Right ventricular failure
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Whilst failure of the left ventricle (LV) has been the subject of intense interest for decades, failure of the right ventricle (RV) has tended to receive scant attention. Indeed, the RV was long considered a relatively passive conduit for blood flow between the systemic and pulmonary circulations.

More recently, the importance of the RV in maintaining haemodynamic stability and organ function has been recognized. It is now known that RV failure is not only as common as LV failure, but also that isolated RV failure may carry a worse prognosis than isolated LV failure.1 RV failure presents unique challenges in identification and management. Therefore, for an anaesthetist, a good understanding of both RV physiology and the impact of RV dysfunction is essential in order to safely manage these potentially complex patients. This review aims to provide a broad overview of RV physiology and of the pathophysiology of RV failure. General haemodynamic aims and specific therapies will be discussed.

Anatomy and physiology

The function of the RV is to receive blood from the right atrium (RA) and to eject blood into the pulmonary artery (PA). The RV can be divided into two sections based on these two functions and on anatomy and embryologic origin. The sinus, or body, receives blood from the RA. The conus, or outflow tract (also called the infundibulum), funnels blood into the PA. They are separated by a muscular ridge extending into the RV cavity termed the crista supraventricularis. Several other internal ridges (trabeculae carnae) line the RV cavity. They are much coarser than those in the LV; they are visible on echo, extending from the base of the anterior papillary muscle to the interventricular septum. This is the moderator band, because it was originally believed to moderate RV distension. However, its function is to convey the right branch of the atroventricular bundle of the conducting system.

When examined in cross-section, the RV is crescent-shaped, due to the fact that its concave free wall wraps around the convex interventricular septum. The RV is comparatively thin walled, with approximately one-sixth the muscle mass of the LV. As such, it is well designed to accommodate increases in preload, but poorly designed to adjust to increases in afterload. The significance of this difference will be discussed below.

Table 1 shows the normal range of pressures in the RV and PA, and the pulmonary vascular resistance, with equivalent values on the left side of the heart for comparison. In contrast to the LV, which pumps blood under high pressure through a vascular system of low compliance, the RV pumps blood under much lower pressures through a highly compliant vascular system. In addition, the high compliance of the RV outflow tract absorbs more of the energy profile of ejected blood (decreasing dP/dT, i.e. the rate of increase in the pulse upstroke).

Figure 1 compares the pressure–volume loop of the RV with that of the LV. The pulmonary valve opens early in systole once RV pressure reaches the (relatively low) PA pressure. Little time is spent in isovolumic contraction, giving a triangular-shaped pressure–volume loop, in contrast to the almost square loop of the LV. Therefore, the RV performs primarily volume rather than pressure work.

Firstly, RV ejection is dependent on the contraction of its free wall, which moves inwards towards the septum. Secondly, important contributions have also been demonstrated from contraction of the interventricular septum and the ‘wringing’ action of the LV.2 For this reason, and because of the importance of
intracavity LV pressure for right coronary perfusion, LV function is an important determinant of RV ejection (e.g. up to 50% under certain loading conditions).

**Pathophysiology of right ventricular failure**

The common causes of RV failure are listed in Table 2. They can be broadly divided into: (a) intrinsic RV failure in the absence of pulmonary hypertension (usually RV infarction); (b) RV failure secondary to increased RV afterload; and (c) RV failure because of volume overload.

A variety of congenital heart lesions are associated with RV failure, usually from increased afterload, volume overload or both. Septal defects are commonly associated with RV failure; the RV is subject to volume overload because of blood shunted from the left side of the heart. Fallot’s tetralogy is another association in which RV hypertrophy, and ultimately RV failure, occur because of RV outlet obstruction. In the adult with a repaired Fallot’s tetralogy, RV failure may still occur because of pulmonary regurgitation, particularly when a transanular patch was used to repair the RV outflow tract.

Figure 2 is a schematic of the consequences of increased RV afterload. First, opening of the pulmonary valve in systole is delayed. Thus, isovolumic contraction time is prolonged and the pressure–volume curve assumes a shape similar to that of the LV. Isovolumic contraction entails pressure work with greater oxygen consumption than volume work. The next consequence is that the relatively compliant RV dilates to maintain stroke volume (Frank–Starling mechanism). However, this causes an increase in myocardial wall stress because of the thin walls of the RV (Law of Laplace). Myocardial wall stress is a major determinant of oxygen demand. An increased right ventricular end-diastolic pressure causes right coronary perfusion to assume a profile similar to that of the left coronary system (flow predominantly or solely in diastole). These factors result in decreased oxygen supply at a time of greatly increased demand.

Dilatation of the RV chamber leads to dilatation of the tricuspid annulus causing tricuspid regurgitation, further exacerbating dilatation. Over time, hypertrophy occurs as a natural response to increased wall stress. As the RV expands, the crescentic shape of the RV cavity is lost (Fig. 3). In addition, the interventricular septum bulges into the LV cavity. This occurs because the pericardium necessarily limits the space available for cardiac expansion, and thus an increase in RV volume must be accommodated by a decrease in LV volume. Septal shift impairs filling of the LV and therefore impairs LV function, a phenomenon termed as ventricular interdependence. As the LV fails, systemic perfusion pressure and right coronary perfusion pressures decrease, further compromising the RV.

In the most severe cases of RV failure, high venous pressures coupled with decreased systemic arterial pressures impair perfusion of major organs. Initially, this will be manifest as a decrease in urine output and creatinine clearance as a result of renal hypoperfusion, and hyperlactataemia, coagulation abnormalities, and elevated liver enzymes because of hepatic hypoperfusion. Unless the RV is unloaded, the vicious cycle outlined above will continue, leading to sustained circulatory failure, ultimately leading to multi-organ failure and death.

RV failure may also occur in the setting of normal RV afterload, most commonly secondary to myocardial infarction (MI). RV MI is a consequence of disease of the right coronary artery, or less commonly, of the left circumflex artery in a left-dominant circulation. As was the case for RV failure in general, interest in isolated RV infarction has tended to be overshadowed by that for LV infarction. More recently, the high mortality in patients with isolated RV infarction has forced a reappraisal of its significance.3

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**Table 1** Normal pressures (ranges, in mm Hg) and vascular resistance in the pulmonary and systemic circulations

<table>
<thead>
<tr>
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<th>Systolic</th>
<th>Diastolic</th>
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<tr>
<td>Right ventricle</td>
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</tr>
<tr>
<td>Pulmonary artery</td>
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<tr>
<td>Pulmonary vascular resistance (dyne s cm$^{-5}$)</td>
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<tr>
<td>Systemic vascular resistance (dyne s cm$^{-5}$)</td>
<td>150–250</td>
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**Table 2** Causes of RV failure

- RV failure with normal afterload
  - RV infarction
  - RV failure secondary to increased afterload
- Pulmonary embolus
- Mitral valve disease with pulmonary hypertension
- Congenital heart disease
- ARDS
- Obstructive sleep apnoea
- Increased afterload complicating cardiac surgery
- Inflammatory effects of CPB
- Protamine
- Increased afterload complicating thoracic surgery
- Extensive lung resection
- Left ventricular assist device
- RV failure secondary to volume overload
- Atrial septal defect, ventricular septal defect

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**Fig. 1** Pressure–volume loops for the RV and LV.
Evaluation of RV function

Failure to consider and identify RV dysfunction in the differential diagnosis of the patient in circulatory shock will have adverse consequences. A high index of suspicion is necessary, particularly for patients in high-risk groups such as those with pre-existing pulmonary hypertension, congenital heart disease, or recent deep vein thrombosis. The following is a non-exhaustive list of clinical signs, and of the utility of investigations.

Clinical signs

Clinical signs include peripheral oedema, jugular venous distension, pulsatile hepatomegaly, right-sided third heart sound, systolic murmur of tricuspid regurgitation, and increased split of the second heart sound. Pulmonary embolus: signs of deep vein thrombosis, increased D-dimers, Type I respiratory failure.

Electrocardiography

The ECG is often normal. Right axis deviation, RVH, RBBB, or S1Q3T3 pattern suggesting that pulmonary embolus may be seen.

Chest X-ray

The chest X-ray has limited utility to specifically identify RV failure. Nonetheless, enlargement of the main PA, a distended azygous vein, and oligemia of a lobe (Westermark’s sign) are all consistent with pulmonary embolus and RV failure.

Invasive monitors

A central line accurately placed in the superior vena cava provides information on filling pressures in the right heart. Severe tricuspid regurgitation is readily seen as a tall CV wave (the CVP trace is said to be ‘ventricularized’) and often indicates RV failure. A PA catheter allows measurement of RV, PA, PA-occlusion pressures, and cardiac output. When each of these values is obtained, it should be possible to distinguish intrinsic RV failure from RV failure secondary to increased afterload and, indeed, from RV failure secondary to disease on the left side of the heart. We find it particularly useful to calculate the transpulmonary gradient (mean PA pressure – mean PA-occlusion pressure). The pulmonary vascular resistance is then calculated by dividing the transpulmonary gradient by the cardiac output. Important limitations to consider when using the PA catheter include unreliable thermodilution measurement of cardiac output with severe tricuspid regurgitation, and hazards of inflating the flotation balloon in a patient with severe pulmonary hypertension.

Echocardiography

An increase in the perioperative use of echocardiography, in particular transoesophageal echocardiography (TOE), has increased appreciation of RV failure; this is now a preferred diagnostic tool. In experienced hands, TOE will allow immediate identification of a dilated, hypertrophic, or poorly contractile RV, and of associated...
phenomena such as tricuspid regurgitation and septal shift. However, because of its complex shape, a single view of the RV gives limited information about overall volume, and even with multiple imaging views, measurements of RV volume (and therefore of RV output) are much more difficult than for the LV, which has a more even ellipsoid shape. In practice, the most useful echo-derived measures of RV loading conditions and performance are as follows:

**RV free wall motion:** Ischaemic or infarcted areas will show motion abnormalities. Abnormalities of free wall motion with apical sparing are considered relatively sensitive for pulmonary embolus (McConnell’s sign).

**Thickness of the free wall:** $>15$ mm at end-diastole in an adult can generally be taken to indicate hypertrophy.

**Dilation may be rapidly assessed by examining the apex in long-axis view.** Normally the apex is formed by the LV, the RV extending only two-thirds the length of the LV. When the RV forms the apex of the heart, RV dilatation is diagnosed.

**Doppler of a regurgitation jet at the tricuspid valve** (which permits estimation of PA pressure).

**Tissue Doppler tricuspid annulus velocity:** a quantitative index of RV free wall motion and function.

**Hepatic venous flow pattern:** it can be used to demonstrate systolic flow reversal, a sign of severe RV failure.

**Perioperative management**

The most common reasons for RV failure in patients presenting for surgery are RV infarction, congenital heart disease, mitral valve disease with pulmonary hypertension, and pulmonary hypertension of other causes. Acute RV failure complicating cardiac surgery may have additional aetiologies, as discussed below.

Irrespective of the cause, certain basic considerations dictate management of patients in or at risk of RV failure. These include, most importantly, preserving myocardial contractility and utilizing ventilatory strategies that minimize increases in pulmonary vascular resistance. In addition, patients must receive adequate analgesia to minimize catecholamine release. For extremity surgery, regional blocks may be a good choice, provided preload and afterload are maintained. The following is a non-exhaustive list of the main tenets of management:

**Optimize preload:** ideally guided by TOE or invasive monitoring

**Maintain AV conduction:** this may be difficult to achieve

**Attention to factors that determine pulmonary vascular resistance:** $P_{aO_2}$, $P_{aCO_2}$, pH, left atrial pressure, airway pressure, reduce preload with nitrates or diuretics, and maintain LV systolic pressure.

When these measures are insufficient, specific measures to reduce RV outflow resistance or increase RV contractility will be necessary. These include: inotropes, particularly those with vasodilator properties; specific therapies for pulmonary hypertension; right ventricular assist devices; biphasic cuirass ventilation; and ultimately, in certain situations, cardiac transplantation.

**The use of inotropes**

If poor contractility is the cause of RV failure, any drug with $\beta_1$ adrenoreceptor agonism is likely to be beneficial. Dobutamine may be preferable to dopamine, because it lacks $\alpha_1$-adrenoreceptor effects, thus limiting pulmonary vasoconstriction. Nonetheless, because of the importance of right coronary artery perfusion for RV function, systemic vasoconstriction may enhance RV function if given in the setting of systemic hypotension. Indeed, in our practice, we frequently obtain benefit from vasoconstrictors, including phenylephrine and norepinephrine, in cases of severe RV dysfunction. Careful consideration of RV loading conditions, systemic and PA pressures, and of the severity of RV dysfunction, will therefore be required for a rational selection of inotrope.

Isoprenaline has been used in RV failure because it combines positive inotropic effects with pulmonary vasodilation. However, tachycardia limits its use. The phosphodiesterase inhibitors enoximone, amrinone, and milrinone are more useful. They have an established role in short-term treatment of cardiac failure, particularly for patients with RV failure. Inhibition of phosphodiesterase enhances intracellular concentrations of cAMP which, in cardiac muscle, enhances contractility, whereas in vascular smooth muscle it promotes vasodilation. These drugs are therefore described as ‘modulators’. Because of the sensitivity of the RV to increased afterload, these drugs are most useful in RV failure resulting from pulmonary hypertension, combining pulmonary vasodilation with positive RV inotropy. It may be necessary to additionally infuse a low dose of norepinephrine to counteract the tendency for systemic vasodilation.

**Treatment of pulmonary hypertension**

**Inhaled nitric oxide (NO)**

NO enters vascular smooth muscle in pulmonary vessels where it activates guanylate cyclase. This leads to increased levels of cGMP causing vasodilation. Excess NO rapidly binds to haemoglobin; therefore, minimal quantities reach the systemic circulation. While clinical trials have verified the reduction in pulmonary vascular resistance, improved survival has not been demonstrated. There is the tendency for rebound pulmonary hypertension when the drug is withdrawn and patients with long-standing pulmonary hypertension are generally poor responders. Best results have been shown for neonates with persistent pulmonary hypertension of the newborn (reduced requirement for ECMO) and infants undergoing surgery for congenital heart disease. Results in adults are disappointing. Nonetheless, a trial of inhaled NO may be indicated in selected patients, particularly in the setting of cardiac transplantation. An increase in $P_{aO_2}$ may be seen because of preferentially improved perfusion of ventilated areas.
Intravenous PGE\textsubscript{1} and inhaled prostacyclin

These prostaglandins act on specific receptors in the vasculature, yielding a vasodilatory result that is at least as potent as that of NO. Intravenous PGE\textsubscript{1} has been used successfully to treat acute RV failure related to pulmonary hypertension during cardiac surgery, but norepinephrine, delivered directly into the left side of the heart, was required to counteract the intense systemic vasodilation.\textsuperscript{5} More practical is inhalation administration of prostacyclin and its analogues. These have been used with some success in acute perioperative RV failure.\textsuperscript{6} As with inhaled NO, rebound hypotension on drug withdrawal has been reported.

Sildenafil

There are several isoforms of phosphodiesterase; in pulmonary vascular smooth muscle, the main isoform is phosphodiesterase-5. Sildenafil, a specific inhibitor of this enzyme, has been validated as a long-term treatment for selected patients with pulmonary hypertension. In the perioperative setting, pretreatment of patients with sildenafil has been reported to have a synergistic effect with inhaled NO in patients with severe RV failure.\textsuperscript{7} There is an increase in the use of this agent to aid weaning from mechanical ventilation in infants who have undergone surgery for congenital heart disease.

Nesiritide

Nesiritide is a synthetic B-type natriuretic peptide; it has a pulmonary vasodilatory action and, additionally, inhibits proliferation of pulmonary vascular smooth muscle cells. Early experience, primarily case reports and small trials, suggests it has promise as a therapy for severe pulmonary hypertension.

Endothelin antagonists

Endothelin is an endothelium-derived vasoconstrictor, excess of which contributes to pulmonary hypertension in a significant subset of patients. Inhibition of the endothelin receptor with bosentan is reported to improve outcome in adults with pulmonary hypertension.\textsuperscript{8} Again, there is limited experience in perioperative use of this drug.

Right ventricular assist devices (RVAD)

In specialist centres, the use of RVAD can be life saving in patients with critical RV failure refractory to general measures and to pharmacological therapy. RVADs are most commonly used to aid separation from cardiopulmonary bypass or as a bridge to transplantation.

Biphasic cuirass ventilation

External cuirass ventilation, using negative or biphasic (positive and negative) pressures, provides an alternative to positive pressure ventilation via a tracheal tube. These devices have been demonstrated to reduce RV afterload, improve pulmonary blood flow, and augment cardiac output in patients with RV dysfunction and cardiac surgery.\textsuperscript{9}

Right ventricular failure complicating cardiac surgery

In the case of failure to separate from cardiopulmonary bypass, or of postoperative haemodynamic instability, particularly if LV function appears good, RV failure must be considered. There are several possible reasons for RV failure in the cardiac surgery patient, including:

- **New onset of right ventricular ischaemia/infarction**, consequent upon graft thrombosis.
- **Air embolus**. The right coronary artery is particularly susceptible because of its anterior position in the aortic root, which means it lies uppermost in the supine patient.
- **Pre-existing pulmonary hypertension** exacerbated by positive pressure ventilation, atelectasis and inadequate oxygenation.
- **Cardiopulmonary bypass** may itself contribute to pulmonary vascular resistance, because activation of inflammatory systems leads to generation of vasoactive mediators and the accumulation of extravascular lung water.
- **Protamine**, used to reverse the effects of heparin after termination of bypass, may, in some patients, cause an extreme pulmonary vasoconstriction, thought to be related to generation of thromboxane A2.

Exclusive use of retrograde cardioplegia through the coronary sinus may poorly protect the RV, particularly in the setting of RV hypertrophy, because the coronary sinus primarily drains the left coronary system.

Following cardiac transplantation, the allograft may be unable to adapt rapidly to a high pulmonary vascular resistance.

References


Please see multiple choice questions 18–22