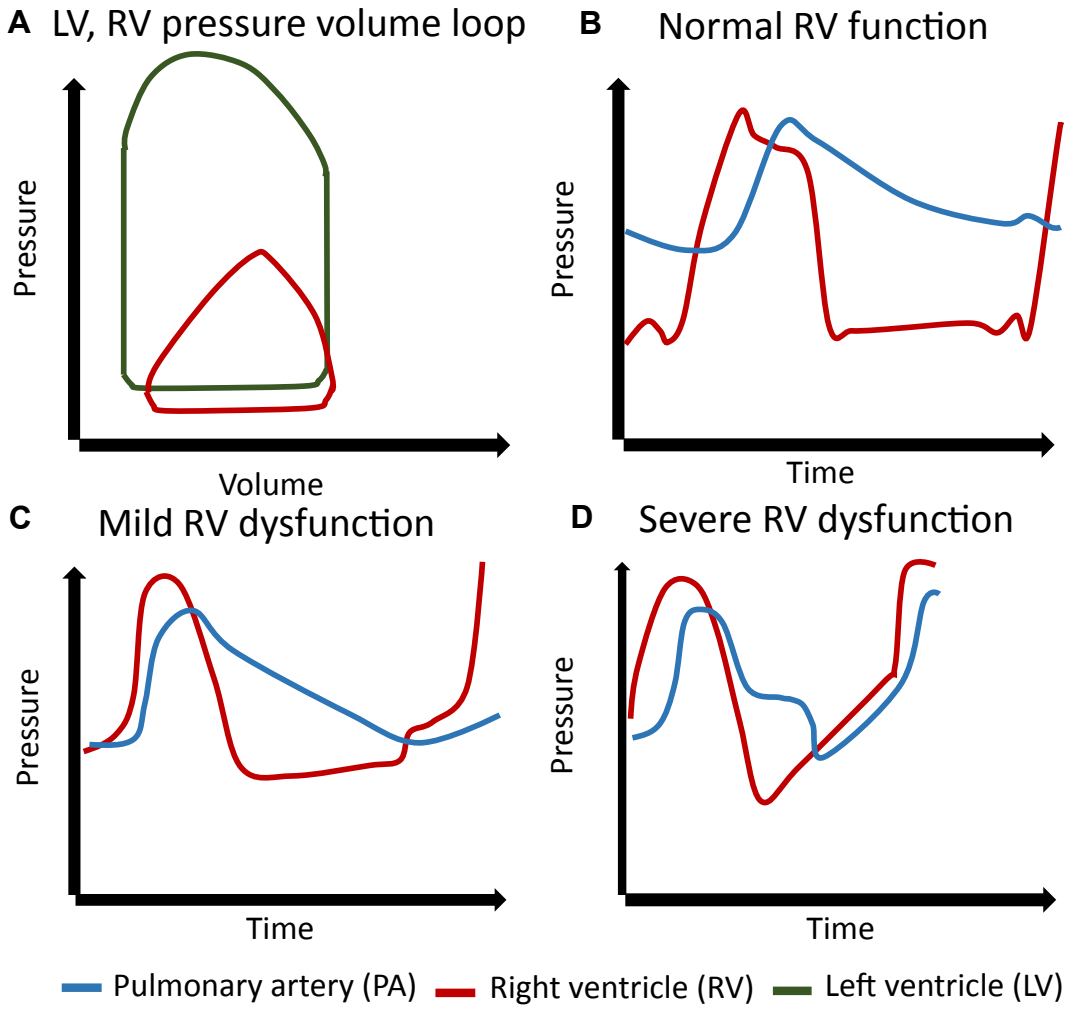

Figure 8. Right ventricle (RV)/left ventricle (LV) pressure-volume relationship and continuous RV/pulmonary artery (PA) pressure monitoring. (**A**) Normal RV and LV pressure-volume relationship; (**B**) normal PA and RV pressure on PA catheter (PAC) tracing; (**C**) mild RV dysfunction on PAC tracing; (**D**) Severe RV dysfunction on PAC tracing. Reproduced from Denault et al.[28] with permission from Wolters Kluwer Health, Inc.

failing RV should be aggressively volume-loaded is not accurate. Overfilling will stretch the tricuspid valve annulus, increase TR, aggravate organ congestion, decrease TSG, and decrease CO. In contrast, underfilling places the RV on a deleterious part of the Frank-Starling curve. What complicates volume determination is that CVP might be in a range that is typically adequate (> 10 mm Hg), and echocardiography might show a dilated RV. The other common determinants of volume responsiveness, such as pulse pressure variation and systolic pressure variation, cannot be relied on for volume responsiveness because of the beat to beat variability in RV stroke volume that will lead to variation not necessarily related to volume status. A good technique to determine if the failing RV is volume-responsive involves the administration of a fluid bolus (250-500 mL of Lactated Ringers), with cautious monitoring. Ongoing fluid is indicated if there is a modest increase in CVP (2-5 mm Hg, and remains < 20 mm Hg), together with a significant improvement in systemic perfusion (CO, mean arterial pressure, and other clinical findings). If only the CVP increases, with little evidence of improved perfusion, then deleterious RV distention might occur.[9] Autotransfusion with the passive leg raise test is an alternative method to determine RV volume responsiveness.

Maintaining RV coronary perfusion. In the normal RV, perfusion occurs in systole and diastole (Fig. 2). However, when the RV pressures are elevated, perfusion takes on some aspects of left-sided physiology; the normal systolic dominant RV perfusion shifts and flow occurs primarily in diastole (Fig. 2). In acute RV failure, RV pressures are high, LV filling is reduced, and CO is reduced. The low BP is deleterious to RV perfusion, and the lethal cycle of RV failure ensues. The emergent first step RV shock should be the immediate increase in BP, improving the RV perfusion as well as TSG. In this regard, vasopressin causes little or no increase in PVR, whereas norepinephrine, through its α-1 agonism, increases PVR. Although vasopressin might be the agent of choice, the inotropic benefit of norepinephrine is often required. A combination of vasopressin and norepinephrine (and an inotrope) is usually needed in acute RV failure. The traditional dose of vasopressin is intravenous 0.02-0.04 IU/min, although intravenous doses as high as 0.06 IU/min have been described

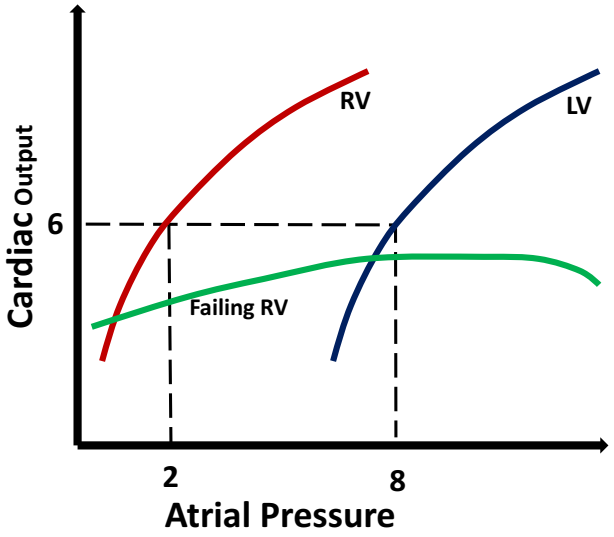

Figure 9. The Frank-Starling curves of normal ventricles and failing right ventricle (RV). Left ventricle (LV) requires higher atrial filling pressures for the same cardiac output.

in shock. However, the safety of these higher doses in RV failure is not well established.[29-31]

The effects of the various vasoactive agents in RV shock are shown in Table 5. Concomitant with starting inotropic support, initial efforts include correcting metabolic abnormalities contributing to decreased contractility (eg, acidosis, hypoxemia, hypocalcemia, sepsis, and hypothermia). Because RV function depends on LV function and BP, restoration of BP and LV function is important. Consideration must be given to the contribution of the IVS to RV contraction; the TSG must be re-established to ensure proper RV contraction.

Inotropic choice is either a β-agonist (eg, dobutamine) or a phosphodiesterase-3 inhibitor (eg, milrinone). However, their increased contractility might be offset by their effect on reducing SVR, especially milrinone. Dobutamine, starting at 2.5-5.0 mcgr/kg/min, causes much less vasodilation. In severe RV shock, combination inotropy, with low-dose milrinone (0.2 mcgr/kg/min) and low dose dobutamine (2.5 mcgr/kg/min), might be the best choice for increasing contractility with fewer side effects than drug alone. Reduced SVR and possible reduced BP might be mitigated by simultaneously starting vasopressin (and adding norepinephrine if required). Levosimendan, a calcium sensitizer, increases cardiac contractility and relaxation without altering myocardial demand and can improve coronary perfusion,[21] although its use in acute RV shock is not well defined.

Reducing PVR and the use of selective pulmonary vasodilators. When RV failure is a consequence of elevated PVR, an important part of therapy is reducing PVR. First, nonpharmacologic means of reducing PVR are used. Overdistention of the lungs as well as atelectasis increase PVR (Fig. 4). Ventilator adjustments must be made to optimize PEEP, reduce acidosis, hypercarbia, and hypoxemia. The endotracheal tube position must be correct; a main stem positioning can be lethal. Peak pressures should be maintained below 30 cm H_2O, and atelectasis must be avoided. Sedation and short-term paralysis might be necessary to avoid coughing, straining, shivering, and ventilator dyssynchrony. Adequate arterial partial pressure of oxygen (PaO_2) should be maintained because pulmonary vasoconstriction occurs with low PaO_2. Pleural effusions should be drained.

Only after these nonpharmacologic treatments have been tried, should selective PA vasodilators be entertained. Chronic PA vasodilator therapy, whether oral, inhaled, intravenous, or subcutaneous, should be continued. Powerful intravenous vasodilators, such as prostanoids, nitroglycerin, or calcium channel blockers, have little or no role in the management of acute RV shock. These agents, although they might dilate the pulmonary vasculature, cause systemic hypotension and decrease the right coronary artery perfusion and TSG. Furthermore, intravenous agents inhibit protective hypoxic pulmonary vasoconstriction, potentially worsening ventilation/perfusion mismatch and hypoxia.[6] In contrast, inhaled PA vasodilators directly reduce PVR in well-ventilated lung regions, and improve ventilation/perfusion matching by increasing flow to the ventilated areas; the improved oxygenation further reduces PVR.[28] Inhaled PA vasodilators include inhaled nitric oxide, inhaled nitric oxide donors (nitroglycerin and sodium nitroprusside), and inhaled prostanoids. Nitric oxide is easy to use but is expensive and requires toxicity monitoring.[32,33] The prostanoids that have been used by inhalation include prostacyclin, iloprost, and treprostinil.[34,35] Inhaled iloprost is a water-soluble analogue of prostacyclin with a longer half-life (20-30 minutes vs 6 minutes) and a longer duration of action (60 minutes vs 15 minutes), which makes it suitable for intermittent nebulization.[34] Inhaled milrinone is available, and has less systemic hypotension than intravenous administration.[36,37] Inhaled prostacyclin and inhaled milrinone might be beneficial in combination.[38-41] The choice of agent is on the basis of physiological rationale and institutional experience; there are no good outcome studies favouring any agent.

In addition to use of inhaled vasodilators, short-term use of sildenafil in the intensive care unit might be effective in managing RV cardiogenic shock due to PH. Through its phosphodiesterase V inhibition, it is a potent pulmonary vasodilator. The effect on BP, if any, is easily offset by the use of vasopressin. It is also important to anticipate a potential worsening of hypoxemia in susceptible patients by reducing hypoxic pulmonary vasoconstriction. The sublingual sildenafil route is particularly useful[42]; 25-50 mg of sildenafil easily dissolves in 0.5-1 mL of water and the sublingual use avoids the issues related to gut edema, access to the gastrointestinal tract, and avoids the first pass hepatic metabolism.[6]

A combination of selective pulmonary vasodilating agents, working on different receptors, might be beneficial.

Specific circumstances

PE. In acute PE, the RV has not had time to adapt to a high PA pressure; RV failure occurs early.[9] In patients with low BP (< 90 mm Hg) and who do not have a high bleeding risk, systemic thrombolysis is recommended.[43] Surgical embolectomy might be indicated in patients with hemodynamic instability, failed or contraindications to thrombolytic therapy, and possibly for free-floating clot in the RA/RV.[44,45] Percutaneous catheter-directed treatment can also be

Table 5. Physiologic effects of various vasoactive medication classes

Vasoactive agent	RV inotropy	PVR	PVR with selective PA vasodilator*	SVR	TSG	CO	Comment
α-Agonist (eg, phenylephrine, norepinephrine)	← →	↑ ↑	↓ ↓	↑ ↑	← →	↓	For temporary treatment of hypotension while the typical RV-support regime is prepared. Phenylephrine is rarely used because it has no inotropic effect. Norepinephrine is the drug of choice because it has concomitant β-1 agonism
AVP (arginine vasopressin)	← →	← →	↓	↑ ↑	← →/↑	← →/↑	Ideal because of minimal effect on PVR. Increased LV pressure pushes the IVS back to the RV, increases RCA blood flow
PDE_3I (eg, milrinone)	↑ ↑	↓ ↓	↓ ↓	↓ ↓	↓ ↓	↑ ↓	Good inotrope but potentially dangerous decrease in BP and TSG. Must start with VP or "ready to go"
β-1/2 agonists (eg, dobutamine)	↑ ↑	↓	↓	↓	↓	↑ ↓	Good inotrope; less effect on SVR, BP, and TSG at lower doses. Also have VP "ready to go". Dobutamine is preferred to epinephrine because it is a pure β-1/2 agonist with no α-agonism, allowing independent titration of vasopressor
Ca^{2+} sensitizers (eg, levosimendan)	↑ ↑	↓ ↓	↓ ↓	↓ ↓	↓ ↓	↑	Risk similar to PDE_3I with regard to SVR; there is limited experience in acute RV shock
Combination of inotropes (eg, dobutamine, milrinone, or combination) with VP	↑ ↑	↓ ↓	↓ ↓	← →/↑	← →	↑	Combination of lower dose PDE_3I and β-1/2 agonists have additive effects, but less profound decrease in SVR. Adding VP mitigates SVR with minimal effect on PVR

BP, blood pressure; CO, cardiac output; IVS, interventricular septum; LV, left ventricular; PA, pulmonary artery; PDE_3I, phosphodiesterase inhibitor; PVR, pulmonary vascular resistance; RCA, right coronary artery; RV, right ventricle; SVR, systemic vascular resistance; TSG, transseptal gradient; VP, vasopressin.

*Selective PA vasodilator (eg, inhaled nitric oxide, inhaled milrinone, inhaled prostanoid, sublingual sildenafil, or combinations).

considered.[45] Extracorporeal membrane oxygenation might be indicated for some patients with massive PE.[46]

RV infarction. Isolated RV infarction is a unique and relatively uncommon situation. The management of RV infarction starts with expeditious acute coronary syndrome care. Most patients will have a degree of LV involvement, and much of the hemodynamic support will be for the LV. However, in a small group of patients with isolated RV infarction, there will be unique management challenges. In patients with normal lungs and normal PVR, isolated RV infarcts will do well as CO is maintained with Fontan-type flow through the pulmonary circulation. In patients with concomitant infarction of the LV, elevated LAP will increase PAP and hence Fontan-type flow will not occur.

Acute or chronic PH. Patients with known PH who present for surgery or with acute illness are at risk of aggravating underlying PH or RV failure. More patients with PH are presenting for noncardiac surgery because of improved survival and quality of life. Because these patients have an increased perioperative morbidity and mortality risk, their surgeries should preferably be performed in centres experienced in dealing with their complex disease.[25]

ARDS. Patients with ARDS are at high risk for RV failure as a result of increased PVR, sepsis-induced RV dysfunction, and RV dysfunction as a consequence of systemic hypotension, acidosis, and metabolic derangements. The principles of management are similar, but there is potential reversibility of elevated PVR (hypoxemia, hypercarbia, decreased functional residual capacity).

Mechanical circulatory support. When acute RV failure is refractory to medical management, mechanical circulatory support might be indicated in the form of a right ventricular assist device for primary RV failure not due to PH. Devices can be inserted centrally or peripherally and are used for a variety of indications including RV infarct, myocarditis, postcardiotomy, post-LVAD RV failure, and post-transplantation.[47] In one study, 78% of patients' function recovered enough to allow explantation, and 50% survived to a year.[47] In patients with acute RV failure secondary to PH, right ventricular assist device support is not effective. The forced increase in CO through a high PVR system will lead to pulmonary hemorrhage.

Conclusions

Acute RV failure can be a diagnostic and therapeutic challenge. Early diagnosis and intervention is required to prevent the rapid and potentially lethal cycle of multiple organ failure. When possible, specialty centres should be involved in patient care.

We propose the following simplified approach to acute RV failure:

1. Recognize RV failure early
   a. Systemic hypoperfusion
   b. Low pulse pressure
   c. Elevated CVP
   d. Signs of abdominal organ failure
2. Search for underlying etiology and treat accordingly
3. Urgent hemodynamic stabilization
   a. Increase systemic BP to normalize TSG, RV perfusion
4. Hemodynamic optimization of the RV
   a. Preload: avoid hypovolemia and overfilling of the RV
   b. Rate: higher heart rate generally well tolerated to minimize associated TR (approximately 80-100 bpm)
   c. Rhythm: early cardioversion
   d. Contractility: either dobutamine, milrinone, or a combination in lower doses. Treat hypotension with vasopressin and norepinephrine
   e. Afterload: first reduce PVR through nonpharmacologic measures. Add inhaled PA vasodilator or a combination of vasodilators if PVR is still elevated
5. Consider mechanical RV circulatory assist, where appropriate, before multiple organ failure.

Disclosures

The authors have no conflicts of interest to disclose.

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