OXFORD

Revalidation FOR ANAESTHETISTS RCA Revalidation matrix Matrix reference 1A01, 2A05, 3G00

BJA Education, 17 (7): 228–234 (2017)

doi: 10.1093/bjaed/mkw074
Advance Access Publication Date: 22 February 2017

Critical care management of pulmonary hypertension

R Condliffe MD* and DG Kiely MD

Consultant Physicians, Sheffield Pulmonary Vascular Disease Unit, Sheffield, S10 2JF, UK

*To whom correspondence should be addressed. E-mail: robin.condliffe@sth.nhs.uk

Abstract

Patients with pulmonary hypertension (PH) can be extremely challenging to manage in the critical care setting. In this article we review the classification, diagnosis, and chronic management of PH. An approach to the management of the critically unwell PH patient is discussed. Initial management involves treating underlying precipitants of deterioration and optimizing right ventricular (RV) preload. Reduction of RV afterload with pulmonary vasodilators is also required. Augmentation of cardiac function and perfusion pressures with inotropes and vasopressors may additionally be needed. Advanced renal and respiratory support may be appropriate depending on the clinical context. Patients with known PH who have undergone major surgery or who are in the immediate postpartum period are also at significant risk of deterioration and require management in the critical care setting. Although pulmonary vasodilators are associated with improvements in pulmonary haemodynamics and oxygenation in patients with acute respiratory distress syndrome or after cardiac surgery, there is currently no evidence demonstrating improved outcomes.

Key points

- Current classification of pulmonary hypertension comprised five diagnostic groups based on shared pathophysiology.
- Diagnostic approach includes echocardiography, the exclusion of thromboembolic disease, and right heart catheterization.
- The majority of evidence for the use of pulmonary vasodilators is in patients with pulmonary arterial hypertension.
- Critical care management of the acutely unwell patient should involve:
  a. treating precipitating factors.
  b. optimizing right ventricular preload and afterload.
  c. maintaining perfusion pressures.
  d. increasing right ventricular contractility.

Background

Classification, epidemiology, and survival

Pulmonary hypertension (PH) is defined as a mean pulmonary artery pressure, measured at right heart catheterization, of ≥25 mm Hg.[1] Current classification describes five main groups of PH based on shared pathophysiological characteristics (Fig. 1).[2] Group 1 (Pulmonary arterial hypertension, PAH) can be idiopathic (IPAH) or heritable or can be associated with other conditions, including connective tissue disease (most commonly systemic sclerosis), congenital heart disease, HIV, and portal hypertension. It can also be associated with various drugs, including amphetamines and interferon. Group 2 (PH secondary to left heart disease, PH-LHD) is predominantly caused by passive transmission of elevated left atrial pressure (pulmonary arterial wedge pressure >15 mm Hg) to the pulmonary circulation and can be caused by left ventricular dysfunction (systolic or diastolic) or valvular disease. Group 3 (PH secondary to respiratory disease, PH-Lung) is common in the presence of severe respiratory disease but is generally relatively mild, where it is often termed cor pulmonale. Group 4 (chronic thromboembolic PH, CTEPH) is caused by obstruction and

Editorial decision: March 2, 2016; **Accepted:** November 21, 2016

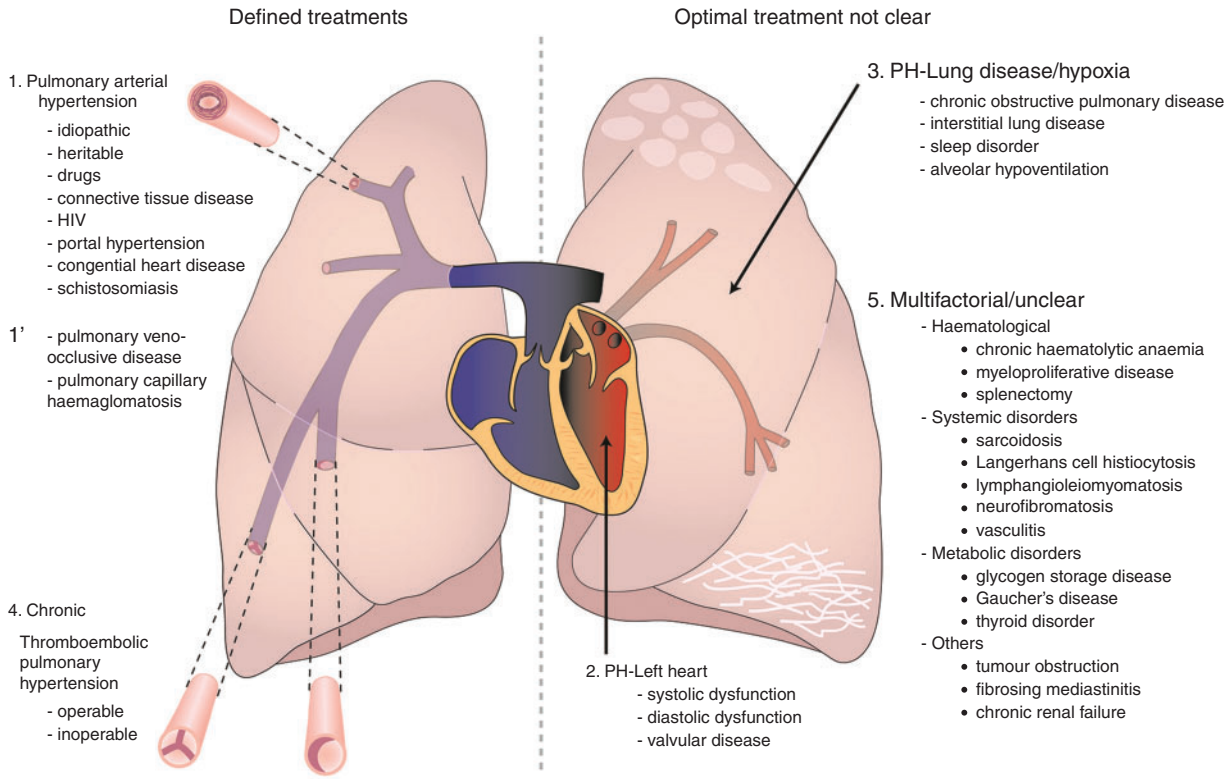

Fig 1 Current classification of pulmonary hypertension (used with permission, first published in *Br Med J*).[2]

narrowing of the pulmonary arterial bed by chronic, organized thromboembolic disease. Group 5 (miscellaneous) consists of associated conditions that may have multiple or uncertain mechanisms of disease and includes sarcoidosis and myeloproliferative disease.

Idiopathic PAH (IPAH) is a rare condition in the general population with an incidence of ~3/million/yr. PAH can occur commonly in specific at-risk groups (e.g. ~10% of patients with systemic sclerosis and ~2% of patients with portal hypertension will develop PAH). CTEPH complicates ~1–4% of patients after an acute pulmonary embolism. PH-LHD and PH-Lung are not uncommon, complicating severe chronic obstructive pulmonary disease in ~50% of patients, whereas estimates of prevalence in patients with left ventricular diastolic dysfunction range from 7 to 83%. Intensivists will therefore rarely manage patients with pre-existing precapillary pulmonary hypertension (i.e. PAH and CTEPH) but will more commonly manage patients with other forms of pre-existing PH. Patients with acute cardiorespiratory failure may also develop acute RV impairment and PH. In this article, we will focus mainly on patients with PAH and CTEPH who require critical care involvement.

Before the availability of specific therapies, IPAH was associated with a median survival of 2.8 years.[3] Outcomes have improved with a 5-yr survival of 75–80% in IPAH patients <50 yr old (similar to the age of patients seen in historical registry data).[4] Patients with Eisenmenger syndrome tend to have a well-conditioned hypertrophied RV and so have superior survival to other forms of PAH.[5]

Diagnosis

The commonest presenting symptom in PAH is progressive exertional dyspnoea. As the RV begins to fail, patients develop peripheral oedema and presyncope. Clinical signs suggestive of PAH include peripheral oedema, an increased jugular venous pulse, a loud P2, and a right ventricular heave. Chest X-ray may show cardiomegaly and enlarged pulmonary arteries, while ECG often demonstrates right axis deviation and anterior and inferior T wave inversion. If PH is suspected then trans-thoracic echocardiography should be performed, with a systolic PAP of ≥ 36 mm Hg being suggestive of PH. An enlarged left atrium, left ventricular hypertrophy, and elevated E/e' (ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity) suggest left ventricular diastolic dysfunction as the cause of PH. If initial investigations suggest that significant PH is likely then radiological assessment is required to exclude thromboembolic disease. Although isotope perfusion scanning is the most sensitive method of excluding clot, computed tomography pulmonary angiography can also be useful in excluding thromboembolic disease while also providing useful information regarding the lungs and heart.[6] Finally, right heart catheterization is performed to accurately measure pulmonary arterial pressure, pulmonary arterial wedge pressure, and cardiac output. If idiopathic PAH is suspected then an acute vasodilator challenge is performed, most commonly with inhaled nitric oxide. In 10% of patients there is a rapid reduction in mPAP by >10–<40 mm Hg, with no reduction in cardiac output. This phenomenon suggests a predominant vasoconstrictive pathophysiology to their increased pulmonary vascular resistance (PVR), and half of these patients will have an excellent haemodynamic response and prognosis with high-dose calcium channel blockade therapy. Conditions associated with the development of PAH should be considered, which may include checking anti-nuclear antibodies, extractable nuclear antibodies, double-stranded DNA antibodies for undiagnosed connective tissue disease, and HIV serology.

Table 1 Therapies in chronic and acute management. neb, nebulized; NS, normal saline; D5W, 5% dextrose; c/i, contraindicated

Therapy	Chronic	Acute	Comments
Prostanoid			
Epoprostenol	i.v.: 2–20 ng/kg/min	i.v.: 1–2 ng/kg/min, increase as tolerated with initial target 10 ng/kg/min after 48–72 h neb: 0.2–0.3 ml/min of 10–20 μg/ml	Limiting side-effects: systemic hypotension, flushing, headache, diarrhoea, leg and jaw pain
Iloprost	i.v.: 1–10 ng/kg/min neb: 5 μg 7 times/day	i.v.: 1–2 μg/h, increase as tolerated with initial target 6 ml/h after 48–72 h (100 μg in 100 ml NS) neb: 5 μg 7 times/day	Limiting side-effects: systemic hypotension, flushing, headache, diarrhoea, leg and jaw pain
Treprostinil	i.v.: 1–60 ng/kg/min sc: 1–60 ng/kg/min oral: up to 6 mg tds		Limiting side-effects: systemic hypotension, flushing, headache, diarrhoea, leg and jaw pain
Selexipag	oral: up to 800 mg bd		Not yet available
ERA			
Bosentan	oral: 125 mg bd		Abnormal LFT 5%
Ambrisentan	oral: 5–10 mg od		
Macitentan	oral: 10 mg od		
NO pathway			
Nitric oxide		neb: 5–80 ppm	Rebound PH, methaemaglobinaemia
Sildenafil	oral: 20–100 mg tds	i.v.: 10 mg tds	c/i with nitrates
Tadalafil	oral: 10–40 mg od		c/i with nitrates
Riociguat	oral: up to 2.5 mg tds		c/i with nitrates
Inotropes			
Dobutamine		i.v.: 2.5–10 μg/kg/min (250 mg in 50 ml NS)	Tachycardia, hypotension
Dopamine		i.v.: 0.5–10 μg/kg/min (200 mg in 50 ml NS)	Tachyarrythmias
Inodilators			
Milrinone		i.v.: 50 μg/kg over 10 min, then 0.375–0.75 μg/kg/min (10 ml in 50 ml NS) neb: 0.2–0.3 ml/min	Hypotension
Enoximone		i.v.: 0.5–1 mg/kg slow injection then 5–20 μg/kg/min	Hypotension
Levosimendan		i.v.: loading 6–12 μg/kg/min over 10 min, then 0.1 μg/kg/min	Not widely available
Pressors			
Norepinephrine		i.v.: 0.01–0.4 μg/kg/min (4 mg in 50 ml D5W)	Bradycardia
Phenylephrinine		i.v.: 40–100 μg bolus, 50–300 μg/min infusion (30 mg in 500 ml NS)	Peripheral May ↑PVR Bradycardia
Metaraminol		i.v.: 1–5 mg/h (20 mg in 40 ml NS)	Peripheral No data in PH
Vasopressin		i.v.: 0.01–0.04 U/min (200 U in 250 ml D5W)	Bradycardia Higher doses may be cardiodepressive

Chronic treatment of PAH and CTEPH

Currently available PAH therapies, which in the UK are only reimbursed via a specialized PH centre, target three pathways (Table 1).

Prostacyclin is produced endogenously in the pulmonary arterial endothelial cells and has vasorelaxant and antiproliferative properties. Prostacyclin (epoprostenol, Flolan™) is infused continuously from a small portable pump via an indwelling line and was shown to improve haemodynamics and mortality in a landmark randomized controlled trial (RCT). Epoprostenol has a short half-life ($t_{1/2} < 10$ min) and is unstable at room temperature, necessitating the use of cold packs or twice daily change of medication. Iloprost is a more stable prostacyclin analogue ($t_{1/2} \approx 30$ min), which can be administered continuously via an indwelling line or nebulized ~6 times a day (Ventavis™). I.V. therapy is generally considered the 'gold standard' therapy although it is associated with a risk of line infection and is not appropriate for a proportion of patients owing to the technical and invasive nature of its administration.

Endothelin-1 is a potent vasoconstrictor and antiproliferative molecule. Blocking its receptor with an oral endothelin receptor antagonist (ERA) has been demonstrated to be effective in a number of RCTs. Three ERAs are currently available: bosentan (Tracleer™), ambrisentan (Volibris™), and macitentan (Opsumit™). Both ambrisentan and macitentan have been demonstrated to lengthen time to clinical worsening when used in combination with phosphodiesterase-5 (PDE5) inhibitors.

Nitric oxide is a potent vasorelaxant agent derived in endothelial cells. It acts via cyclic GMP (cGMP), which is broken down by phosphodiesterase-5 (PDE5). Two inhibitors (PDE5-I) are licensed for use in PAH, sildenafil (Revatio™) and tadalafil (Cialis™). The most important drug–drug interaction is with nitrates, which are contraindicated owing to a high risk of significant systemic hypotension. Riocuguat (Adempas™) is an alternative oral agent, which targets the nitric oxide pathway by stimulating soluble guanylate cyclase, which has been shown to improve haemodynamics and exercise capacity in PAH and in residual or inoperable CTEPH.

Current guidelines suggest oral therapies, either in upfront combination or as monotherapy with possible subsequent sequential combination therapy, in patients with mild to moderate symptoms [World Health Organization (WHO) functional classes II and III].[7] Subsequent addition of a prostanoid ('triple therapy') may subsequently be necessary, especially in patients being considered for lung transplantation. Patients presenting with severe symptoms (WHO functional class IV) should be considered for first-line i.v. prostanoid therapy.

Several observational studies have suggested a mortality benefit from anticoagulation in idiopathic disease and so most patients with IPAH are anticoagulated. If a patient has particular bleeding risks then anticoagulation should not be used and it can be reversed/withheld if indicated. Anticoagulation is generally not indicated in other forms of PAH unless there is another clear indication. Clearly, long-term anticoagulation is indicated in patients with CTEPH.

The majority of patients with CTEPH are candidates for potentially curative surgery in the form of pulmonary endarterectomy (PEA).[8] In the UK, one centre (Papworth) has been commissioned to provide a national PEA service. Perioperative mortality is now <5%, and 80% of patients surviving surgery have minimal breathlessness 1 yr following surgery. Operability is assessed on a patient-by-patient basis by assessing both the extent and location of chronic thromboembolic disease and the severity of pulmonary haemodynamic abnormality. In some patients, the severity of PH is disproportionate to the extent of surgically accessible disease; these patients are termed inoperable or as having distal disease. Some patients may have an operable distribution of disease but may have comorbidities (especially severe lung disease) that preclude PEA surgery. Patients with inoperable disease may develop a pulmonary vasculopathy in unobstructed pulmonary arteries/arterioles, which is indistinguishable from that seen in PAH, and so PAH-specific therapies are used in distal CTEPH.

Patients who deteriorate despite optimal chronic PAH therapy should be considered for transplantation (usually double-lung) and referred in a timely manner. Currently in the UK, there is no routine super-urgent transplantation service and so this option will not be open to the majority of patients who deteriorate despite critical care management.

Critical care management in the acutely unwell PAH or CTEPH patient

Management of the acutely unwell patient can be summarized in a step-wise approach (Fig. 2).[9,10] Early discussion with the local PH centre regarding patients with suspected treatable PH is advised (www.pulmonaryhypertensioncentres.co.uk).

Treatment of underlying cause for deterioration

Significant clinical deterioration in a previously relatively stable patient may occur as a result of cardiac arrhythmia or sepsis. Other underlying causes of clinical deterioration that should also be considered include anaemia, thromboembolic disease, pericardial effusion, metabolic abnormalities, and exacerbations of any coexisting chronic conditions. Patients with precapillary PH are especially prone to developing atrial flutter, which may occur at some point in up to 25% of patients.[11] Patients with a dilated right atrium who develop atrial flutter with 2:1 block tend to have a slower ventricular rate than the 'usual' rate of 150 beats per minute. The development of atrial flutter is associated with a poorer survival, and current evidence suggests that restoring sinus rhythm improves outcomes more than mere rate control. Methods of restoring sinus rhythm include chemical cardioversion (e.g. amiodarone), DCCV (direct cardiac cardioversion), or ablation therapy. Sepsis is a common cause of acute deterioration, and an elevated C-reactive protein (CRP) should lead to a careful search for a focus of infection. Broad-spectrum antibiotics may be indicated, even in the absence of a clear source, when infection is suspected. As discussed earlier, patients receiving continuous i.v. prostanoid are at risk of developing a catheter-related bloodstream infection (CRBSI).[12] Patients with a CRBSI will often have no external signs of line infection and may present with non-specific worsening of breathlessness. An elevated, unexplained, CRP in such patients should lead to exclusion of a line infection with peripheral and central blood cultures and antibiotic therapy to cover gram-positive and gram-negative organisms while cultures are pending.

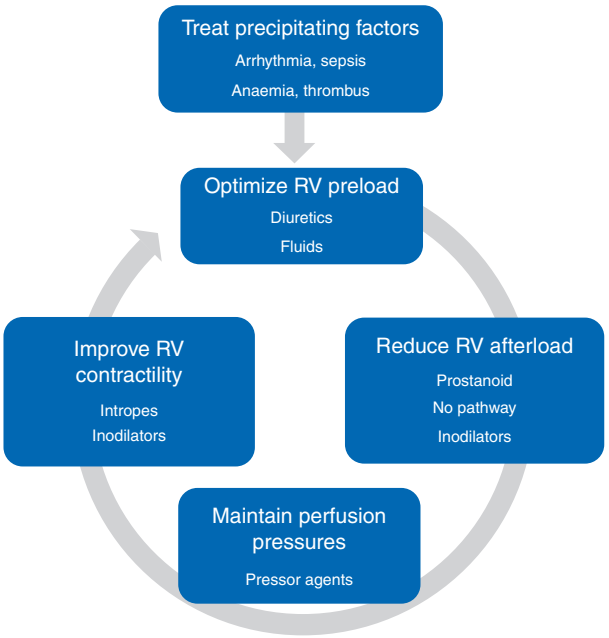

Fig 2. Approach to management of the sick PH patient.

Optimize RV preload

Acute clinical deterioration may be related to relative hypovolaemia, especially if there have been fluid losses (e.g. vomiting), fluid intake has been poor, or in sepsis. More commonly, deterioration in RV function is associated with the development of peripheral oedema. Excess volume loading of the right ventricle can reduce RV contractility, and posterior bowing of the interventricular septum can lead to underfilling of the left ventricle and further reduction in cardiac output. Renal congestion attributable to RV failure is also associated with the development of worsened renal function. Patients with peripheral oedema attributable to RV failure therefore benefit from diuresis with a combination of loop diuretics, aldosterone antagonists, and sometimes thiazide diuretics. Often a continuous infusion of loop diuretic is used, although evidence to demonstrate superiority over a bolus approach is lacking. Continuous veno-venous haemofiltration (CVVH) may be considered in selected instances of resistant heart failure.

Reduce RV afterload

Patients presenting to critical care with *de novo* PAH will generally require urgent commencement of i.v. prostanoid. Doses

should be gradually increased as tolerated; commencing too high a dose or increasing the dose too rapidly can be associated with systemic hypotension and side-effects, including flushing, headache, jaw pain, nausea, diarrhoea, and leg pain. If i.v. prostanoid therapy is tolerated then a PDE5-I (most commonly sildenafil given its shorter half-life) may be added. I.V. sildenafil is available for patients where the enteral route is not possible. Inhaled pulmonary vasodilators may also have a role. Inhaled nitric oxide (NO) can be an effective way of reducing RV afterload, but its use may be limited by lack of availability, the development of methaemaglobinaemia, and rebound pulmonary hypertension on cessation. Nebulized prostanoid therapy may also be considered, especially in the presence of coexisting lung disease, as this approach is not associated with the same worsening of ventilation–perfusion mismatch. Accurate dosing and administration in the acutely unwell patient may, however, be challenging. Decompression of the RV using balloon atrioseptostomy is a potential therapy for patients with severe PAH, although it is rarely performed in the UK. Very high right atrial pressure and significant hypoxaemia are significant risk factors for mortality related to this procedure and so many patients in the critical care setting may be poor candidates.

Improve cardiac function and maintain perfusion pressures

Inotropic therapy to improve RV contractility and hence stroke volume may be indicated if steps 1–3 do not result in satisfactory clinical improvement (Table 1). Dobutamine is the most common β_1 agonist used, although medium dose dopamine may also be used. Dobutamine dosing is often limited by tachycardia and systemic hypotension. The phosphodiesterase-3 inhibitors, milrinone and enxoimone, have positive inotropic effects combined with the capacity to reduce RV afterload ('inodilators') without significant chronotropic effect, but they can be associated with significant systemic hypotension. Levosimendan is a calcium-sensitizing agent, which also has inodilating properties but may result in less systemic hypotension.

Vasopressor agents are often required in combination with inotropes to augment systemic vascular resistance and hence maintain systemic blood pressure (Table 1). Norepinephrine is a potent α_1 agonist and so there is a concern of increasing pulmonary (in addition to systemic) vascular resistance. However, norepinephrine also has inotropic properties owing to β_1 effects and appears to improve coupling between RV function and afterload. Vasopressin may have pulmonary vasodilatory effects in addition to a systemic vasoconstrictive effect. In our clinical practice, we would consider adding vasopressin in patients resistant to norepinephrine. Both norepinephrine and vasopressin require central administration and so peripherally administered vasopressors may be required initially. Phenylephrine has been shown to improve right coronary artery perfusion in RV failure (owing to improved aortic root perfusion) but may worsen coupling between RV function and afterload by increasing PVR. Metaraminol is an alternative peripherally administered α_1-agonist, although there are no data in patients with PH.

Extracorporeal support and surgical treatment

If steps 1–4 do not result in clinical improvement then extracorporeal support and transplantation may be considered. Venoarterial extracorporeal membrane oxygenation (v/a ECMO) results in a significant reduction in RV afterload with dramatic clinical responses reported. v/a ECMO can be performed using right atrial cannulation via the femoral vein, with oxygenated blood being returned to the aorta via a femoral arterial cannula. Patients undergoing v/a ECMO cannot fully ambulate and require close monitoring of anticoagulation to prevent both catastrophic clotting of the device and bleeding.[10] An alternative mechanical approach to reducing RV afterload is a pumpless membrane oxygenator (Novalung™) inserted between the pulmonary artery (PA) and left atrium (LA). This approach can allow patient mobility but requires surgical insertion. Both v/a ECMO and PA:LA Novalung can result in significant clinical improvement, but unless super-urgent lung transplantation is available, or unless there is a clear, very reversible precipitating factor, then their utility in clinical practice may be limited. Patients may present with CTEPH *in extremis*, and direct transfer for urgent PEA surgery may be indicated.

Monitoring

Most patients needing critical care management will require arterial line insertion and often central venous access. Several methods of more advanced cardiovascular monitoring may be considered. Pulmonary artery catheter insertion provides accurate measurements of pulmonary pressures, cardiac output, and LA filling pressures but has been shown not to improve outcomes in other groups of patients and is associated with a risk of pulmonary arterial rupture. Outside of cardiothoracic surgery, pulmonary artery catheterization is therefore rarely indicated in the critically ill PH patient. Regular measurement of central venous oxygen saturations, drawn from a standard central line, may reflect changes in cardiac output. Several non-invasive means of estimating cardiac output are available, and in our centre we use a lithium dilution method (LiDCO™), which provides estimates of cardiac output, stroke volume, and systemic vascular resistance (SVR).

Limits to critical care management

The appropriateness and extent of critical care management depends on the clinical context. A patient with progressive 'end stage' disease in whom super-urgent transplantation is not an option may well be best served by ward-based care. A newly diagnosed, treatment-naive patient is likely to be a candidate for more aggressive management. In addition to cardiovascular support as described above, renal support in the form of CVVH and respiratory support in the form of continuous positive airways pressure (CPAP), non-invasive ventilation (NIV), and invasive ventilation may be required. Data from our unit suggest that around 50% of patients receiving CVVH leave hospital alive and so this should be considered, especially in treatment-naive patients and where there is a clear reversible precipitating factor to acute kidney injury.[13] Invasive ventilation is infrequently appropriate in the critically sick PAH patient, although we have successfully ventilated patients where clinical deterioration has been caused by severe pneumonia.

Outcomes in critical care

A study of 43 patients admitted to critical care with severe heart failure secondary to PAH who required catecholamines observed in-hospital mortality of 43%. Low systemic blood pressure at admission, lower sodium, and higher creatinine, N-terminal pro-brain natriuretic peptide, and CRP were associated with worse outcome.[14] Haddad and colleagues[15] studied 119 patients admitted to hospital with right heart failure secondary to PAH. Ninety day mortality of 29% was observed, with

respiratory rate, renal function, hyponatraemia, and severity of tricuspid regurgitation predicting poor outcome.

Surgery and pregnancy in patients with pulmonary hypertension

Several groups have reported outcomes of non-obstetric, non-cardiac surgery in patients with PH. Ramakrishna and colleagues[16] reported a 7% 30-day mortality in 145 patients. Surgery that was major, prolonged, and an emergency was associated with increased morbidity, as was a requirement for dopamine or epinephrine. Price and colleagues reported 7% mortality in 28 patients with mild to moderate pulmonary hypertension. There was a trend towards regional anaesthesia being associated with better outcomes than general anaesthesia. Again, poorer outcome was associated with surgery that was emergency, prolonged, and major in nature. Baseline pulmonary arterial saturations, but not other haemodynamic measurements, were also predictive of complications.[17] Finally, Meyer and colleagues[18] observed a 3.5% mortality in 114 patients with mild PAH. In this cohort, emergency surgery, baseline 6 min walk distance, and mean right atrial pressure predicted major complications.

Pregnancy is associated with significant cardiovascular demands, with the need for a significant increase in cardiac output. As such, it is poorly tolerated in patients with PH, with historical series reporting maternal mortality of 30–56%. More recent series have reported improved outcomes but with maternal mortality still between 10 and 20%. In Sheffield, we have adopted an approach of early elective delivery at 34–36 weeks via Caesarean section using a combined spinal–epidural approach (to minimize the effect on the SVR).[19] Care must be taken with the use of oxytocin for the management of the third stage as it may increase PVR and reduce SVR and so we use a low-dose infusion rather than a bolus. Similarly, nitrous oxide should also be avoided owing to adverse effects on PVR. The immediate postpartum period appears to be a particularly dangerous time and so patients require close monitoring in a critical care unit for at least 72 h. We monitor the patients with LiDCO™, arterial, and central lines. If the central venous pressure (CVP) increases then diuretics are administered.

Critical care management of patients with RV dysfunction secondary to severe acute cardiopulmonary disease or postcardiothoracic surgery

Severe acute cardiorespiratory disease, most notably adult respiratory distress syndrome (ARDS), can be associated with acute RV dysfunction. Short-term improvements in haemodynamics and oxygenation have been described with inhaled NO, inhaled epoprostenol, and iloprost. Although i.v. epoprostenol and oral sildenafil have been shown to improve RV function in the setting of ARDS, this occurs at the expense of poorer oxygenation. No studies have, to date, demonstrated a mortality benefit from pulmonary vasodilators in patients with ARDS and so their routine use cannot currently be recommended. Pulmonary vasodilators have also been assessed in patients undergoing cardiac surgery and may have a role in selected patients who are difficult to wean from cardiopulmonary bypass or ventilation. Hypoxia, acute hypercapnia, and atelectasis can all result in increased PVR. High lung volumes can result in both reduced RV return and increased RV afterload. A reduction in airways plateau pressure used in protective ventilation for ARDS has been associated with a reduction in acute RV dysfunction from 60 to 25%.[20]

Conclusion

Critically unwell patients with PAH and CTEPH have a high mortality, and critical care involvement will often be appropriate. Initial management involves treating underlying precipitants of deterioration and optimizing RV preload. Reduction of RV afterload with pulmonary vasodilators is also required. Augmentation of cardiac function and perfusion pressures with inotropes and vasopressors may additionally be needed. Advanced renal and respiratory support may be appropriate depending on the clinical context. Patients with known PAH or CTEPH who have undergone major surgery or who are in the immediate postpartum period are also at significant risk of deterioration and require management in the critical care setting. Although pulmonary vasodilators are associated with improvements in pulmonary haemodynamics and oxygenation in patients with acute respiratory distress syndrome or after cardiac surgery, there is currently no evidence demonstrating improved outcomes.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to *BJA Education*.

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