Netherlands Journal of Critical Care
Submitted April 2017; Accepted August 2017

REVIEW

Right ventricular failure in the intensive care unit: mechanisms and medical therapy

M.J. Schuuring[1,2], W.K. Lagrand[3]

[1]Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands
[2]Department of Cardiology, Haga Teaching Hospital, the Hague, the Netherlands
[3]Department of Intensive Care, Academic Medical Center, Amsterdam, the Netherlands

Correspondence
M.J. Schuuring - m.j.schuuring@amc.uva.nl

Keywords - **right ventricular failure, intensive care unit, medical therapy**

Abstract

Right ventricular (RV) failure is frequently encountered in the intensive care unit. This clinical syndrome may be difficult to diagnose and treat. RV failure is commonly characterised by oedema, elevated jugular venous pressure, hypotension and in worse cases shock or multi-organ failure. High-risk patients include those with cardiac surgery, ARDS, ischaemia (inferior infarction, RV involvement), recent myocardial infarction, pulmonary hypertension and patients with congenital heart disease. Besides supportive treatment, medical therapies are available that are targeted to RV failure including inotropic and vasodilatory agents. Mechanical and surgical therapy of RV failure is beyond the scope of this article. Larger prospective studies are needed to determine optimal diagnostic and medical therapy for patients with RV failure in the intensive care unit.

Introduction

The clinical syndrome of right ventricular (RV) failure was first described by Cohn et al. and was associated with a native transmural posteroinferior myocardial infarction.[1] More than 40 years later there is no single accepted definition of RV failure. The Heart Failure Association and the working group on pulmonary circulation and right ventricular function of the European Society of Cardiology defined right ventricular (RV) failure as a rapidly progressive syndrome with systemic congestion resulting from impaired RV filling and/or reduced RV output.[2] However, others define RV failure as a clinical entity characterised by oedema, elevated jugular venous pressure, hypotension and, in worse cases, shock or multi-organ failure.[3,4] The right ventricle of the heart differs structurally and functionally from the left ventricle. Insufficient RV contractility is induced by three interrelated factors.[5] Firstly, overstretching of the RV free wall places myocytes at a mechanical disadvantage. Secondly, derangements in cellular metabolism lead to decreased myocardial contractile forces. Thirdly, in case of coronary ischaemia, insufficient oxygen delivery leads to decreased coronary arterial perfusion, and subsequent decreased myocardial contractility. There are multiple causes of RV failure *(table 1)*; the most common causes are discussed here.

Table 1. Causes of right ventricular failure in the intensive care unit

Cardiac surgery
Acute respiratory distress syndrome (ARDS)
Ischemia or air emboli
Inflammation or myocarditis
Pulmonary embolism
Lung disease
Pulmonary hypertension
Tamponade
Congenital heart disease
Cardiac valvulopathy
Cardiomyopathy

The main cause of RV failure in the intensive care unit (ICU) is cardiac surgery.[6] Furthermore, acute respiratory distress syndrome (ARDS) has a reported incidence of RV failure ranging from 25% to 50%, depending on severity and mechanical ventilation settings.[2,7–9] ARDS patients are frequently under positive pressure ventilation. This can result in increased RV afterload, and thereby RV failure, despite decreased left ventricular (LV) afterload. It has been postulated that the right ventricle is less sensitive to ischaemia than the left ventricle because of the smaller muscle mass, lower workload, more favourable ratio between oxygen delivery and consumption,

and better collateral circulation. However, RV infarction results from acute occlusion of the right coronary artery proximal to the RV branches. With a left dominant system, proximal occlusion of the circumflex may also result in RV involvement. Other causes of RV failure are air embolism, pulmonary embolism, lung disease, pulmonary hypertension, tamponade, cardiac valvulopathy (tricuspid valve insufficiency, pulmonary valve stenosis), cardiomyopathy, drug toxicity, or congenital heart disease. Particularly Ebstein malformation and atrial or ventricular septal defects are seen as congenital heart diseases causing RV failure. Patients with congenital heart disease often undergo right-sided surgery and, especially in patients with congenital heart disease, the contribution of the right ventricle to cardiac pump function is essential.[10] RV failure has also been associated with inflammation or myocarditis. It is possible that the thin-walled right ventricle may be more susceptible to dysfunction secondary to inflammation or pericardial effusions, particularly after cardiac surgery.[10] These effusions may result from local tissue damage or from a systemic inflammatory response. Cytokines may play a role in affecting RV performance. In a state of cardiopulmonary bypass the body releases cytokines which initiate inflammation and pulmonary vasoconstriction.[11] One of these cytokines is endothelin-1. Endothelin-1 has a vasoconstrictive effect on the pulmonary arterioles and might consequently influence RV afterload.[12] This might indicate a central role for cardiopulmonary bypass in the development of RV failure.

RV failure may be difficult to diagnose. There can be various clinical signs at physical examination, such as peripheral oedema, ascites, central venous pressure increase, hypoxaemia, a third heart sound on auscultation, murmur of valvular insufficiency, hypotension, tachycardia, cold extremities or oliguria.[2] The ECG can be initially normal at RV ischaemia, but can also demonstrate an inferior wall myocardial infarction. In suspected RV involvement in myocardial infarction (inferior wall infarcts), it is important to also perform a right-sided ECG recording. ST elevation in V4R of more than 1 mm is suggestive of transmural ischaemia of the right ventricle.[13] Furthermore, at RV infarction, (AV-nodal) conduction problems are more in the foreground than ventricular arrhythmias due to ischaemia of the AV node. Echocardiography is a cornerstone in estimating RV function, as it is for the diagnosis of RV failure. Echocardiographic evidence of RV failure is: dilatation of the right ventricle with impaired contractility, reduced tricuspid annular plane systolic excursion, reduced tissue Doppler derived systolic velocity of the tricuspid annulus (RV S'), increased end-diastolic volume, decreased filling of the left ventricle and abnormal movements of the interventricular septum.[2] As a result of the dilation of the right ventricle a pronounced tricuspid insufficiency may occur. Transoesophageal echocardiography might be indicated if transthoracic echocardiography is not conclusive. Right heart catheterisation and continuous cardiac output monitoring using a Swan-Ganz catheter can be useful in establishing a diagnosis and guiding clinicians in therapeutic management.[14] Instant monitoring of right ventricular ejection fraction and end-diastolic volume index reflects RV function.

The aim of this narrative review is to describe mechanisms of RV failure and to summarise supportive and medical therapies available for RV failure in the ICU. Mechanical and surgical therapy of RV failure is beyond the scope of this article.

Treatment goals

There are seven important goals in the management of RV failure *(figure 1)*. The most important step is to identify and treat reversible causes of RV failure, such as right coronary artery occlusion, pulmonary embolism, toxic drugs, sepsis, and hypoxia, congenital heart disease, valvular disease.[15] Secondly, if none of these reversible causes are identified and pulmonary arterial hypertension (PAH) is suspected, expert advice is needed to identify whether vasoreactivity testing or specific therapy for PAH is indicated. Specific subgroups of patients with pulmonary hypertension, namely those with PAH or chronic thromboembolic pulmonary hypertension (CTEPH), may benefit from specific pulmonary vasodilators or surgical thrombectomy (pulmonary thromboendarterectomy). However, these agents are potentially dangerous to specific patients so transfer of these patients to a specialised centre should be considered. Thirdly, it is important to ensure adequate preload and coronary perfusion. Fourthly, it is important to optimise myocardial oxygen supply and

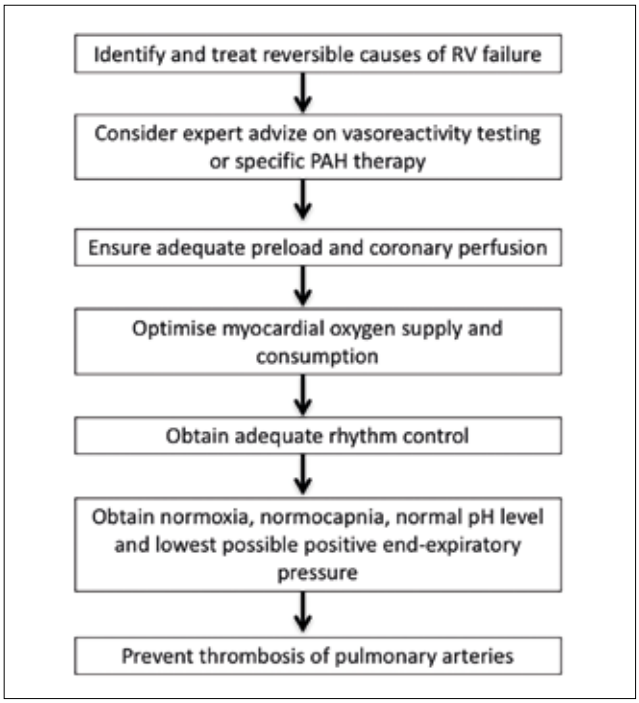

Figure 1. Treatment goals in management of right ventricular failure in the intensive care unit

consumption. As fifth goal, adequate rhythm control should be obtained. Maintenance of sinus rhythm in patients with RV failure and atrial tachyarrhythmias is recommended.16 Synchronised atrial and ventricular contraction seems critical for patients with RV failure to sustain sufficient cardiac output. Atrioventricular synchronous pacing is helpful during cardiogenic shock because of RV infarction from right coronary artery ischaemia, leading to atrioventricular node dysfunction and consequently loss of atrioventricular synchrony. The sixth goal is to obtain normoxia, normocapnia, a normal pH level and the lowest possible positive end-expiratory pressure (PEEP).[17] Lastly, thrombosis of pulmonary arteries should be prevented. Anticoagulation should be considered on an individual basis and haemoptysis may represent a contraindication to anticoagulant therapy. Anticoagulation is recommended lifelong in CTEPH patients and may be considered in patients with idiopathic PAH, heritable PAH and PAH due to use of anorexigens.[18]

Repeated echocardiographic examination is required to evaluate the response to therapy. Haemodynamic monitoring using a Pulse Contour Cardiac Output (PiCCO) monitor (especially in combination with echocardiography) is often sufficient to optimise treatment. Pulmonary artery catheterisation, as an alternative haemodynamic monitoring device, can provide additional diagnostic information (high central venous pressure, low wedge pressure, reduced cardiac output, and possibly elevated pulmonary pressures), and may be helpful in order to guide therapy. Remember that the cardiac output measurement can be unreliable in the case of tricuspid valve insufficiency. When it is decided to use a pulmonary artery catheter, the benefits must be carefully weighed against the risks, especially in case of ischaemia.

Supportive therapy

Volume optimisation

Proper fluid management is critical for successful management of RV failure, see *figure 2*.[19,20] Adequate RV filling pressure is essential in maintaining the cardiac output in patients with acute RV failure.5 Optimal right-sided filling pressure may vary considerably between individual patients based on RV contractility and afterload. Commonly, preload is aimed to keep RV transmural filling pressures adequate.[5] A tempered approach to volume resuscitation of the failing right ventricle is recommended, and excessive volume loading (more than 2 litres of fluid) should be avoided, especially in patients with mean arterial pressure less than 60 mmHg.[16,21] A PiCCO monitor or Swan-Ganz catheter may be helpful to optimise filling pressures or to evaluate changes in cardiac output.

Protective pulmonary ventilation

PEEP provides increased afterload and reduced preload of the right ventricle, whereas it provides decreased preload and afterload for the left ventricle. The optimal PEEP level is obtained with adequate oxygenation to prevent atelectasis with

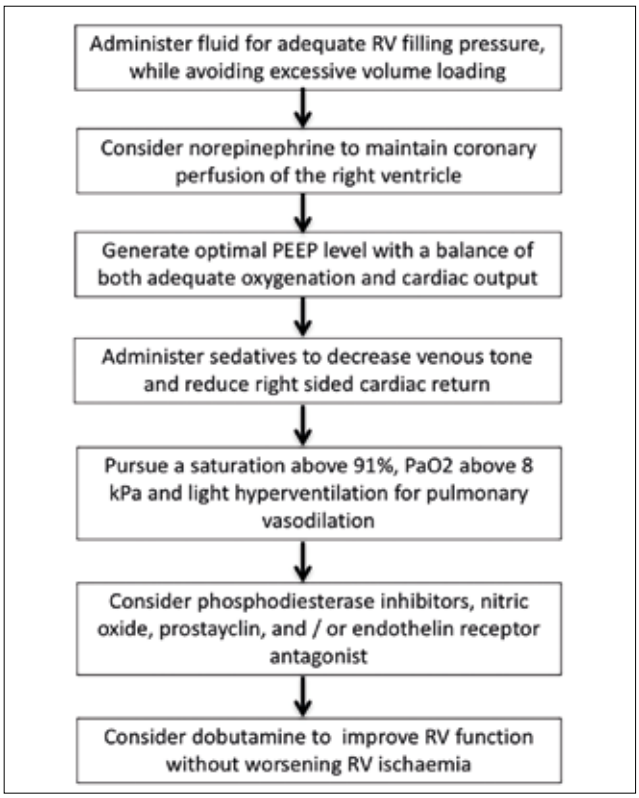

Figure 2. Treatment algorithm in management of right ventricular failure in the intensive care unit

derecruitment, without compromising cardiac output. Guide values are: 5-10 cm H2O PEEP, SpO2> 91%, PaO2> 8 kPa and cardiac index >2.5 l / min / m^2. Protective ventilation strategies (target tidal volume <6 ml/kg) with focus on maintaining plateau pressure <27 cmH2O, PaCO2 <8 kPa (60 mmHg), adapting PEEP to RV function, and considering prone positioning for PaO2/fraction of inspired oxygen (FiO2) <20 kPa (150 mmHg) have been recommended to prevent acute RV failure or counter its complications.[8] In case of treatment failure in combination with high respiratory mechanical driving forces, extracorporeal lung assist treatment can be considered.

Sedation

Sedatives affect sympathetic vasoconstriction of the systemic venous circulation, leading to decreased venous tone and reduced right-sided (cardiac) return. Appropriate sedation (and, if necessary, muscle relaxation) may be used to prevent forceful exhalations.

Oxygen therapy

The most potent pulmonary vasodilator is oxygen. Treating physicians should act according to the resuscitation protocol (SpO2> 91%, PaO2> 8 kPa). Mild hyperventilation (alkalosis, pH 7.45-7.55) supports the vasodilator effect. In patients with RV failure and / or pulmonary hypertension, it can be argued to first reduce the PEEP and then the FiO2.

Drug therapy to reduce RV afterload

Phosphodiesterase inhibitors

Sildenafil is a phosphodiesterase (V) inhibitor, registered for the treatment of pulmonary hypertension. However, little is known about use of sildenafil in critically ill patients. Sildenafil appears to have favourable effects on RV function in the setting of ventilated patients with RV failure due to pulmonary disease.[22] In 12 patients sildenafil improved central haemodynamics and RV function indices in ventilated patients with WHO group-III pulmonary hypertension and RV failure requiring dobutamine infusion, when they respond favourably to the latter. Accordingly, an adequate RV systolic reserve may be compulsory for sildenafil to exert its actions. However, sildenafil must be used cautiously in patients who are haemodynamically unstable, because they have systemic vasodilator effects that can lower blood pressure, and their terminal half-life ranges from 4 to 18 hours. In ten patients with ARDS a single dose of sildenafil reduced pulmonary arterial pressures, but the increased shunt fraction and decreased arterial oxygenation render it unsuitable for the treatment of patients with ARDS.[23] Milrinone is discussed in under the section on vasoactive drugs in RV failure. Importantly, the main effect of milrinone is a vasodilator effect, thereby decreasing the pulmonary vascular resistance.

Nitric oxide

Inhaled nitric oxide causes pulmonary vasodilation with a quick onset of action and an extremely short half-life time, making it an attractive agent for attempting to unload the right ventricle in the ICU.[5,24] Nitric oxide may also improve outcomes in RV failure by decreasing inflammatory cytokine production in the lung.[25] Small studies have demonstrated haemodynamic improvements with inhaled nitric oxide in patients with RV myocardial infarction,[26] after cardiac transplant[27] or in massive pulmonary embolism.[24] In patients with lung injury, however, a randomised controlled trial of 385 patients on inhaled nitric oxide only resulted in short-term oxygenation improvements but had no substantial impact on the duration of ventilatory support or mortality.[28] Furthermore, nitroglycerin is available. Nitroglycerin works as a vasodilator, particularly on venous vasculature and to a lesser extent on the arterial vascular bed. However, arterial (including pulmonary arterial) blood pressure may decrease during nitroglycerin administration. As a result, afterload for both the right and left ventricle may decrease. Under nitroglycerin administration, the oxygen saturation may drop as a result of pulmonary shunting.

Prostacyclin

Epoprostenol is a prostacyclin analogue with a short half-life time (~5 min). In patients with RV failure after cardiac transplant or cardiopulmonary bypass, treatment with inhaled epoprostenol may improve haemodynamics.[29] Use of iloprost, an inhaled prostacyclin, may be limited by the development of hypotension, bradycardia, headache, or flushing.

Endothelin receptor antagonist

Endothelin receptor antagonists have been shown to correlate inversely with cardiac output.[30] Antagonising endothelin has been proven effective in patients with PAH. However, endothelin receptor antagonists have been associated with increased mortality in left heart failure.

Calcium channel blockers

Calcium channel blockers should also be used with caution in the ICU, because they have negative inotropic effects. Moreover, calcium channel blockers have been shown to increase the RV stroke work index.[31]

Vasoactive drugs in RV failure

Catecholamines

Norepinephrine is an alpha-agonist with also some beta-agonist activity, resulting mainly in vasoconstriction (alpha receptor stimulation) with some positive inotropic effect (beta stimulation). Norepinephrine is the only drug that helps to maintain coronary perfusion of the right ventricle.[2,32] Norepinephrine can, however, increase afterload of the right ventricle because of an increase in pulmonary artery pressure; titrate on clinical presence and mean arterial pressure. In a small study of patients with sepsis with right heart failure, norepinephrine use was associated with improved RV myocardial oxygen delivery (via an increase in systemic vascular resistance), although pulmonary vascular resistance was increased. No change was observed with respect to the RV ejection fraction.[33] Epinephrine is an alpha- and beta-agonist which has vasoconstrictor and positive inotropic, chronotropic and dromotropic properties. Epinephrine may be considered when alternative pharmacological inotropic support (e.g. norepinephrine) is insufficient. Dosage should be titrated on clinical presentation and mean arterial pressure.

Phenylephrine is an alpha-$_1$ receptor agonist that increases perfusion of the right coronary artery, but does not impact RV contractility, and can increase pulmonary vascular resistance. It can also cause reflex bradycardia, which can be problematic in case of reduced RV stroke volume.[5] In patients with severe septic shock, RV function improves with epinephrine, by means of an improvement in RV contractility.[34]

Vasopressin

Selectively, vasopressin achieves pulmonary vasodilation because of a release of nitric oxide. Postoperatively, if patients are refractory to catecholamine, vasopressin may be considered. In patients with hypotension, the combination of vasopressin and a catecholamine might be used.

Inotropes

Dobutamine

Dobutamine is a beta-$_1$ agonist with positive inotropic activity and is a mild beta-$_2$ and alpha-1 stimulant. There is a dose-

guided effect, and higher doses should be avoided because of the risk of vasodilatation and hypotension. Traditionally, dobutamine was considered the agent of choice because of its primary effect on beta receptors with minimal propensity for vasoconstriction, and potential to improve RV function without worsening RV ischaemia.[35] Dobutamine has been shown to improve the haemodynamics in patients with pulmonary hypertension after RV infarction.[36] In patients with RV failure, the addition of dobutamine can improve haemodynamics when compared with pure vasodilation with nitroprusside,[37] or an inopressor such as norepinephrine.[38]

Phosphodiesterase inhibitors

Milrinone is a commonly used phosphodiesterase (III) inhibitor which has slightly positive inotropic and positive lusitropic effects. The main effect of milrinone is vasodilation, thereby decreasing the pulmonary vascular resistance. The systemic vascular resistance may decrease during milrinone administration (resulting in hypotension) and the half-life time is long. It is important to realise that a loading dose of milrinone may result in a significant drop in blood pressure.[5] Following cardiac surgery and cardiopulmonary bypass, milrinone decreases pulmonary pressures and improves cardiac output in patients with reduced RV function.[39]

Calcium sensitiser

Levosimendan is a calcium sensitiser with positive inotropic and lusitropic properties. Levosimendan also inhibits phosphodiesterase and has a vasodilator effect. A randomised placebo-controlled trial with levosimendan showed improvement in RV function in patients with left heart failure.[40] Moreover, improved RV function in response to levosimendan has been observed in patients with RV failure associated with chronic thromboembolic pulmonary hypertension and heart transplantation.[41]

Conclusion

RV failure is frequently encountered in the ICU and is associated with high mortality. The main cause of RV failure in the intensive care unit is cardiac surgery. RV failure may be difficult to diagnose and treat. Larger prospective studies are needed to determine optimal diagnostic and medical therapy for patients with RV failure in the intensive care unit.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

References

1. Cohn JN, Guiha NH, Broder MI, Limas CJ. Right ventricular infarction. Clinical and hemodynamic features. Am J Cardiol. 1974;33:209-14.
2. Harjola V-P, Mebazaa A, Čelutkienė J, et al. Contemporary management of acute right ventricular failure: a statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology. Eur J Heart Fail. 2016;18:226-41.
3. Schuuring M, van Gulik C, Koolbergen D, et al. Determinants of clinical right ventricular failure after congenital cardiac surgery in adults. J Cardiothorac Vasc Anesth. 2013;27:723-7.
4. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: II. Pathophysiology, clinical importance, and management. Anesth Analg. 2009;108:422-33.
5. Ventetuolo CE, Klinger JR. Management of acute right ventricular failure in the intensive care unit. Ann Am Thorac Soc. 2014;11:811-22.
6. Bootsma IT, de Lange F, Koopmans M, et al. Right Ventricular Function After Cardiac Surgery Is a Strong Independent Predictor for Long-Term Mortality. J Cardiothorac Vasc Anesth. 2017;
7. Jardin F, Vieillard-Baron A. Is there a safe plateau pressure in ARDS? The right heart only knows. Intensive Care Med. 2007;33:444-7.
8. Vieillard-Baron A, Price LC, Matthay MA. Acute cor pulmonale in ARDS. Intensive Care Med. 2013;39:1836-8.
9. Vieillard-Baron A, Schmitt JM, Augarde R, et al. Acute cor pulmonale in acute respiratory distress syndrome submitted to protective ventilation: incidence, clinical implications, and prognosis. Crit Care Med. 2001;29:1551–5.
10. Schuuring MJ, Bolmers PPM, Mulder BJM, et al. Right ventricular function declines after cardiac surgery in adult patients with congenital heart disease. Int J Cardiovasc Imaging. 2012;28:755-62.
11. Bond BR, Dorman BH, Clair MJ, et al. Endothelin-1 during and after cardiopulmonary bypass: association to graft sensitivity and postoperative recovery. J Thorac Cardiovasc Surg. 2001;122:358-64.
12. Schuuring MJ, Vis JC, Duffels MG, Bouma BJ, Mulder BJ. Adult patients with pulmonary arterial hypertension due to congenital heart disease: a review on advanced medical treatment with bosentan. Ther Clin Risk Manag. 2010;6:359-66.
13. Braat SH, Brugada P, den Dulk K, van Ommen V, Wellens HJ. Value of lead V4R for recognition of the infarct coronary artery in acute inferior myocardial infarction. Am J Cardiol. 1984;53:1538-41.
14. King C, May CW, Williams J, Shlobin OA. Management of right heart failure in the critically ill. Crit Care Clin. 2014;30:475-98.
15. Greyson CR. Right heart failure in the intensive care unit. Curr Opin Crit Care. 2012;18:424-31.
16. Green EM, Givertz MM. Management of acute right ventricular failure in the intensive care unit. Curr Heart Fail Rep. 2012;9:228-35.
17. Girgis K, Hamed H, Khater Y, Kacmarek RM. A decremental PEEP trial identifies the PEEP level that maintains oxygenation after lung recruitment. Respir Care. 2006;51:1132-9.
18. Galiè N, Humbert M, Vachiery J-L, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016;37:67-119.
19. Zamanian RT, Haddad F, Doyle RL, Weinacker AB. Management strategies for patients with pulmonary hypertension in the intensive care unit. Crit Care Med. 2007;35:2037-50.
20. Kholdani CA, Fares WH. Management of Right Heart Failure in the Intensive Care Unit. Clin Chest Med. 2015;36:511-20.
21. Piazza G, Goldhaber SZ. The acutely decompensated right ventricle: pathways for diagnosis and management. Chest. 2005;128:1836-52.
22. Karakitsos D, Papanikolaou J, Karabinis A, et al. Acute effect of sildenafil on central hemodynamics in mechanically ventilated patients with WHO group III pulmonary hypertension and right ventricular failure necessitating administration of dobutamine. Int J Cardiol. 2013;167:848-54.
23. Cornet AD, Hofstra JJ, Swart EL, Girbes ARJ, Juffermans NP. Sildenafil attenuates pulmonary arterial pressure but does not improve oxygenation during ARDS. Intensive Care Med. 2010;36:758-64.
24. Summerfield DT, Desai H, Levitov A, Grooms DA, Marik PE. Inhaled nitric oxide as salvage therapy in massive pulmonary embolism: a case series. Respir Care. 2012;57:444-8.

25. Meldrum DR, Shames BD, Meng X, et al. Nitric oxide downregulates lung macrophage inflammatory cytokine production. Ann Thorac Surg. 1998;66:313-7.
26. Inglessis I, Shin JT, Lepore JJ, et al. Hemodynamic effects of inhaled nitric oxide in right ventricular myocardial infarction and cardiogenic shock. J Am Coll Cardiol. 2004;44:793-8.
27. Ardehali A, Hughes K, Sadeghi A, et al. Inhaled nitric oxide for pulmonary hypertension after heart transplantation. Transplantation. 2001;72:638-41.
28. Taylor RW, Zimmerman JL, Dellinger RP, et al., Inhaled Nitric Oxide in ARDS Study Group. Low-dose inhaled nitric oxide in patients with acute lung injury: a randomised controlled trial. JAMA. 2004;291:1603-9.
29. Gordon C, Collard CD, Pan W. Intraoperative management of pulmonary hypertension and associated right heart failure. Curr Opin Anaesthesiol. 2010;23:49-56.
30. Stewart DJ, Levy RD, Cernacek P, Langleben D. Increased plasma endothelin-1 in pulmonary hypertension: marker or mediator of disease? Ann Intern Med. 1991;114:464-9.
31. Packer M, Medina N, Yushak M. Adverse hemodynamic and clinical effects of calcium channel blockade in pulmonary hypertension secondary to obliterative pulmonary vascular disease. J Am Coll Cardiol. 1984;4:890-901.
32. Hrymak C, Strumpher J, Jacobsohn E. Acute Right Ventricle Failure in the Intensive Care Unit: Assessment and Management. Can J Cardiol. 2017;33:61-71.
33. Hollenberg SM. Vasoactive drugs in circulatory shock. Am J Respir Crit Care Med. 2011;183:847-55.
34. Le Tulzo Y, Seguin P, Gacouin A, et al. Effects of epinephrine on right ventricular function in patients with severe septic shock and right ventricular failure: a preliminary descriptive study. Intensive Care Med. 1997;23:664-70.
35. Greyson C, Xu Y, Lu L, Schwartz GG. Right ventricular pressure and dilation during pressure overload determine dysfunction after pressure overload. Am J Physiol Heart Circ Physiol. 2000;278:H1414-20.
36. Ferrario M, Poli A, Previtali M, et al. Hemodynamics of volume loading compared with dobutamine in severe right ventricular infarction. Am J Cardiol. 1994;74:329-33.
37. Dell'Italia LJ, Starling MR, Blumhardt R, Lasher JC, O'Rourke RA. Comparative effects of volume loading, dobutamine, and nitroprusside in patients with predominant right ventricular infarction. Circulation. 1985;72:1327-35.
38. Kerbaul F, Rondelet B, Motte S, et al. Effects of norepinephrine and dobutamine on pressure load-induced right ventricular failure. Crit Care Med. 2004;32:1035-40.
39. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. Ann Thorac Surg. 2002;73:325-30.
40. Parissis JT, Paraskevaidis I, Bistola V, et al. Effects of levosimendan on right ventricular function in patients with advanced heart failure. Am J Cardiol. 2006;98:1489-92.
41. Pitsiou G, Paspala A, Bagalas V, Boutou AK, Stanopoulos I. Inhaled iloprost plus levosimendan to decompensate right heart failure due to chronic thromboembolic pulmonary hypertension. Anaesth Intensive Care. 2013;41:554-6.