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Clinical Aspects of the Right Ventricle in Anaesthesia and Intensive Care

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Complete List of Authors:	Shelley, Ben; Golden Jubilee National Hospital, Anaesthesia and Critical Care; University of Glasgow School of Life Sciences, Academic Unit of Anaesthesia Murphy, Emma; Golden Jubilee National Hospital, Department of Anaesthesia
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Clinical Presentation and Management of Right Ventricular Dysfunction

Emma Murphy MBCHB, MRCP

Clinical Research Fellow in Cardiothoracic Anaesthesia and Intensive Care

Department of Anaesthesia, Golden Jubilee National Hospital, Glasgow, UK

Academic Unit of Anaesthesia, Critical Care and Pain Medicine, Glasgow, University.

Benjamin Shelley MBCHB, FRCA, FFICM, MD

Consultant in Cardiothoracic Anaesthesia and Intensive Care

Department of Anaesthesia, Golden Jubilee National Hospital, Glasgow, UK

Academic Unit of Anaesthesia, Critical Care and Pain Medicine, Glasgow, University.

Corresponding author:

Dr Benjamin Shelley

Department of Anaesthesia

Golden Jubilee National Hospital

Agamemnon Street

Clydebank

Glasgow

UK

G81 4DY

Email: Benjamin.Shelley@glasgow.ac.uk

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Telephone: 0141 951 5000

Keywords: Right ventricle, Right ventricular dysfunction, anaesthesia, general, and critical care.

Key Points:

1. Right ventricular (RV) dysfunction may be encountered in a wide variety of clinical scenarios
2. Identifying the underlying aetiology is important to optimising the RV.
3. Key management principles involve optimising rate, rhythm, perfusion, and preload, whilst maintaining contractility and minimising afterload.
4. 'Traditional' mechanical ventilation strategies may worsen RV dysfunction.

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Learning Objectives:

By reading this article you should be to:

- Describe a variety of conditions where right ventricular (RV) dysfunction might occur
- Describe a strategy for management of RV dysfunction including an approach to rate, rhythm, perfusion, preload, contractility, and afterload.
- Be aware of the complex interaction between mechanical ventilation and RV dysfunction.
- Have a basic understanding of the mechanical support options available when pharmacological management fails.

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Introduction

The importance of identifying and managing right ventricular (RV) dysfunction is becoming increasingly recognised by both anaesthetist and intensivist. In the face of an ageing population, with a broad range of increasingly complex comorbidities, the importance of RV function is applicable to a far wider population than those undergoing cardiothoracic surgery. Early recognition of RV dysfunction is essential to prevent failure and improve morbidity and mortality. An approach to RV structure and function was discussed in part one of this series with the aim of this second article to provide an overview of the clinical conditions leading to RV dysfunction and outline an approach to managing these patients.[1]

Right ventricular failure (RVF) is a heterogeneous syndrome, with a wide variety of aetiologies (both acute and chronic) requiring individualised treatment.[2] Whilst RVF lacks a validated consensus definition, the term acute right heart syndrome (ARHS) has recently been described, and is defined as a rapidly progressive syndrome with systemic congestion resulting from impaired RV filling and or reduced RV flow output.[2]

A high index of suspicion is required in patients with potential acute RV dysfunction as signs and symptoms may be non-specific. Acute signs of RVF are mainly a result of low cardiac output (CO) or systemic venous congestion and include signs of hypoperfusion with deranged liver function tests, elevated urea and creatinine, high lactate, and low venous oxygen saturations, all of which are non-specific to the diagnosis of RV failure. Signs and symptoms of chronic RV failure, such as ascites, exertional dyspnoea, reduced exercise tolerance, and ankle swelling may not always be present. Early use of transthoracic

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echocardiography (TTE) is recommended in those with a suspicion of RV failure to aid the early diagnosis in a challenging cohort of patients with limited specific clinical signs.[3]

Clinical Conditions in which RV failure may be encountered

RV function can be impaired by either volume or pressure overload states or a reduction in myocardial contractility. Dysfunction is triggered by an injury or stress to the RV with adaptation dependant on the nature of the insult, the duration of the disease, and time of onset (i.e. birth, childhood or adulthood). Acute events, as seen in myocardial infarction (MI) or pulmonary embolism (PE), may quickly progress to RV failure due to impaired contractility or acutely increased afterload. In chronic diseases, such as pulmonary hypertension (PH) or congenital cardiac disease, a gradual increase in RV afterload allows adaptive mechanisms to develop which preserve CO over a longer period of time before decompensation occurs.

Generally, the RV adapts better to volume overload, as seen with tricuspid regurgitation (TR) and atrial septal defects (ASDs), and can withstand these conditions for a long period of time without significant change in RV systolic function. Acute pressure overload, as seen in PE, leads to a rapid rise in pulmonary vascular resistance (PVR), increased afterload and RV wall tension, which quickly leads to RV dilatation and failure. Chronic pressure overload, commonly seen in PH, results in the RV being able to adapt as the pressure increases gradually over time. Multiple compensatory measures exist in chronic pressure overload including myocyte hypertrophy, expansion of the extracellular matrix, reduction in wall stress, and upregulation of neurohormonal systems. Over time, the gradual increase in

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afterload results in a decrease in contractility, leading to progressive RV dilation and ultimately failure.

When considering the aetiology of RV dysfunction, it can be useful to categorise into those affecting preload, afterload and contractility. Increased preload may occur in TR and ASDs. Increased afterload may occur due PH and PE. Decreased contractility may be encountered in RV infarction, arrhythmias or sepsis. In critically ill patients, RV dysfunction can often be multifactorial e.g. with sepsis induced acute respiratory distress syndrome (ARDS) where RV function may be impaired by both increased afterload and reduced contractility.

- *Pulmonary Hypertension*

PH is defined by a mean pulmonary artery pressure ≥25 mm Hg at rest, and is the commonest cause of RV failure.[4] The World Health Organisation classifies PH into 5 broad classifications: 1) pulmonary arterial hypertension, 2) PH secondary to left heart disease, 3) PH associated with lung disease, 4) chronic thromboembolic PH and 5) miscellaneous including haematological, metabolic and systemic disorders.[4] Classifications 1,3, and 4 are 'precapillary' and demonstrate a low or normal pulmonary capillary wedge pressure (a surrogate measure of left atrial pressure).

In PH, remodelling of the pulmonary vasculature, hypoxic vasoconstriction and disruption and fibrosis of small pulmonary vessels result in a steady increase in PVR. Increased afterload and disruption of neuroendocrine and autocrine signals leads to cardiomyocyte loss, myocardial ischaemia and remodelling. Initially, this increased afterload can be

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compensated for by RV hypertrophy, but eventually, the RV can no longer compensate and dilatation and dysfunction occur. The RV's ability to adapt to pressure overload determines prognosis in PH with a dilated RV shown to predict poor survival.[5]

Managing patients with PH in a critical care setting can be challenging and complex; pulmonary vasodilators, less commonly used in a general ICU environment, may be required with consideration given to early advice from a PH centre.[6] Condliffe et al have recently published 'Critical Care Management of Pulmonary Hypertension' which provides an in-depth review of PH in the ICU setting.[6]

Special attention should be given to patients with preexisting PH undergoing surgery as they are at high risk of deterioration. The chosen anaesthetic technique should aim to prevent further iatrogenic increases in PAP by preventing hypoxia, hypercapnia, and acidosis. The use of PEEP, intraoperative patient positioning, and pneumoperitoneum can all increase afterload. Intraoperative invasive monitoring is likely to be required and the use of transoesophageal echocardiography (TOE) and CO monitoring devices may be appropriate. Neuraxial techniques can be used; however, consideration should be given to the risk of cardiovascular instability with sympathetic block. These patients are likely to require critical care following surgery with high-risk of post-operative RV failure. Depending on the nature and urgency of the surgery, referral to a PH centre for advice may be appropriate.

- *Left Ventricular (LV) Failure*

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The commonest cause of PH is left-sided heart failure which includes LV systolic dysfunction, LV diastolic dysfunction and left-sided valvular heart disease.[4] LV failure is classified as post capillary PH (class II) and is associated with a high pulmonary capillary wedge pressure.[4] In this instance, PH develops occurs as a result of passive backward transmission of raised left sided filling pressures. Associated RV dysfunction often goes unrecognised despite a prevalence of around one fifth of patients with LV failure.[7] RV failure is an important independent predictor of survival in patients with LV failure.[7] As with all cases of RV failure, monitoring of both the LV and RV with echocardiography is essential. In patients with RV failure as a result of raised left sided filling pressures, benefit may be derived from left heart failure management strategies including revascularisation, diuresis, and the use of beta blockers and angiotensin converting enzyme inhibitors. In some preoperative patients, it may be beneficial to delay surgery in order to optimise heart failure management prior to surgery.

- *Chronic Obstructive Pulmonary Disease (COPD)*

COPD is the most common cause of cor pulmonale and leads to an increase in RV afterload secondary to changes in pulmonary vascular structure and mechanics, and lung hyperinflation. Patients with COPD who subsequently develop RV dysfunction have an increased risk of admission to hospital and mortality.[8]

It is often not appreciated that these changes are not just limited to those with severe lung disease; studies demonstrate remodelling of the pulmonary vasculature occurs in those with

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mild disease and in smokers with normal lung function.[9] As such, there is good evidence to show that patients with mild to moderate COPD (well within the realms of lung function seen in patients presenting for a wide range of elective surgeries) have exercise limitation resulting from cardiac (i.e. RV) rather than respiratory insufficiency. Arguably, the COPD population should be considered 'at risk' of RV dysfunction during the perioperative period and may be less tolerant of the stresses of mechanical ventilation and critical illness. The development of disproportionate haemodynamic collapse following intubation in the COPD patient with 'single organ' postoperative respiratory failure is a classic example of this.

- *Pulmonary Embolism (PE)*

PE is the commonest cause of acute RV dysfunction; assessment of RV function is essential as mortality is directly related to the extent of RV failure.[10] Mechanical obstruction of pulmonary vessels results in acutely increased RV afterload. Acute dilatation and stretch of the RV muscle occurs when more than 30% of the pulmonary vasculature is blocked, increasing RV wall tension with an increasing oxygen demand whilst simultaneously decreasing perfusion. [11] In most cases of PE, as resolution of the embolus occurs over time, pulmonary artery pressures (PAP) decline and RV function returns to normal.

Chronic thromboembolic PH (CTEPH) is a rare complication of PE and occurs as a result of incomplete resolution of the clot with the formation of a fibrotic and flow limiting thrombus within the pulmonary vasculature. These changes lead to an increase in afterload with

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remodelling of both the pulmonary vasculature and the RV. Pulmonary endarterectomy may be appropriate for some patients; however, RV dysfunction may persist following surgery as a result of the extent of RV remodelling which has taken place.[12]

- *Acute Respiratory Distress Syndrome*

Acute cor pulmonalae has been reported in 20-25% of patients with ARDS with good evidence to suggest that RV dysfunction is independently associated with poor outcome.[13] A high index of suspicion is therefore required for the potential diagnosis of PH and RV dysfunction in those with ARDS as the clinical signs are often non-specific.

ARDS causes direct injury to the pulmonary circulation caused by hypoxic vasoconstriction, extrinsic vascular compression as a result of interstitial oedema, vasoconstrictor mediator release, and blood vessel remodelling. Endothelial dysfunction is a common feature alongside mechanical obstruction as a consequence of thromboemboli particularly in the larger pulmonary arteries, veins, and lymphatics whilst smaller vessels become occluded by neutrophils and platelets. [14] This leads to an increase in PVR , RV afterload, the development of PH and RV failure. In patients with ARDS, these effects are magnified as airway pressures rise in combination with the pulmonary vasoconstrictive effects of hypoxia and hypercapnia.

It is increasingly being recognised that modern ventilatory practices with low tidal volumes and high PEEP have the potential to adversely affect RV function, with some experts recommending an 'RV protective approach' to mechanical ventilation in ARDS, such that

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PEEP is manipulated in parallel with echocardiographic assessment of the RV. Such an RV protective strategy focuses on limiting plateau pressure to reduce lung stress, improving oxygenation to limit the effect of hypoxic vasoconstriction and preventing hypercapnia.[15] Tidal volume and PEEP should aim to maintain a plateau pressure <27cmH_20, a driving pressure <18cmH_20 and ideally a $PaC0_2$ <48mmHg.[15] If the respiratory rate is adjusted, this should be done carefully as this may induce intrinsic PEEP and dynamic hyperinflation worsening RV dysfunction. Ventilation in the prone position has been shown to induce alveolar recruitment and reduce RV afterload.[16]

- *Obesity and Obstructive Sleep Apnoea*

Obesity is an independent risk factor for cardiovascular disease and has been shown to cause a wide spectrum of cardiovascular changes which can ultimately result in heart failure. Obesity can lead to RV dysfunction as a result of increased CO, obesity hypoventilation syndrome and obstructive sleep apnoea (OSA). Studies have shown the presence of RV dilatation, increased RV wall thickness and subclinical RV diastolic and systolic impairment may be present in young obese patients with no pre-existing cardiovascular disease. [17]

In OSA, hypoxic pulmonary vasoconstriction occurs during apnoeic episodes leading to remodelling of the pulmonary microcirculation increasing PVR, and ultimately leading to the development of PH and subsequent RV dysfunction.[18] Negative intrathoracic pressure, occurring during inspiration against an occluded pharynx, increases venous return, and RV

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preload.[18] Co-existing cardiovascular disease and hypoxaemia may also play an important role in RV dysfunction in this patient population. Imaging of the RV by TTE can be challenging in this cohort of patients and consideration may be given to more advanced techniques.

Careful attention to mechanical ventilation strategies is also required to prevent atelectasis but prevent further RV dysfunction (necessitating a similarly balanced ventilation strategy as described in ARDS).

- *Right ventricle myocardial infarction (RVMI)*

As the RV is supplied by the right coronary artery (RCA) in 80% of the population, RCA occlusion can lead to significant RV ischaemia. Generally, the RV is considered to more tolerant of an ischemic insult compared with the LV as a result of coronary perfusion occurring throughout the cardiac cycle, and reduced myocardial oxygen demand[19]. Patients with a proximal RCA MI, however, have an increased risk of tachyarrhythmia, cardiogenic shock and death because of the interruption of the blood flow to the AV node and the lack of collateral blood supply present in the RV. Prognosis in RVMI is dependent on the location of the MI, presence of complications, preexisting RV dysfunction, and successful coronary reperfusion. Similar to LVMI, patients who survive RVMI, may recover their systolic function following the initial ischaemic episode as 'stunning' resolves.

- *Congenital Heart Disease*

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Several different types of congenital heart disease are associated with RV dysfunction. Both atrial and ventricular septal defects (A- and V-SD) with left to right shunt and tricuspid and pulmonary regurgitation may lead to volume overloaded RV failure. Chronically increased pulmonary blood flow can occur in large septal defects leading to pulmonary endothelial damage, thrombosis, RV hypertrophy and pulmonary vascular remodelling. If unchecked, progressive hypertrophy and increasing right sided systolic pressure result in 'suprasystemic' right sided pressures and reversal of the initially left-to-right shunt. This results in right-to-left shunting and consequent systemic hypoxemia as seen in Eisenmenger's syndrome. [19 20]

Pressure-overloaded RV failure occurs with pulmonary stenosis, RV outflow tract (RVOT) obstruction after correction of tetralogy of Fallot (TOF), and repair of transposition of the great arteries. Whilst the RV is initially able to adapt, (if untreated) longstanding obstruction leads to progressive TR and RV dilation and failure.[20] Over time pulmonary regurgitation leads to progressive RV dilatation necessitating timely PV replacement before RV dysfunction ensues.[20] Adult patients with TOF repaired in childhood are becoming an increasingly large cohort in congenital cardiac centres.

- *Cardiac Surgery*

A degree of RV dysfunction following cardiac surgery is commonplace; however, the underlying aetiology is not clear. Besides the effects of myocardial stunning resulting from direct myocardial ischaemia during cardiopulmonary bypass, the RV is particularly susceptible to post-operative dysfunction because of air embolization (to which the RV is

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particularly predisposed as a result of the anterior location of the right coronary ostia), and increased PVR postoperatively. Where systemic vasodilatation is common following cardiopulmonary bypass, PVR commonly rises as a result of the activation of inflammatory mediators, the accumulation of extravascular lung water, persistent pulmonary de-recruitment and protamine-induced PH.

PH, RV dilatation and dysfunction, and functional TR are common sequelae of mitral valve disease. At the time of mitral valve surgery, the tricuspid vale (TV) may also be repaired. Careful attention to the RV following TV surgery is paramount. Pre-operatively TR can lead to overestimation of baseline RV function as it is 'flattered' by the presence of TR (i.e. the ease of emptying when blood may flow in an anterograde or retrograde direction can make the function 'look' better than it is). Repair of the valve can then lead to an effective increase in afterload which may unmask impaired RV function.

- *Left Ventricular Assisted Devices (LVAD)*

LVADs are used as a bridge to transplant or recovery in patients with severe heart failure. An inlet cannula is inserted into the LA or LV cavity, whilst an outflow graft is attached to the ascending aorta providing isolated support to the left-side of the heart. Adequacy of RV function is a major determinant of outcome following LVAD insertion. In comparison to the low cardiac output state encountered pre-operatively, following LVAD implantation, the RV is challenged by the need to match the increased LV output which leads to an effective increase in preload. In addition, unloading of the LV by a VAD can alter the shape and size of the RV leading to a direct effect on function.[21]

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- *Heart Transplantation*

Despite advances in the perioperative management of heart transplantation, acute RV failure still accounts for a significant number of complications and early deaths. Whilst the aetiology for RV failure following transplantation is multifactorial, two predominant mechanisms are described. Firstly, that of an ischaemic insult to the RV occurring as a result of prolonged ischaemic time and sub-optimal myocardial protection leading directly to primary graft failure. Secondly, the presence of pre-existing or acquired PH in the recipient can result in the exposure of the previously 'afterload-naive' (and therefore not adapted) transplanted organ to acutely increased afterload.

Management:

The management of RV failure should naturally aim to identify and treat any underlying aetiology. Generic treatment goals include optimising rate, rhythm, perfusion, preload, augmenting myocardial contractility and minimising afterload (Figure 1). This requires a careful balance of cardiac filling combined with vasopressor and inotropic support. In rare cases, surgical management may be required in the form of mechanical circulatory support**.**

- *Optimise rate and rhythm*

In general, it is considered preferable to keep the RV beating faster and where possible in sinus rhythm (SR). A relatively high heart rate (it is not uncommon to pace the immediately post-transplanted heart at 110 bpm), prevents excessive RV distention and subsequent

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distortion of the LV and minimises TR. Additionally in conditions of failure where stroke volume may be limited, a higher heart rate promotes cardiac output. Clinicians should always be aware however of the effects of tachycardia on the LV blood supply and on its function.

In theory, preservation of SR offers significant haemodynamic benefits, improving ventricular preload as well as improving atrial emptying and reducing atrial pressures. In many patients, non-sinus rhythm is a chronic situation however; attempts to restore SR through chemical or electrical cardioversion should therefore be reserved for circumstances where acute or paroxysmal arrhythmias are causing or exacerbating a patient's condition.

- *Maintaining Perfusion*

The importance of maintaining systemic arterial pressure, and right coronary perfusion pressure is often under-appreciated in RV dysfunction where systemic hypotension can be detrimental to the failing RV. Vasoconstrictor agents, such as noradrenaline or vasopressin (Table 1), are often required to maintain systemic pressure, indirectly resulting in improved RV function and global tissue perfusion.

Intra-aortic balloon pump counter pulsation (IABP) is a commonly used circulatory assist device improving coronary and systemic blood flow.[22] Whilst these devices are generally considered to provide left sided support; improvement of right coronary perfusion can aid RV function. The IABP inflates and deflates in harmony with the cardiac cycle; as diastolic

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aortic pressure is augmented, coronary perfusion pressure is increased, improving coronary blood flow and increasing myocardial oxygen supply.

- *Optimise preload*

Optimising RV preload by ensuring adequate filling pressure is important in patients with RV dysfunction; even a functionally impaired ventricle has an optimal level of filling. Given the potential for deleterious effects of over-distention however, it is common practice to assess fluid responsiveness in patients with RV dysfunction by using small volume fluid boluses (50-100ml) whilst paying close attention to CVP. In patients with RV dilatation, any increase in intravascular volume can worsen dilatation and further impair LV diastolic filling. In the dilated RV, marked diuresis is often warranted to offload the ventricle and reduce right-sided filling pressures.

Exaggerated, ventilation induced (i.e. in response to cyclically varying afterload) changes in SV and CO are common in the failing RV and can easily be misinterpreted as signs of 'fluid responsiveness', rendering monitors assessing SV or systolic pressure variation less useful in this context. Often the only reliable method of assessing preload responsiveness is the judicious administration of a fluid bolus and observing the net change in SV or CO using an appropriate CO monitor.

- *Reduce afterload*

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Minimising afterload is a key component of RV management, though many patients presenting with RV failure have chronic lung or cardiac diseases and consequently PH that cannot easily be reversed. Iatrogenic increases in PVR should be avoided by careful avoidance of hypoxia, hypercapnia and acidosis. When ventilating patients with RV failure airway pressures should be minimised and PEEP used judiciously; both atelectasis and excessive PEEP will increase PVR (Figure 2). Again, these goals appear in conflict to those employed in patients with ARDS, where permissive hypercapnia and higher levels of PEEP are commonplace.

Intravenous (IV) or inhaled pulmonary vasodilators may be used to reduce afterload by targeting pathways implicated in PH. IV pulmonary vasodilators (e.g. GTN, flolan, inodilators) cause indiscriminate vasodilation of the pulmonary vascular bed, blunting hypoxic pulmonary vasoconstriction, leading to a worsening of any ventilation-perfusion mismatch (V/Q) and potentially causing hypoxia. Systemic vasodilation occurs in parallel and can cause systemic hypotension.

Inhaled vasodilators, such as nitric oxide, reduce PVR only in areas of the lung that are well ventilated and so improve the V/Q matching by increasing flow to these areas, improving oxygenation and decreasing PVR. Nitric oxide has a fast-onset of action with a short half-life and has been shown to improve RV systolic function, mixed venous oxygen saturations and haemodynamics in patients with acute RV failure. Nitric oxide may be of benefit in the peri-operative and early post-operative period in patients with PH during cardiac surgery. There is evidence for a reduction in PAP and an improvement in hypoxia in other clinical scenarios such as ARDS, PE, and COPD; however, the evidence for an improvement in overall outcome

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is lacking. Disadvantages include expense, the need for toxicity monitoring, platelet inhibition, prolonged bleeding time and the potential for rebound hypoxaemia and PH. Weaning of nitric oxide can be challenging and slow weaning over hours to days may be required to avoid vasoconstriction and rebound pulmonary hypertension or hypoxaemia.

Oral phosphodiesterase type-5 inhibitors, such as sildenafil, reduce PVR and improve RV contractility but caution should be exercised because of their long terminal half-life (4-18hours) and risk of systemic hypotension as a result of systemic vasodilatation. In practice, these agents tend to be used in stable disease rather than in the acute phase.

- *Optimise contractility*

Inodilatory vasoactive drugs, such as dobutamine, a beta agonist, or milrinone a phosphodiesterase-3 inhibitor, are a natural choice in RV dysfunction promoting increased contractility with a simultaneous reduction in afterload (Table 1). Both agents cause a reduction in SVR and can lead to profound systemic hypotension, especially with milrinone. As such, systemic vasoconstrictors are often required in conjunction with ino-dilators to counteract the side effects described.

Levosimendan, a calcium sensitizer, may improve coronary perfusion and contractility without increasing myocardial demand; however, its role in RV failure needs further exploration.

- *Mechanical Support*

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In isolated RV failure refractory to medical therapy or RV failure in the context of an LV support device several options exist for mechanical circulatory support of the RV. It is important to consider mechanical support early in order to prevent irreversible end organ damage.

Peripheral venoarterial extracorporal membrane oxygenation (ECMO - in contrast to venovenous ECMO) provides respiratory and biventricular support via cannulae in the right atrium (inserted via a peripheral vein) and in the subclavian or femoral artery.

Surgically implanted VADs provide isolated RV support classically via cannulae in the RA or RV and an outflow cannula in the pulmonary artery. In recent years, so called 'percutaneously inserted' VAD devices such as the Impella RP and TandemHeart RVAD devices have become increasingly popular, providing isolated RV support without the need for sternotomy by accessing the pulmonary circulation via a transvalvular systemic venous approach.

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Conclusions

RV dysfunction and failure can occur as a result of a wide variety of pathophysiology and is becoming more frequent in the general anaesthetic and intensive care population. Initial management should aim to identify potential underlying reversible causes, optimise preload and reduce afterload. Close attention should be paid to rate, rhythm and perfusion.

Pharmacological management may include a combination of inotropes, vasopressors, and pulmonary vasodilators.

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MCQs

Question1:

A 64-year-old male is admitted to ICU with Type 1 respiratory failure. His chest xray findings are consistent with acute respiratory distress syndrome (ARDS). He has an endotracheal tube placed and is ventilated. His current ventilation settings are Fi02 0.9, TV 550ml, RR 18, PEEP 8cmH_20. His observations include BP 74/47mmHg MAP 58, HR 108bpm, lactate 6, venous oxygen saturations 48%. The following statements are true:

a) An increased pulmonary vascular resistance (PVR) occurs during mechanical ventilation because of alveolar distension and extra-alveolar capillary compression.
b) A bedside transthoracic echocardiograph would be an appropriate investigation in this patient.
c) A driving pressure of >18cm H_20 is considered a risk factor for acute cor pulmonale.
d) Proning may be beneficial in this patient to increased afterload.
e) 'RV protective' ventilation strategies include adjusting tidal volume and PEEP to achieve a plateau pressure of >27cm H_20

Answers:

a) True. Alveolar distention during mechanical ventilation leads to compression of extra-alveolar capillaries increasing pulmonary vascular resistance (PVR) and RV afterload. In patients with ARDS, these effects are magnified as airway pressures rise in combination with the pulmonary vasoconstrictive effects of hypoxia and hypercapnia.

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b) True. This patient is demonstrating non-specific signs of RV dysfunction including evidence of hypoperfusion. A bedside TTE may demonstrate evidence of RV dysfunction which occurs in around 15% of patients with ARDS.

c) True. Risk factors for acute pulmonale include an P_{a02}/F_{i02} of < 150mmHg (20 kPa), P_{aCo2} > 48mmHg (6.3kPa) and a driving pressure of > 18cm H_20.

d) False. Proning could be useful in this patient as it has been shown to *reduce* afterload and improve alveolar recruitment.

e) False. Tidal volume and PEEP should aim to maintain a plateau pressure less than 27cmH_20, a driving pressure < 18cmH_20 and ideally a $PaC0_2$ < 48mmHg

Question 2:

Appropriate statements regarding pharmacological management of right ventricular failure (RVF) include:

a) Milrinone leads to an increase in pulmonary vascular resistance as a result of its role as a PDE3 inhibitor

b) Noradrenaline works on the α1 and β1receptors leading to vasoconstriction and increased myocardial oxygen delivery.

c) Sildenafil can be inhaled via a nebuliser, administered intravenously or orally.

d) Vasopressin causes pulmonary vasodilatation

e) Nitric oxide has a half-life of less than 5 seconds

Answers:

For Peer Review

Question 2

a. False. Milrinone is an ino-dilator that works on the PDE3 receptor causing a decrease in pulmonary and systemic vascular resistance.
b. True. Noradrenaline works on the $\alpha 1$, $\beta 1$ with effects including vasoconstriction, increased systemic and pulmonary vascular resistance, and increased myocardial oxygen delivery.
c. False. Sildenafil has an oral and IV preparation but no nebulised form. Other pulmonary vasodilators such as prostacyclin may be given in the nebulised form.
d. True. Vasopressin causes pulmonary vasodilatation as a result of its stimulation of endothelial nitric oxide.
e. True. Inhaled NO reacts with oxidised haemoglobin to produce methaemoglobin with a half-life of less than 5 seconds.

Question 3:

Regarding clinical conditions associated with right ventricular dysfunction:

a. Right ventricular myocardial infarction occurs traditionally because of occlusion of the left anterior descending artery.
b. Atrial septal defects (ASD) can lead to volume overloaded RV failure.
c. Repair of the tricuspid valve during cardiac surgery may lead to an increase in preload.
d. Pre-existing pulmonary hypertension is a risk factor for developing post-operative RV dysfunction in cardiac transplant patients.

For Peer Review

e. Following left ventricular assisted device insertion, the RV has to work harder as a result of an increase in contractility.

Answers 3:

a. False. RVMI classically occurs because of an occlusion of the right coronary artery.
b. True. ASD defects are associated with volume overloaded RV failure. Other causes include VSDs, pulmonary regurgitation and tricuspid regurgitation.
c. False. Repair of the tricuspid valve leads to an effective increase in afterload which may affect RV function.
d. True. The transplanted heart may be exposed to increased afterload from pre-existing pulmonary hypertension resulting in RV failure.
e. False. In comparison to the low cardiac output state encountered pre-operatively, following LVAD implantation, the RV has to work harder to match the increased LV output which leads to an effective increase in preload.

For Peer Review

Question 4:

Regarding the aetiology of right ventricular failure, the following statements are true:

a. During cardiac surgery, RV dysfunction may occur because of air embolism.
b. Negative intra-thoracic pressure, encountered in OSA, increases venous return and consequently RV preload.

c. Patients with large VSD defects will present with pressure-overloaded RV failure.

d. RV failure may be encountered following LVAD insertion as a result of an increased preload.

e. LV failure is classified as WHO Class 1 Pulmonary Hypertension.

Answers:

a. True. The RV is particularly susceptible to post-operative dysfunction because of air embolization. The RV is particularly predisposed because of the anterior location of the right coronary ostia.

b. True. The negative intra-thoracic pressure, occurring during inspiration against an occluded pharynx, increases venous return, and RV preload.

c. False. Ventricular septal defects (A- and V-SD) with left to right shunt and tricuspid and pulmonary regurgitation may lead to volume-overloaded RV failure.

d. True. Following LVAD implantation, the RV is challenged by the need to match the increased LV output which leads to an effective increase in preload and therefore potential RV failure.

e. False. LV failure is classified as post-capillary PH (WHO class II PH) and is associated with a high pulmonary capillary wedge pressure

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Figure 1: Management of Right Ventricular Failure Algorithm.

NO: nitric oxide. PH: pulmonary hypertension. DCCV: direct current cardioversion. CVP: central venous pressure. CVVH: continuous venous-venous hemofiltration. IABP: intra-aortic balloon pump. ECMO: extra-corpeal membrane oxygenation. VAD: ventricular assist device. HR: Heart rate. SR: sinus rhythm. IV: Intravenous.

Figure 2. Schematic representation of the relationship between lung volume and pulmonary vascular resistance.

The relationship of PVR and lung volumes. Atelectasis compresses extra-alveolar bloods vessels which increases PVR. Alveolar distention, occurring at high lung volumes, compresses intra-alveolar blood vessels which increases PVR.

RV - Residual volume (RV). Functional Residual Capacity (FRC). Total Lung Capacity (TLC).

Table 1. Commonly used pharmacological agents in RV failure.

IV: intravenous. Neb: Nebulised. SVR: systemic vascular resistance. PVR: pulmonary vascular resistance. PH: Pulmonary hypertension. [a] A loading dose of milrinone may be given.

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MCQs

Question1:

A 64-year-old male is admitted to ICU with Type 1 respiratory failure. His chest x-ray findings are consistent with acute respiratory distress syndrome (ARDS). He has an endotracheal tube placed and is ventilated. His current ventilation settings are Fi02 0.9, TV 550ml, RR 18, PEEP 8cmH_20. His observations include BP 74/47mmHg MAP 58, HR 108bpm, lactate 6, venous oxygen saturations 48%. The following statements are true:

a) An increased pulmonary vascular resistance (PVR) occurs during mechanical ventilation due to alveolar distension and extra-alveolar capillary compression.
b) A bedside transthoracic echocardiograph would be an appropriate investigation in this patient.
c) A driving pressure of >18cm H_20 is considered a risk factor for acute cor pulmonale.
d) Proning may be beneficial in this patient to increased afterload.
e) 'RV protective' ventilation strategies include adjusting tidal volume and PEEP to achieve a plateau pressure of >27cm H_20

Answers:

a) True. Alveolar distention during mechanical ventilation leads to compression of extra-alveolar capillaries increasing pulmonary vascular resistance (PVR) and RV afterload. In patients with ARDS, these effects are magnified as airway pressures rise in combination with the pulmonary vasoconstrictive effects of hypoxia and hypercapnia.

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b) True. This patient is demonstrating non-specific signs of RV dysfunction including evidence of hypoperfusion. A bedside TTE may demonstrate evidence of RV dysfunction which occurs in around 15% of patients with ARDS.

c) True. Risk factors for acute pulmonale include an P_{a02}/F_{i02} of < 150mmHg (20 kPa), P_{aCo2} > 48mmHg (6.3kPa) and a driving pressure of > 18cm H_20.

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e. False. LV failure is classified as post-capillary PH (WHO class II PH) and is associated with a high pulmonary capillary wedge pressure.

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Drug	Classification	Dose	Receptor	Effects	Onset	Advantages	Disadvantages
Noradrenaline	Vasopressor	IV:0.02 – 0.2mcg/kg/min	α1, β1	Vasoconstriction ↑SVR, ↑Myocardial O_2 delivery ↑PVR	Quick (mins)	Cheap Easy to titrate Familiarity	Arrhythmias ↑ PVR in higher doses
Vasopressin	Vasopressor	IV.: 1-4 units/min	V1, V2	Vasoconstriction, ↑SVR, Pulmonary vasodilatation at low doses via endothelial nitric oxide pathway ↑myocardial O_2 delivery	Quick (mins)	Catecholamine sparing Less ↑ PVR than Noradrenaline Easy to titrate	Expensive Bradycardia Splanchnic ischaemia
Dobutamine	Inodilator	IV: 2.5-10mcg/kg/min	β1,β2	Inotropy ↑contractility ↓SVR, PVR	Quick (mins)	Easy to titrate Cheap	↑ O_2 demand Tachy-arrhythmias Systemic hypotension
Milrinone	Inodilator	IV 0.375–0.75 mcg/kg/min[a]	PDE3 inhibitor	Inotropy ↑Contractility ↓SVR, PVR	Long half-life (2.5h)	Pulmonary vasodilatation	Systemic hypotension Expensive
Levosimendan	Inodilator	IV loading: 6–12 mcg/kg/min over 10 min followed by 0.1	Calcium sensitizer	↑Contractility	Slow	No effect on myocardial oxygen demand	Expensive Tachycardia Hypotension Headache

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		mcg/kg/min					
Sildenafil	Pulmonary vasodilator	IV: 10mg TDS Oral: 20–100 mg TDS	PDE5 inhibitor	↓PVR ↑Contractility	Slow	Oral admin for patients with chronic disease.	Long terminal half-life (4-18h), ↓SVR
Epoprostenol	Pulmonary vasodilator	IV:1-2ng/kg/min Neb: 0.2–0.3 ml/min of 10–20 µg/ml	Prostacyclin	↓PVR ↑V/Q mismatch	Quick	As efficient as nitric oxide	Systemic hypotension with IV admin Flushing Headaches

Table 1. Commonly used pharmacological agents in RV failure.
IV: intravenous. Neb: Nebulised. SVR: systemic vascular resistance. PVR: pulmonary vascular resistance. PH: Pulmonary hypertension. [a] A loading dose of milrinone may be given but increases risk of systemic hypotension.

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Management of Acute Right Ventricular Failure

In all cases identify and treat underlying aetiologies where possible

Maintain rate and rhythm:

Higher HR

Aim to maintain SR

Cardioversion if new onset/instability

Amiodarone +/- DCCV

Optimise Preload:

Optimise cardiac filling

Under-filled: Small fluid boluses (50-100ml, close attention to CVP)

Overfilled: Diuresis with loop diuretics

CVVH may be required

Improve contractility and maintain perfusion:

Inodilators (dobutamine, milrinone)

Vasopressors (noradrenaline, vasopressin)

Reduce afterload:

Prevent hypoxia, hypercapnia, acidosis

Reduce PEEP and airway pressures

Avoid atelectasis

Inhaled pulmonary vasodilators

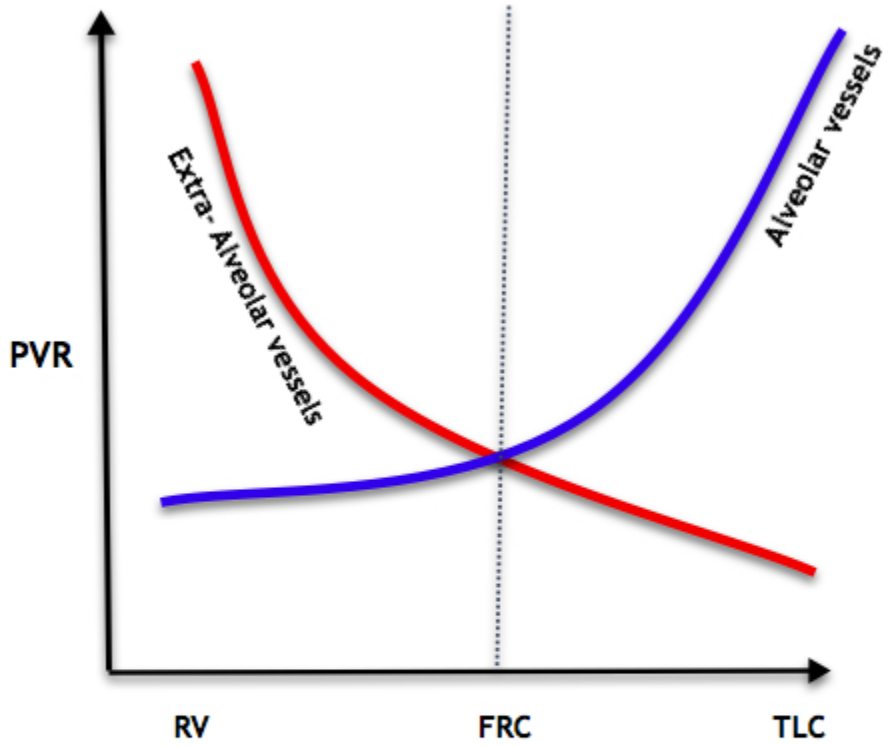
Intravenous pulmonary vasodilators

Mechanical Circulatory Support:

IABP

ECMO

VAD



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