The Right Ventricle in Cardiac Surgery, a Perioperative Perspective: II. Pathophysiology, Clinical Importance, and Management

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The importance of right ventricular (RV) function in cardiovascular disease and cardiac surgery has been recognized for several years. RV dysfunction has been shown to be a significant prognostic factor in cardiac surgery and heart transplantation. In the first article of this review, key features of RV anatomy, physiology, and assessment were presented. In this second part, we review the pathophysiology, clinical importance, and management of RV failure in cardiac surgery.
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Acute right ventricular (RV) failure after cardiac surgery continues to be a significant cause of morbidity and mortality. Acute refractory RV failure occurs in approximately 0.1% of patients following cardiotomy, in 2%–3% of patients following heart transplantation, and in 20%–30% of patients requiring left ventricular (LV) assist device (LVAD) insertion.[1] Acute refractory RV failure is also associated with a high in-hospital mortality rate that may reach 70%–75%.[1–3] In recent years, our understanding of postoperative RV failure has improved, leading to better prevention and management strategies.

In the first part of this review series, the anatomy, physiology, and assessment of the RV were discussed. In the second part, we will discuss the pathophysiology, clinical importance, and management of RV failure in cardiac surgery. We recently reviewed the role of the RV in cardiovascular disease.[4,5] In this article, we will review RV function from the perspective of the surgeon and anesthesiologist caring for the perioperative patient undergoing cardiac surgery.

PATHOPHYSIOLOGY OF RV FAILURE AFTER CARDIAC SURGERY

Postcardiotomy RV failure is often precipitated by an element of ischemia and myocardial depression after cardiopulmonary bypass (CPB).[1] Myocardial dysfunction and pulmonary hypertension (PH) after CPB are usually mild and do not lead to postoperative circulatory failure. However, in vulnerable patients, CPB may contribute to postoperative RV failure.[1,6,7] In patients requiring LVAD support, unloading of the LV alters RV size and shape and may lead to RV failure.[8] In heart transplant recipients, donor heart ischemia and preexisting pulmonary vascular disease increase the risk of postoperative RV failure.[9–11] Other factors which may contribute to postoperative RV failure include 1) suboptimal myocardial protection during surgery, 2) long CPB time, 3) RV myocardial ischemia or infarction caused by coronary embolism or coronary bypass graft occlusion, 4) atrial arrhythmias or loss of atrioventricular synchrony, 5) reperfusion lung injury with secondary PH, 6) postoperative pulmonary embolism, 7) preexisting pulmonary vascular disease, 8) protamine-induced PH, or 9) sepsis-associated myocardial depression (Table 1).

When the RV fails, maintenance of hemodynamic stability depends on LV contraction, especially that of the septum, atrial contraction, atrioventricular synchrony, and RV perfusion. Experimental studies have shown that in models where the RV was replaced with a noncontractile patch, the septum was able to maintain circulatory stability as long as the RV was not dilated.[12–15] Although volume loading may improve RV function, excessive volume loading may contribute to low cardiac output through ventricular interdependence (Fig. 1). RV dilation causes a leftward shift of the ventricular septum, increases pericardial constraint, and modifies LV geometry. As a consequence both LV distensibility and contractility may be decreased resulting in reduced cardiac output.[16]

Acute RV failure may lead to systemic congestion and circulatory failure. Tricuspid regurgitation is usually a prominent feature of acute RV failure and may be the result of RV dilation and PH.[4,16] Hypoxemia is

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Table 1. Common Causes of Right Ventricular Failure in Cardiac Surgery

Mechanism of postoperative RV failure	Specific etiologies
Preexisting RV dysfunction	Preoperative RV dysfunction associated with pulmonary hypertension or congenital, valvular or coronary disease
RV myocardial infarction	Coronary embolism (air, thrombus), thrombotic occlusion, graft dysfunction
Postsurgical myocardial dysfunction	Suboptimal myocardial protection, long cardiopulmonary bypass time
Postoperative pulmonary hypertension	Preexisting pulmonary hypertension Ischemia-reperfusion injury Pulmonary embolism Left ventricular failure Excessive blood transfusions
Dynamic obstruction of the RVOT	Volume depletion, high dose of inotropes
Excessive volume loading of the RV	Excessive transfusions or volume infusion Severe tricuspid regurgitation
Acute unloading of the LV	Following LVAD support
Transplantation	Pulmonary hypertension, prolonged ischemic time, acute rejection, obstruction at the pulmonary artery anastomosis
Pericardial constriction	Postcardiotomy syndrome

LVAD = left ventricular assist device; RV = right ventricular; RVOT = right ventricular outflow tract.

often noted in patients with severe RV failure and may occur as a consequence of increased right to left shunting through a patent foramen ovale or increased ventilation-perfusion mismatches associated with low cardiac output. Alternatively, hypoxemia may be a reflection of the underlying pulmonary disease.

THE IMPORTANCE OF RV FUNCTION IN CARDIAC SURGERY

Over the last three decades, emphasis in cardiology and cardiac surgery has mainly been placed on LV function. Recent data also suggest that RV function may improve risk stratification of patients undergoing surgery for coronary artery disease, valvular heart disease, congenital heart disease (CHD), heart transplantation, or in patients requiring mechanical assist devices and those experiencing postoperative hemodynamic instability (Table 2). In contrast to the evidence that supports LV function in cardiac surgery, most of the evidence that supports the importance of RV function in cardiac surgery is based on retrospective or small prospective studies. Variables of RV function have not yet been included in large-scale risk stratification models. Thus, their inclusion in the Parsonnet score or the Euroscore has not been well established.[17–20] The absence of RV functional parameters in large-scale models may be explained by the more challenging assessment of the RV. However, novel indices of RV function, such as the myocardial performance index (RVMPI) or the tricuspid annular plane systolic excursion, may allow more routine inclusion in risk stratification models.[4]

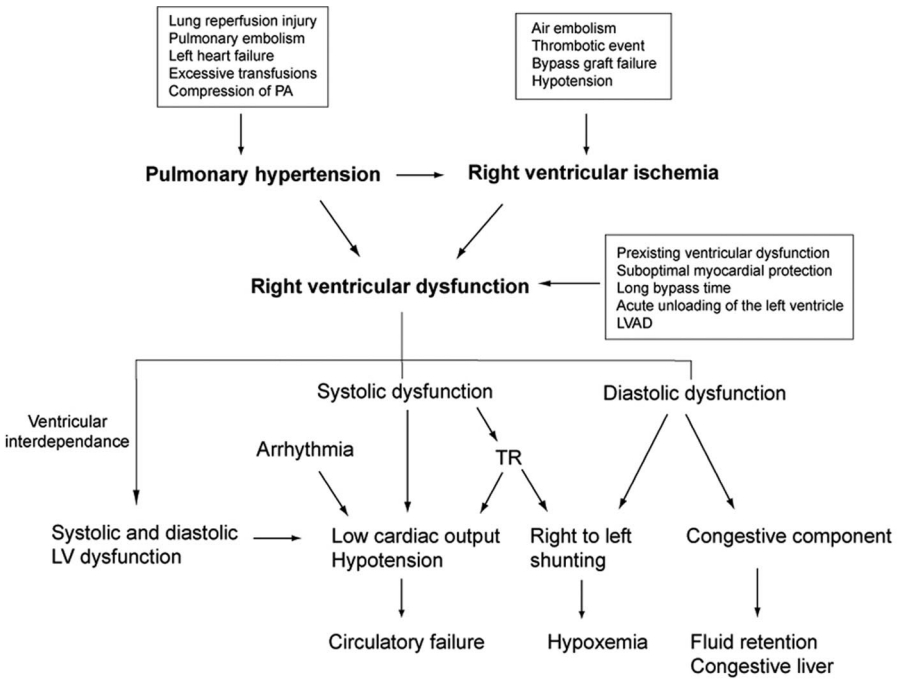

Figure 1. Pathophysiology of right ventricular (RV) failure in cardiac surgery. (LV = left ventricular; LVAD = left ventricular assist device; PA = pulmonary artery; TR = tricuspid regurgitation). Adapted with permission from Haddad F, Denault AY, Couture P, Cartier R, Pellerin M, Levesque S, Lambert J, Tardif JC. Right ventricular myocardial performance index predicts perioperative mortality or circulatory failure in high-risk valvular surgery. J Am Soc Echocardiogr 2007;20:1065–72.

Table 2. Prognostic Value of Right Ventricular Function in Cardiac Surgery

Study	Population	Study design	RV dysfunction	Results
Maslow et al.[21]	CAD undergoing coronary bypass surgery with LVEF <25%	Retrospective $n = 41$	RVFAC < 35%	RV dysfunction is associated with decreased long term survival
Pinzani et al.[22]	Mitral and combined mitro-aortic surgery	Retrospective $n = 382$	Clinical definition	Postoperative RV failure is the strongest predictor of postoperative mortality
Haddad et al.[24]	High-risk valvular surgery	Prospective $n = 50$	RVFAC < 32% or RVMPI > 0.50	Preoperative RV dysfunction was associated with a higher incidence of postoperative circulatory failure
Denault et al.[51]	Patients undergoing cardiac surgery with CPB	Retrospective and prospective $n = 800$	Dynamic obstruction of RVOT (gradient > 25 mm Hg)	Incidence: 4%, dynamic obstruction of RVOT was associated with a higher incidence of difficult weaning from bypass
Reichert et al.[50]	Unstable postoperative patients	Prospective $n = 60$	RVFAC < 35%	RV dysfunction associated with high mortality rates
Webb et al.[34,39]	Atrial septal defect	Retrospective series	RV remodeling	Older age at repair and abnormal RV myocardial relaxation were associated with incomplete RV remodeling
Cullen et al.[42]	Tetralogy of Fallot	Prospective $n = 35$	Restrictive RV physiology	Restrictive physiology predicts longer intensive care unit stay post repair and lower cardiac output
Gatzoulis et al.[43]	Tetralogy of Fallot	Prospective $n = 41$	Restrictive RV physiology	Restrictive physiology predicts smaller RV and better exercise tolerance
Therrien et al.[38]	Tetralogy of Fallot	Prospective $n = 17$	RV remodeling	Severe RV dilatation (RVEDV >170 mL/m^2 or RVESV >85 mL/m^2) associated with incomplete RV remodeling
Kormos et al.[48]	LVAD and RV failure	Retrospective $n = 31$	Clinical mean RVEF = 11.8%	Preoperative clinical factors such as fever, pulmonary edema and intraoperative blood transfusions were associated with RVAD need
Ochiai et al.[2]	LVAD	Retrospective $n = 245$	RV failure requiring RVAD	23 patients (9%) required RVAD. The need for circulatory support, female gender, and non-ischemic etiology predictors of RVAD need.
Hosenpud et al.[9]	Heart transplantation	Retrospective (ISHLT database)	RV failure associated with circulatory failure	RV failure accounts for up to 20% of early deaths

CAD = coronary artery disease; CPB = cardiopulmonary bypass; ISHLT = International Society of Heart Lung Transplantation; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; RV = right ventricular; RVAD = right ventricular assist device; RVED = right ventricular end-diastolic volume; RVEF = right ventricular ejection fraction; RVESV = right ventricular end-systolic volume; RVFAC = right ventricular fractional area change; RVMPI = right ventricular myocardial performance index; RVOT = right ventricular outflow tract.

Perioperative Risk Stratification in Coronary Bypass and Valvular Surgery

In patients with ischemic cardiomyopathy and severe LV systolic dysfunction undergoing nonemergent coronary artery bypass surgery, Maslow et al.[21] showed that the presence of significant RV dysfunction was associated with an increased risk of postoperative and long-term morbidity and mortality. Significant RV dysfunction was defined by a RV fractional area change (RVFAC) inferior to 35%.[21] In their retrospective study, patients with RV dysfunction had a higher incidence of postoperative inotropic or mechanical support, required longer intensive care unit and hospital stays, and had reduced short-term and long-term survival rates.[21]

Retrospective or small prospective studies also support the prognostic value of RV function in patients undergoing valvular heart surgery. In a retrospective study of patients undergoing mitral and mitral-aortic valvular surgery, Pinzani et al.[22] demonstrated that preoperative RV failure was a strong predictor of perioperative mortality. In this same study, postoperative RV failure was the most important independent predictor of late survival. In a small prospective study

of 14 patients with severe nonischemic mitral regurgitation and reduced LV and RV function, Wencker et al.[23] found that preoperative RV ejection fraction ≤20% was associated with late postoperative death. In a small prospective study (n = 50), Haddad et al.[24] have shown that preoperative RV dysfunction, as assessed by RVFAC or RVMPI, was associated with postoperative circulatory failure.

The Importance of RV Function in Patients with PH

PH is a major risk factor for mortality in patients undergoing cardiac surgery.[17,25] PH is included in both the Parsonnet and Euroscore models, where it significantly contributes to risk stratification.[17,25] In noncardiac surgery, PH has also been associated with worse outcome.[26,27]

In both the surgical and medical setting, there is growing evidence that morbidity and mortality associated with PH is dependent on RV adaptation to pulmonary vascular disease rather than on the absolute value of pulmonary arterial pressure.[24,26–29] In patients undergoing mitral valve surgery, RV dysfunction defined by a RVMPI >0.50 or a RVFAC <32% was a better predictor of postoperative circulatory failure than pulmonary arterial pressure.[24] In patients undergoing pulmonary embolectomy for chronic thromboembolic PH, studies suggest that preoperative RV failure, manifested by increased right atrial pressure, has been recognized as a risk factor for perioperative mortality.[30,31] Recent studies, however, emphasize that postoperative residual PH is the most important predictor of death.[30] In patients undergoing lung transplantation for PH, reverse cardiac remodeling and recovery of RV function occurs in most of the patients. Predictors of persistence of RV dysfunction have not been yet established.[32] In patients with PH undergoing noncardiac surgery, RV dysfunction, as assessed by the RVMPI, was also a better predictor of survival than absolute pulmonary arterial pressure.[26]

Congenital Heart Disease

The RV plays an important role in CHD, where it may support the pulmonary circulation (pulmonary RV) or the systemic circulation (systemic RV).[4,33,34] Recent studies have demonstrated that RV function is one of the most important predictors of survival and postoperative outcome in patients with CHD and RV pressure or volume overload.[34–37]

In patients with isolated atrial septal defect (ASD) and normal pulmonary pressure or mild PH, closure of the defect usually results in progressive remodeling of the RV.[38] Incomplete RV remodeling in ASD may, however, be seen in older patients (>40 yr old) or in patients with abnormal preoperative RV myocardial relaxation.[38] Atrial arrhythmias in ASD may also persist or develop in adults undergoing cardiac surgery after the age of 40 yr.[34,39] In contrast, closure of an ASD in patients with severe pulmonary vascular disease usually precipitates RV failure. In patients with significant systemic to pulmonary shunting ($Q_p/Q_s > 1.5$) and severe PH, several centers use a preoperative pulmonary vascular resistance (PVR) <15 Wood units and pulmonary to systemic resistance ratio ≤2/3 as a threshold beyond which surgery would carry unacceptable mortality risk.[40,41] However, individual centers vary these thresholds according to pulmonary vascular reactivity and specific anatomic lesions.[41] Closure of the defect is contraindicated in patients with Eisenmenger physiology, unless significant regression of pulmonary vascular disease occurs with pharmacological therapy.

In patients with repaired tetralogy of Fallot (TOF), severe pulmonary regurgitation is the most common cause of progressive RV dilation and failure and is associated with decreased exercise tolerance, atrial and ventricular arrhythmias, and sudden death.[34] Severe RV dilation, especially when progressive, may be the first sign of a failing RV and should prompt consideration of pulmonary valve replacement. Pulmonary valve replacement generally results in a decrease in RV volume.[34] Incomplete RV remodeling with persistence of RV dilation is more common in patients with severely dilated RVs (preoperative RV end-diastolic volume >170 mL/m^2).[38,42] Some patients with TOF exhibit a "restrictive RV physiology," which is defined by the presence of forward and laminar late diastolic pulmonary flow throughout respiration.[34] Early after TOF repair, restrictive RV physiology is associated with a low cardiac output and longer intensive care stay.[34,42] Late after TOF repair, however, restrictive RV physiology counteracts the effects of chronic pulmonary regurgitation. It is associated with a smaller RV, shorter QRS duration, and increased exercise tolerance.[34,43]

Ebstein's anomaly is characterized by an apical displacement of the septal and inferior tricuspid leaflet exceeding 8 mm/m^2.[34] This malformation results in atrialization of a portion of the RV and moderate-to-severe tricuspid regurgitation. The size of the functional RV and tricuspid valve morphology (attachment, commissures, surface) determines the best surgical approach. Preoperative assessment of Ebstein's anomaly is best achieved by combining echocardiography and magnetic resonance imaging.[34,35]

The RV usually adapts well to pulmonary valve stenosis, even when severe. Long-standing severe pulmonary stenosis, however, may lead to RV dilation, RV failure, and tricuspid regurgitation. Percutaneous valvuloplasty is usually considered as the intervention of choice in patients with moderate-to-severe pulmonary valve stenosis.

In transposition of the great arteries (TGA), the anatomic RV supports the systemic circulation.[34,44,45] Because the RV is not well suited to support the systemic circulation, RV failure occurs and is closely related to outcome.[34,44,45] In patients with L-TGA

(congenitally corrected TGA), moderate-to-severe systemic atrioventricular valve (tricuspid valve) regurgitation and RV failure are associated with increased mortality.[34,45] In patients with D-TGA who have undergone an atrial switch operation, myocardial perfusion defects, uncoordinated myocardial contraction, and systemic atrioventricular valve (tricuspid valve) regurgitation may contribute to a progressive decline in RV function.[34,45] Tricuspid valve replacement may slow the progression of RV failure in patients with L-TGA. Late arterial switch operation is also occasionally considered in selected patients, although its benefits have not yet been clearly demonstrated. As patients with TGA get older, many of them may be considered for heart transplantation or mechanical support.

Heart Transplantation

Despite advances in the perioperative management of heart transplantation, acute RV failure still accounts for a significant number of early complications and early deaths in up to 20% of patients in some reports.[9–11] Many factors contribute to the development of acute RV failure and include 1) preexisting or acquired PH, 2) marginal organ preservation and long ischemic time, 3) mechanical obstruction at the level of the pulmonary artery anastomosis, 4) significant donor-recipient mismatch with a much smaller donor heart (more than 20% mismatch in size), and 5) acute allograft rejection.[10] Several studies have demonstrated that preoperative PVR ≥6 Wood units and transpulmonary gradient ≥15 mm Hg are associated with increased perioperative mortality, most probably associated with an increased incidence of acute RV failure.

Left Ventricular Assist Devices

Acute RV failure after LVAD insertion occurs in approximately 10%–30% of patients and is associated with a high mortality.[2,46,47] Many factors may contribute to acute RV failure after LVAD insertion. The most important factor appears to be the acute unloading of the left heart, which results in shifting of the ventricular septum, potentially altering RV geometry, and contractility as well as worsening tricuspid regurgitation. The septal shift results in lower work of the septum and lower septal contribution to RV contraction. This is especially important in patients with baseline RV dysfunction. Predicting acute RV failure after LVAD insertion has proven to be challenging, although several reports have greatly increased our understanding of this problem.[2,46,47] Ochiai et al.[2] reviewed preoperative data for 245 patients, who underwent LVAD implantation. The most significant predictors for RV assist device (RVAD) use after LVAD insertion were the need for circulatory support before LVAD insertion, female gender, and a nonischemic etiology. The most important hemodynamic variables predictive of RVAD use were low-mean pulmonary arterial pressure and low RV stroke work index.[2] Low pulmonary artery pressure in this context was most probably a reflection of a failing RV incapable of generating high, or even normal, pulmonary artery pressures. In a smaller study, Kromos et al.[48] found that preoperative clinical factors, such as fever, pulmonary edema, and intraoperative blood transfusions, were better predictors of RVAD requirements than preimplantation measurement of RV function or hemodynamic variables. A larger study with adequate power to establish a reliable composite predictive risk factor for improving outcome in these patients would be helpful.[47]

Unstable Postoperative Patients

In the hemodynamically unstable postoperative cardiac surgery patient, RV dysfunction is a frequent finding. Costachescu et al.[49] found that RV systolic dysfunction, defined by an RVFAC ≤25% or severe RV dilation, was present in almost half of the patients with hemodynamic compromise. In patients with hypotension requiring inotropic support after cardiac surgery, Reichert et al.[50] have demonstrated that RV failure, defined by RVFAC of <35%, was associated with a high mortality rate. In their study, patients with biventricular failure had a mortality rate as high as 86%. This contrasted with a mortality of 30%–40% for patients with predominately LV failure and a mortality of only 15% for those with normal RV and LV function who were hemodynamically unstable.[50] More recently, dynamic obstruction of the RV outflow tract (RVOT), defined by a RVOT gradient ≥25 mm Hg, was also recognized as a potential cause of difficult weaning from bypass in adults.[51]

PREVENTION AND MANAGEMENT OF POSTOPERATIVE RV FAILURE

Managing acute RV failure after cardiac surgery remains challenging, particularly in certain cardiac surgical settings such as mitral disease, PH, ischemic cardiomyopathy, CHD, heart transplantation, and after the insertion of an LVAD.

Strategies to Minimize the Risk of Postoperative RV Failure

Prevention of acute RV failure after cardiac surgery begins with the identification of high-risk patients. This group includes patients with preexisting PH or preexisting RV dysfunction, patients undergoing surgery with long CPB times, patients receiving cardiac allografts with either long ischemic time or mismatched in size or patients receiving a LVAD.[52] Strategies that may reduce the risk of severe postoperative RV failure include 1) selecting the appropriate timing for surgery, 2) optimizing myocardial protection, 3) selective use of pulmonary vasodilators in the perioperative period, and 4) avoiding liberal transfusion strategies and the use of older blood products.[53]

Avoiding hypotension, optimizing preload, and careful adjustment of ventilation settings by avoiding hypoxemia and hypercapnia are also important principles in the prevention of postoperative RV failure.

Timing of Surgery

Choosing the appropriate timing for surgery may significantly decrease the risk of postoperative RV failure. In patients with valvular heart disease or CHD, cardiac surgery should be considered before the development of severe RV dysfunction develops.[4,54] In patients presenting with an acute RV myocardial infarction, it is usually considered reasonable to delay coronary artery bypass graft surgery for 4 wk to allow for the recovery of RV contractile performance. This approach is suggested if early reperfusion either percutaneously or with thrombolytics cannot be achieved.[55]

Myocardial Protection

Over the last five decades, advances in myocardial protection have significantly improved outcomes in cardiac surgery.[56] Several studies have shown that warm cardioplegia may improve myocardial protection and postoperative outcomes.[56–59] No study, however, has studied the effects of warm cardioplegia on postoperative RV function using echocardiography.

In heart transplantation, continuous perfusion of the donor hearts may reduce ischemic time and allow better myocardial protection and recovery. Continuing prospective studies (PROCEED trial) will determine whether this new strategy will reduce the incidence of postoperative RV failure and improve graft function.

Surgical Approach

Tailoring the surgical procedure in high-risk patients could potentially reduce the incidence of acute RV failure or postoperative RV remodeling. In patients with coronary artery disease and RV dysfunction, the integrity of the RV blood supply must be considered for revascularization.[1] Some surgeons recommend that revascularization of RV marginal arteries may need to be included in the revascularization plan, not only for long-term perfusion but also for delivery of cardioplegia during a cardiac surgical procedure.[1]

Off-pump surgery could have the theoretical benefit of improving myocardial protection in high-risk candidates although an unexpected increase in pulmonary pressures may occur during cardiac manipulation.[60] In low-risk patients undergoing coronary artery bypass surgery, Pegg et al.[60] have recently shown that early and late postoperative RV function was similar between patients undergoing on-pump or off-pump coronary artery bypass surgery.

In patients with functional tricuspid regurgitation associated with dilation of the tricuspid annulus, there is growing evidence that favors repair.[61] Several studies have demonstrated that annuloplasty of the tricuspid valve based on tricuspid dilation improves functional status independent of the degree of tricuspid regurgitation and may improve RV remodeling.[61] On-pump beating heart tricuspid annuloplasty is sometimes considered to improve postsurgical RV remodeling.

Anesthetic Drugs

Studies comparing different anesthetics or techniques on RV function have not been extensively conducted. In clinical practice, various anesthetic regimens have been used successfully in patients with PH who are at risk for postoperative RV dysfunction.[6] In patients with PH, isoflurane is usually recommended for anesthesia, although it may have significant negative inotropic effects when given at clinical concentrations.[62,63]

The Preventive Use of Pulmonary Vasodilators

The prevention of PH and its consequences is a promising strategy for preventing postoperative RV failure. The primary end point in most studies has been pulmonary hemodynamics with limited information available on RV function.

Some investigators believed that the administration of pulmonary vasodilators before CPB could minimize the effects of the pulmonary reperfusion syndrome. In that regard, inhaled prostacyclin and inhaled milrinone have been shown to decrease pulmonary arterial endothelial dysfunction induced by CPB in pig models.[64,65] In small clinical studies, inhaled prostacyclin or inhaled milrinone have been associated with a decrease in postoperative PH. Hache et al.[66] conducted a pilot, randomized, controlled trial in patients with preoperative PH and demonstrated that inhaled prostacyclin given before CPB was superior to placebo in reducing PH. Furthermore, in patients who received inhaled prostacyclin, the amount of vasoactive support was reduced.[67] In a study of high-risk patients by Lamarche et al.,[68] the administration of inhaled milrinone before CPB with PH ($n = 30$) was associated with a lower rate of reinitiation of CPB than when the pulmonary vasodilator was administered after weaning from CPB (9 vs 1; $P = 0.021$). Additionally, postoperative pulmonary artery pressures were lower in the prophylactically treated group. Further prospective and randomized studies will, however, be required to determine the efficacy of this approach. In a recent trial, Fattouch et al.[67] studied patients with PH ($n = 58$) undergoing mitral valve replacement for mitral stenosis. Inhaled prostacyclin and inhaled nitric oxide (iNO) were compared with conventional IV vasodilators. The inhaled drugs were given just before the end of CPB. Inhaled medications were associated with a significant reduction in indices of PH as well as with an increase in cardiac output and in RV ejection fraction compared with conventional treatment. In addition, in both inhaled groups, separation from CPB was easier, the amount of vasoactive drugs administered was smaller, and the duration of stay in the intensive care unit and hospital was shorter. The same

group also compared similar strategies in the treatment of PH after mitral valve replacement upon arrival in the intensive care unit.[67] Inhalation of prostacyclin was associated with a reduction in PVR and an increase in stroke volume. iNO reduced PVR but did not increase stroke volume, and nitroprusside was associated with a reduction in systemic arterial pressure and systemic vascular resistance.

Prevention of Protamine-Induced PH

Inhaled pulmonary vasodilators have also been used to prevent protamine-induced PH and RV failure. In a study of patients undergoing coronary revascularization (n = 3800), Ocal et al.[69] compared two therapeutic approaches in the treatment of the protamine reaction observed in 68 patients (1.8%). One group received inhaled prostacyclin and the other IV nitroglycerin in addition to standard vasoactive drugs. The inhaled prostacyclin group showed improved hemodynamics, and only 14 patients (39%) developing protamine-induced PH had to return to CPB compared with all 30 patients (100%) in the nitroglycerin group. A tendency for shorter length of stay in the intensive care unit and reduced mortality was observed in the inhaled prostacyclin group, but the numbers were too small to be statistically significant. To avoid protamine reactions, heparinase, a heparin degrading enzyme, was compared with placebo in a multicentered, randomized, controlled trial that included 167 patients.[70] The results of the trial, however, were negative. Heparinase was not associated with any reduction in the intervention to treat PH or any reduction in bleeding.

Managing Acute RV Failure After Cardiac Surgery

One of the most important principles in managing postoperative RV failure is to be able to maintain systemic blood pressure while minimizing RV dilation. Maintenance of sinus rhythm and atrioventricular synchrony is also especially important in RV failure, as atrial fibrillation and high-grade atrioventricular block may have profound hemodynamic consequences.[71] Therefore, placement of atrial epicardial leads should be considered in patients at risk of postoperative RV failure. Other important principles include reducing RV afterload, minimizing blood transfusions that may exacerbate PH, and optimizing ventilator settings.[52,72] It is also essential to tailor therapy to the specific etiology of postoperative RV failure (Fig. 2).

Vasopressor and Inotropic Support

In patients with severe postoperative RV failure, vasopressor or inotropic support may be required to maintain hemodynamic stability and prevent the vicious cycle of hypotension and RV ischemia.[1,52] Only a few small studies have compared the efficacy of different vasopressor or inotropic drugs in patients with RV failure or PH after cardiac surgery.

In patients with RV failure and hypotension associated with an acute or chronic increase in pulmonary artery pressure, norepinephrine may be useful in maintaining systemic pressure, increasing cardiac index, and reducing pulmonary pressure.[6,73,74] In an experimental dog model of pulmonary embolism, norepinephrine appeared to be superior to phenylephrine in improving cardiac output.[75] In another experimental animal model, phenylephrine had a negative inotropic effect on RV function.[76] In patients with mild-to-moderate RV dysfunction after cardiac surgery, but without severe hypotension, dobutamine or milrinone are both recommended and may increase cardiac output while decreasing pulmonary pressures.[6,77] In patients with low cardiac output syndrome after cardiac surgery (cardiac output below 2 $L \cdot min^{-1} \cdot m^{-2}$ with pulmonary capillary wedge pressure >10 mm Hg), Feneck et al.[78] compared milrinone with dobutamine in 120 patients. In a subset of patients with PH (defined as PVR >200 $dyn \cdot s \cdot cm^{-5}$ or mean pulmonary artery pressure >25 mm Hg), milrinone had a similar effect to dobutamine on reducing PVR and increasing in cardiac index. The pulmonary capillary wedge pressure and systemic vascular resistance were reduced more significantly by milrinone. Enoximone, an imidazole phosphodiesterase inhibitor, and the combination of dobutamine and nitroglycerine were evaluated in patients with mitral valve regurgitation and pulmonary venous hypertension.[79] Both regimens had comparable effects on mean systemic arterial pressure and heart rate, but enoximone was more effective in reducing mean pulmonary artery pressure. In patients with severe RV failure associated with circulatory failure, epinephrine may also be considered if patients fail to respond to norepinephrine with or without the addition of dobutamine.[80] If a dynamic RVOT obstruction is noted when using large inotropic support, it is usually recommended to reduce the dose, as it may lead to paradoxical decreases in cardiac output.[51] Levosimendan, a calcium sensitizer, has been used in low-output heart failure,[81] but its promise, specifically for RV failure, has been explored only in small human studies[82] and an experimental model.[83–85]

Optimization of RV Preload

In patients with postoperative RV failure and low filling pressures (right atrial pressure <15 mm Hg), preload should be optimized to increase cardiac output. Excessive volume loading should be avoided, however, as it may lead to LV dysfunction through the mechanisms of ventricular interdependence. It may also diminish the contribution of septal contraction to RV function.[1,6]

Inhaled Pulmonary Vasodilators

Inhaled pulmonary vasodilators may be helpful in the treatment of postoperative PH or RV failure. The most commonly used inhaled pulmonary vasodilators

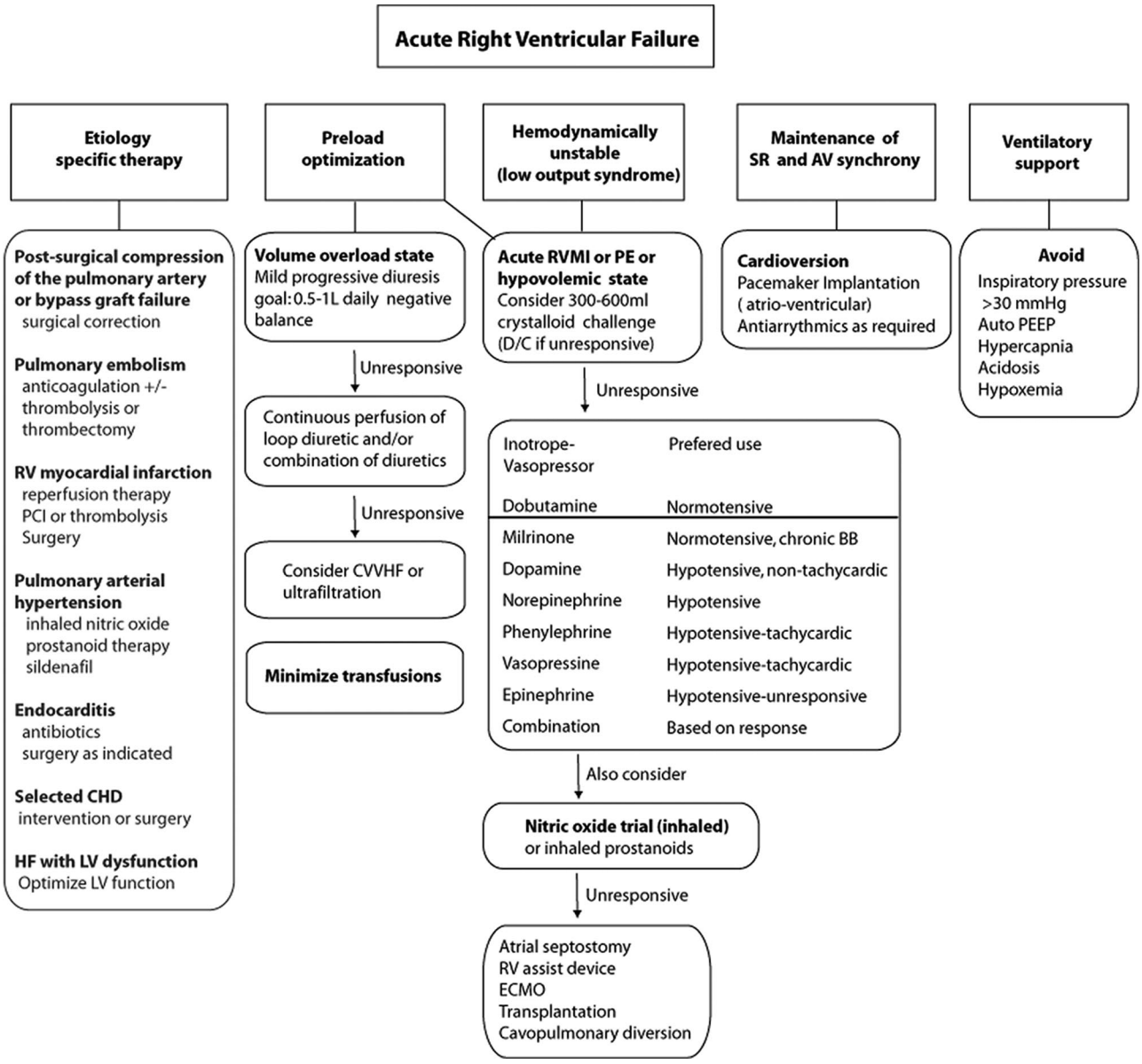

Figure 2. Proposed approach to acute right ventricular failure. AV = atrioventricular; BB = β-blockade; CHD = congenital heart disease; CVVHF = continuous veno-venous hemofiltration; D/C = discontinue; ECMO = extracorporeal membrane oxygenation; HF = heart failure; L = Liter; LV = left ventricular; PCI = percutaneous coronary intervention; PE = pulmonary embolism; PEEP= positive end-expiratory pressure; RV = right ventricular; RVMI = right ventricular myocardial infarction; SR = sinus rhythm. Adapted with permission from Haddad F, Hunt SA, Rosenthal DN, Murphy DJ. Right ventricular function in cardiovascular disease. I. Anatomy, physiology, aging, and functional assessment of the right ventricle. Circulation 2008;117:1436–48.

include iNO, inhaled prostacyclin, iloprost, and inhaled milrinone.[6,86–89] Inhaled sildenafil has been also recently studied in experimental models of lung reperfusion injury.[90] Compared with systemic drugs, inhaled drugs have the advantage of improving pulmonary hemodynamics without increasing ventilation-perfusion mismatches or causing systemic hypotension.

Evidence from retrospective studies and small randomized trials suggest that iNO may decrease the incidence of refractory postoperative RV failure after heart transplantation or CHD surgery.[87,91–94] In patients requiring LVAD support, Argenziano et al.[95] demonstrated in a randomized crossover trial of 11 patients with severe RV failure that iNO led to significant improvement in hemodynamics. RVAD insertion was required in one patient and was partially attributable to abrupt discontinuation of iNO.[95] Retrospective studies also suggest that the use of iNO decreases the need for RVAD insertion after LVAD insertion.[87,96] Comparative studies on different inhaled drugs suggest that iNO and inhaled prostacyclin have equivalent efficacy.[87] Inhaled prostacyclin may have the advantage of lower cost and does not cause methemoglobinemia.[87]

Ventilation

Optimal ventilation settings in patients with severe RV failure may increase RV preload and decrease RV afterload. In general, hyperinflation of the lungs should be avoided, as it may significantly increase

Table 3. Selected Reports of Right Ventricular Assist Device Use for Right Ventricular Failure[a]

Author	Surgical procedure	No. of patients with RVAD use	Survivors
Pae et al.[99]	Postcardiotomy	121	30/121 (25%)
Chen et al.[8]	Postcardiotomy	18/151	6/18 (30%)
McGovern et al.[100]	Postcardiotomy	6/15,000	2/6 (33%)
Pennington et al.[97]	Postcardiotomy	7/4695	0/7 (0%)
Mundth et al.[98]	Postcardiotomy	11	6/11 (54%)
Ochiai et al.[2]	Post LVAD insertion	23/245 (9%)	4/23 (17%) survival to transplant
Barnard et al.[101]	Heart transplant	6	2/6 (33%)
Jacquet et al.[102]	Heart transplant and LVAD	11	6/11 (54%)

[a] Duration of support varied from 2 h to 8 d. Advised caution in patients of age above 70 yr. LVAD = left ventricular assist device; RVAD = right ventricular assist device. Adapted from Kaul TK, Fields BL. Postoperative acute refractory right ventricular failure: incidence, pathogenesis, management and prognosis. Cardiovasc Surg 2000;8:1–9.

PVR.[6] Application of high levels of positive end-expiratory pressure will also narrow the capillaries in the well-ventilated areas and divert flow to less well ventilated or nonventilated areas.[6] Therefore, an increase in ventilation-perfusion mismatch resulting in a decrease in arterial oxygen content can be expected.[6] Hypoxemia, hypercapnia, or acidosis should also be avoided, as they may exacerbate PH.

Surgical Management

In cases where RV failure results from a compression of the pulmonary artery, a stricture at the pulmonary anastomotic site (heart transplantation) or mechanical complication of coronary bypass graft, surgery may correct the underlying cause of failure.[1,52]

Most cases of refractory RV failure will, however, require short-term mechanical support. In the early 1980s, pulmonary artery balloon pumps were used to support the failing RV. Clinical studies have shown that these pumps reduce pulmonary pressures and offload the RV. Because pulmonary artery balloon pumps are less reliable than RVAD, and can only provide short-term support, their use was abandoned in favor of the RVAD.[1] The Thoratec system is the most commonly used RVAD in clinical practice and offers the advantage of longer-term support.[1] Although RVAD reestablishes hemodynamic stability in most cases, the hospital discharge rate following a successful weaning may be as low as 25%–30%[8,97–102] (Table 3). This is in contrast to the 40%–60% salvage rate seen in patients with isolated LVAD support in the acute setting.[1] Occasionally, when time does not allow for surgical insertion of a RVAD or in the presence of associated acute lung injury, an extracorporeal membrane oxygenator is used as a bridge to RVAD or transplantation.[1] In selected cases not considered candidates for RVAD or transplantation and with normal PVR, cavo-pulmonary shunting has been successfully performed in specialized centers.[1]

CONCLUSION

Acute RV failure in cardiac surgery remains a significant cause of morbidity and mortality. Recognition of high-risk patients and early management of RV dysfunction may decrease the incidence of refractory postoperative RV failure. This will be particularly important in high-risk surgeries, such as CHD, multiple valve surgery, and during LVAD insertion. Advances in myocardial protection, prophylactic use of inhaled pulmonary vasodilators, and better RVAD technology will hopefully improve outcomes in this high-risk population.

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REFERENCES

1. Kaul TK, Fields BL. Postoperative acute refractory right ventricular failure: incidence, pathogenesis, management and prognosis. Cardiovasc Surg 2000;8:1–9
2. Ochiai Y, McCarthy PM, Smedira NG, Banbury MK, Navia JL, Feng J, Hsu AP, Yeager ML, Buda T, Hoercher KJ, Howard MW, Takagaki M, Doi K, Fukamachi K. Predictors of severe right ventricular failure after implantable left ventricular assist device insertion: analysis of 245 patients. Circulation 2002; 106:I198–I202
3. Moazami N, Pasque MK, Moon MR, Herren RL, Bailey MS, Lawton JS, Damiano RJ Jr. Mechanical support for isolated right ventricular failure in patients after cardiotomy. J Heart Lung Transplant 2004;23:1371–5
4. Haddad F, Hunt SA, Rosenthal DN, Murphy DJ. Right ventricular function in cardiovascular disease. I. Anatomy, physiology, aging, and functional assessment of the right ventricle. Circulation 2008;117:1436–48
5. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease. II. Pathophysiology, clinical importance, and management of right ventricular failure. Circulation 2008;117:1717–31
6. Fischer LG, Van AH, Burkle H. Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists. Anesth Analg 2003;96:1603–16
7. Voelkel NF, Quaife RA, Leinwand LA, Barst RJ, McGoon MD, Meldrum DR, Dupuis J, Long CS, Rubin LJ, Smart FW, Suzuki YJ, Gladwin M, Denholm EM, Gail DB. Right ventricular function and failure: report of a National Heart, Lung, and Blood Institute working group on cellular and molecular mechanisms of right heart failure. Circulation 2006;114:1883–91
8. Chen JM, Levin HR, Rose EA, Addonizio LJ, Landry DW, Sistino JJ, Michler RE, Oz MC. Experience with right ventricular assist devices for perioperative right-sided circulatory failure. Ann Thorac Surg 1996;61:305–10
9. Hosenpud JD, Bennett LE, Keck BM, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: seventeenth official report-2000. J Heart Lung Transplant 2000;19:909–31
10. Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. J Am Coll Cardiol 2001;38:923–31

11. Taylor DO, Edwards LB, Boucek MM, Trulock EP, Aurora P, Christie J, Dobbels F, Rahmel AO, Keck BM, Hertz MI. Registry of the International Society for Heart and Lung Transplantation: twenty-fourth official adult heart transplant report-2007. J Heart Lung Transplant 2007;26:769–81
12. Goldstein JA, Harada A, Yagi Y, Barzilai B, Cox JL. Hemodynamic importance of systolic ventricular interaction, augmented right atrial contractility and atrioventricular synchrony in acute right ventricular dysfunction. J Am Coll Cardiol 1990;16:181–9
13. Dell'Italia LJ. The right ventricle: anatomy, physiology, and clinical importance. Curr Probl Cardiol 1991;16:653–720
14. Hoffman D, Sisto D, Frater RW, Nikolic SD. Left-to-right ventricular interaction with a noncontracting right ventricle. J Thorac Cardiovasc Surg 1994;107:1496–502
15. Goldstein J. The right ventricle: what's right and what's wrong. Coron Artery Dis 2005;16:1–3
16. O'rourke RA, Dell'Italia LJ. Diagnosis and management of right ventricular myocardial infarction. Curr Probl Cardiol 2004;29:6–47
17. Bernstein AD, Parsonnet V. Bedside estimation of risk as an aid for decision-making in cardiac surgery. Ann Thorac Surg 2000;69:823–8
18. Nashef SA, Roques F, Hammill BG, Peterson ED, Michel P, Grover FL, Wyse RK, Ferguson TB. Validation of European System for Cardiac Operative Risk Evaluation (EuroSCORE) in North American cardiac surgery. Eur J Cardiothorac Surg 2002;22:101–5
19. Shroyer AL, Coombs LP, Peterson ED, Eiken MC, DeLong ER, Chen A, Ferguson TB Jr, Grover FL, Edwards FH. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. Ann Thorac Surg 2003;75:1856–64
20. Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Pi-by-no, simple risk stratification model for heart valve surgery. Circulation 2005;112:224–31
21. Maslow AD, Regan MM, Panzica P, Heindel S, Mashikian J, Comunale ME. Precardiopulmonary bypass right ventricular function is associated with poor outcome after coronary artery bypass grafting in patients with severe left ventricular systolic dysfunction. Anesth Analg 2002;95:1507–18
22. Pinzani A, de GG, Pinzani V, Ninet J, Milon H, Delahaye JP. [Pre- and postoperative right cardiac insufficiency in patients with mitral or mitral-aortic valve diseases]. Arch Mal Coeur Vaiss 1993;86:27–34
23. Wencker D, Borer JS, Hochreiter C, Devereux RB, Roman MJ, Kligfield P, Supino P, Krieger K, Isom OW. Preoperative predictors of late postoperative outcome among patients with nonischemic mitral regurgitation with 'high risk' descriptors and comparison with unoperated patients. Cardiology 2000; 93:37–42
24. Haddad F, Denault AY, Couture P, Cartier R, Pellerin M, Levesque S, Lambert J, Tardif JC. Right ventricular myocardial performance index predicts perioperative mortality or circulatory failure in high-risk valvular surgery. J Am Soc Echocardiogr 2007;20:1065–72
25. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9–13
26. Yeo TC, Dujardin KS, Tei C, Mahoney DW, McGoon MD, Seward JB. Value of a Doppler-derived index combining systolic and diastolic time intervals in predicting outcome in primary pulmonary hypertension. Am J Cardiol 1998;81: 1157–61
27. Ramakrishna G, Sprung J, Ravi BS, Chandrasekaran K, McGoon MD. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. J Am Coll Cardiol 2005;45:1691–9
28. D'Alonzo GE, Barst RJ, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Kernis JT. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. Ann Intern Med 1991;115:343–9
29. Ghio S, Gavazzi A, Campana C, Inserra C, Klersy C, Sebastiani R, Arbustini E, Recusani F, Tavazzi L. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. J Am Coll Cardiol 2001;37:183–8
30. Tscholl D, Langer F, Wendler O, Wilkens H, Georg T, Schafers HJ. Pulmonary thromboendarterectomy—risk factors for early survival and hemodynamic improvement. Eur J Cardiothorac Surg 2001;19:771–6
31. Hoeper MM, Mayer E, Simonneau G, Rubin LJ. Chronic thromboembolic pulmonary hypertension. Circulation 2006; 113:2011–20
32. Kasimir MT, Seebacher G, Jaksch P, Winkler G, Schmid K, Marta GM, Simon P, Klepetko W. Reverse cardiac remodelling in patients with primary pulmonary hypertension after isolated lung transplantation. Eur J Cardiothorac Surg 2004; 26:776–81
33. Wu JC, Child JS. Common congenital heart disorders in adults. Curr Probl Cardiol 2004;29:641–700
34. Davlouros PA, Niwa K, Webb G, Gatzoulis MA. The right ventricle in congenital heart disease. Heart 2006;92(suppl 1):i27–i38
35. Chauvaud S. Ebstein's malformation. surgical treatment and results. Thorac Cardiovasc Surg 2000;48:220–3
36. Therrien J, Warnes C, Daliento L, Hess J, Hoffmann A, Marelli A, Thilen U, Presbitero P, Perloff J, Somerville J, Webb GD. Can Cardiovascular Society Consensus Conference 2001 update: recommendations for the management of adults with congenital heart disease part III. Can J Cardiol 2001;17:1135–58
37. Atik FA, Atik E, da Cunha CR, Caneo LF, Assad RS, Jatene MB, Riso A, Barbero-Marcial M. Long-term results of correction of tetralogy of Fallot in adulthood. Eur J Cardiothorac Surg 2004;25:250–5
38. Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G. Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. Am J Cardiol 2005;95: 779–82
39. Webb G, Gatzoulis MA. Atrial septal defects in the adult: recent progress and overview. Circulation 2006;114:1645–53
40. Steele PM, Fuster V, Cohen M, Ritter DG, McGoon DC. Isolated atrial septal defect with pulmonary vascular obstructive disease—long-term follow-up and prediction of outcome after surgical correction. Circulation 1987;76:1037–42
41. Landzberg MJ. Congenital heart disease associated pulmonary arterial hypertension. Clin Chest Med 2007;28:243–53, x
42. Cullen S, Shore D, Redington A. Characterization of right ventricular diastolic performance after complete repair of tetralogy of Fallot. Restrictive physiology predicts slow postoperative recovery. Circulation 1995;91:1782–9
43. Gatzoulis MA, Clark AL, Cullen S, Newman CG, Redington AN. Right ventricular diastolic function 15 to 35 years after repair of tetralogy of Fallot. Restrictive physiology predicts superior exercise performance. Circulation 1995;91:1775–81
44. Gatzoulis MA, Till JA, Somerville J, Redington AN. Mechanoelectrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. Circulation 1995;92:231–7
45. Warnes CA. Transposition of the great arteries. Circulation 2006;114:2699–709
46. Fukamachi K, McCarthy PM, Smedira NG, Vargo RL, Starling RC, Young JB. Preoperative risk factors for right ventricular failure after implantable left ventricular assist device insertion. Ann Thorac Surg 1999;68:2181–4
47. Furukawa K, Motomura T, Nose Y. Right ventricular failure after left ventricular assist device implantation: the need for an implantable right ventricular assist device. Artif Organs 2005;29:369–77
48. Kormos RL, Gasior TA, Kawai A, Pham SM, Murali S, Hattler BG, Griffith BP. Transplant candidate's clinical status rather than right ventricular function defines need for univentricular versus biventricular support. J Thorac Cardiovasc Surg 1996; 111:773–82
49. Costachescu T, Denault AY, Guimond JG, Couture P, Carignan S, Sheridan P, Hellou G, Blair L, Normandin L, Babin D, Allard M, Harel F, Buithieu J. The hemodynamically unstable patient in the intensive care unit: hemodynamic vs. transesophageal echocardiographic monitoring. Crit Care Med 2002;30:1214–23
50. Reichert CL, Visser CA, van den Brink RB, Koolen JJ, van Wezel HB, Moulijn AC, Dunning AJ. Prognostic value of biventricular function in hypotensive patients after cardiac surgery as assessed by transesophageal echocardiography. J Cardiothorac Vasc Anesth 1992;6:429–32

51. Denault AY, Chaput M, Couture P, Hebert Y, Haddad F, Tardif JC. Dynamic right ventricular outflow tract obstruction in cardiac surgery. J Thorac Cardiovasc Surg 2006;132:43–9
52. Vlahakes GJ. Right ventricular failure following cardiac surgery. Coron Artery Dis 2005;16:27–30
53. Koch CG, Li L, Sessler DI, Figueroa P, Hoeltge GA, Mihaljevic T, Blackstone EH. Duration of red-cell storage and complications after cardiac surgery. N Engl J Med 2008;358:1229–39
54. Bonow RO, Carabello BA, Kanu C, de LA Jr, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'gara PT, O'rourke RA, Otto CM, Shah PM, Shanewise JS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Circulation 2006;114:e84–e231
55. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, Hochman JS, Krumholz HM, Lamas GA, Mullany CJ, Pearle DL, Sloan MA, Smith SC Jr, Anbe DT, Kushner FG, Ornato JP, Pearle DL, Sloan MA, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Halperin JL, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B, Tarkington LG, Yancy CW. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2008;51:210–47
56. Jacob S, Kallikourdis A, Sellke F, Dunning J. Is blood cardioplegia superior to crystalloid cardioplegia? Interact Cardiovasc Thorac Surg 2008;7:491–8
57. Al-Ruzzeh S, Nakamura K, Athanasiou T, Modine T, George S, Yacoub M, Ilsley C, Amrani M. Does off-pump coronary artery bypass (OPCAB) surgery improve the outcome in high-risk patients?: a comparative study of 1398 high-risk patients. Eur J Cardiothorac Surg 2003;23:50–5
58. Carrier M, Pellerin M, Perrault LP, Bouchard D, Page P, Searle N, Lavoie J. Cardioplegic arrest with L-arginine improves myocardial protection: results of a prospective randomized clinical trial. Ann Thorac Surg 2002;73:837–41
59. el-Hamamsy I, Stevens LM, Pellerin M, Bouchard D, Page P, Carrier M, Perrault LP. A prospective randomized study of diluted versus non-diluted cardioplegia (minicardioplegia) in primary coronary artery bypass surgery. J Cardiovasc Surg (Torino) 2004;45:101–6
60. Pegg TJ, Selvanayagam JB, Karamitsos TD, Arnold RJ, Francis JM, Neubauer S, Taggart DP. Effects of off-pump versus on-pump coronary artery bypass grafting on early and late right ventricular function. Circulation 29;117:2202–10
61. Shah PM, Raney AA. Tricuspid valve disease. Curr Probl Cardiol 2008;33:47–84
62. Ewalenko P, Brimioulle S, Delcroix M, Lejeune P, Naeije R. Comparison of the effects of isoflurane with those of propofol on pulmonary vascular impedance in experimental embolic pulmonary hypertension. Br J Anaesth 1997;79:625–30
63. Cheng DC, Edelist G. Isoflurane and primary pulmonary hypertension. Anaesthesia 1988;43:22–4
64. Fortier S, DeMaria RG, Lamarche Y, Malo O, Denault AY, Desjardins F, Carrier M, Perrault LP. Inhaled prostacyclin reduces cardiopulmonary bypass-induced pulmonary endothelial dysfunction via increased cyclic adenosine monophosphate levels. J Thorac Cardiovasc Surg 2004;128:109–16
65. Lamarche Y, Malo O, Thorin E, Denault AY, Carrier M, Roy J, Perrault LP. Inhaled but not intravenous milrinone prevents pulmonary endothelial dysfunction after cardiopulmonary bypass. J Thorac Cardiovasc Surg 2005;130:83–92
66. Hache M, Denault AY, Belisle S, Robitaille D, Couture P, Sheridan P, Pellerin M, Babin D, Noel N, Guertin MC, Martineau R, Dupuis J. Inhaled epoprostenol (prostacyclin) and pulmonary hypertension before cardiac surgery. J Thorac Cardiovasc Surg 2003;125:642–9
67. Fattouch K, Sbraga F, Sampognaro R, Bianco G, Gucciardo M, Lavalle C, Vizza CD, Fedele F, Ruvolo G. Treatment of pulmonary hypertension in patients undergoing cardiac surgery with cardiopulmonary bypass: a randomized, prospective, double-blind study. J Cardiovasc Med (Hagerstown) 2006;7:119–23
68. Lamarche Y, Perrault LP, Maltais S, Tetreault K, Lambert J, Denault AY. Preliminary experience with inhaled milrinone in cardiac surgery. Eur J Cardiothorac Surg 2007;31:1081–7
69. Ocal A, Kiris I, Erdinc M, Peker O, Yavuz T, Ibrisim E. Efficiency of prostacyclin in the treatment of protamine-mediated right ventricular failure and acute pulmonary hypertension. Tohoku J Exp Med 2005;207:51–8
70. Stafford-Smith M, Lefrak EA, Qazi AG, Welsby IJ, Barber L, Hoeft A, Dorenbaum A, Mathias J, Rochon JJ, Newman MF. Efficacy and safety of heparinase I versus protamine in patients undergoing coronary artery bypass grafting with and without cardiopulmonary bypass. Anesthesiology 2005;103:229–40
71. Goldstein JA, Barzilai B, Rosamond TL, Eisenberg PR, Jaffe AS. Determinants of hemodynamic compromise with severe right ventricular infarction. Circulation 1990;82:359–68
72. Vlahakes GJ. Management of pulmonary hypertension and right ventricular failure: another step forward. Ann Thorac Surg 1996;61:1051–2
73. Ghignone M, Girling L, Prewitt RM. Volume expansion versus norepinephrine in treatment of a low cardiac output complicating an acute increase in right ventricular afterload in dogs. Anesthesiology 1984;60:132–5
74. Kwak YL, Lee CS, Park YH, Hong YW. The effect of phenylephrine and norepinephrine in patients with chronic pulmonary hypertension. Anaesthesia 2002;57:9–14
75. Hirsch LJ, Rooney MW, Wat SS, Kleinmann B, Mathru M. Norepinephrine and phenylephrine effects on right ventricular function in experimental canine pulmonary embolism. Chest 1991;100:796–801
76. Wang GY, McCloskey DT, Turcato S, Swigart PM, Simpson PC, Baker AJ. Contrasting inotropic responses to alpha1-adrenergic receptor stimulation in left versus right ventricular myocardium. Am J Physiol Heart Circ Physiol 2006;291:H2013–H2017
77. Elatrous S, Nouira S, Besbes-Ouanes L, Boussarsar M, Boukef R, Marghli S, Abroug F. Dobutamine in severe scorpion envenomation: effects on standard hemodynamics, right ventricular performance, and tissue oxygenation. Chest 1999;116:748–53
78. Feneck RO, Sherry KM, Withington PS, Oduro-Dominah A. Comparison of the hemodynamic effects of milrinone with dobutamine in patients after cardiac surgery. J Cardiothorac Vasc Anesth 2001;15:306–15
79. Hachenberg T, Mollhoff T, Holst D, Hammel D, Brussel T. Cardiopulmonary effects of enoximone or dobutamine and nitroglycerin on mitral valve regurgitation and pulmonary venous hypertension. J Cardiothorac Vasc Anesth 1997;11:453–7
80. Le TY, Seguin P, Gacouin A, Camus C, Suprin E, Jouannic I, Thomas R. 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
81. Follath F, Cleland JG, Just H, Papp JG, Scholz H, Peuhkurinen K, Harjola VP, Mitrovic V, Abdalla M, Sandell EP, Lehtonen L. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. Lancet 2002;360:196–202
82. Morelli A, Teboul JL, Maggiore SM, Vieillard-Baron A, Rocco M, Conti G, De GA, Picchini U, Orecchioni A, Carbone I, Tritapepe L, Pietropaoli P, Westphal M. Effects of levosimendan on right ventricular afterload in patients with acute respiratory distress syndrome: a pilot study. Crit Care Med 2006;34:2287–93
83. Leather HA, Ver EK, Segers P, Herijgers P, Vandermeersch E, Wouters PF. Effects of levosimendan on right ventricular function and ventriculovascular coupling in open chest pigs. Crit Care Med 2003;31:2339–43
84. Kerbaul F, Gariboldi V, Giorgi R, Mekkaoui C, Guieu R, Fesler P, Gouin F, Brimioulle S, Collart F. Effects of levosimendan on acute pulmonary embolism-induced right ventricular failure. Crit Care Med 2007;35:1948–54

85. Missant C, Rex S, Segers P, Wouters PF. Levosimendan improves right ventriculovascular coupling in a porcine model of right ventricular dysfunction. Crit Care Med 2007;35:707–15
86. Haraldsson A, Kieler-Jensen N, Ricksten SE. The additive pulmonary vasodilatory effects of inhaled prostacyclin and inhaled milrinone in postcardiac surgical patients with pulmonary hypertension. Anesth Analg 2001;93:1439–45, table of contents
87. Oz MC, Ardehali A. Collective review: perioperative uses of inhaled nitric oxide in adults. Heart Surg Forum 2004;7: E584–E589
88. Sablotzki A, Starzmann W, Scheubel R, Grond S, Czeslick EG. Selective pulmonary vasodilation with inhaled aerosolized milrinone in heart transplant candidates: [La vasodilatation pulmonaire selective avec l'inhalation de milrinone en aerosol chez des candidats a la greffe cardiaque]. Can J Anaesth 2005;52:1076–82
89. Denault AY, Lamarche Y, Couture P, Haddad F, Lambert J, Tardif JC, Perrault LP. Inhaled milrinone: a new alternative in cardiac surgery? Semin Cardiothorac Vasc Anesth 2006;10: 346–60
90. Aubin MC, Laurendeau S, Mommerot A, Lamarche Y, Denault AY, Carrier M, Perrault LP. Differential effects of inhaled and intravenous sildenafil in the prevention of the pulmonary endothelial dysfunction due to cardiopulmonary bypass. J Cardiovasc Pharmacol 2008;51:11–7
91. Jois D, Pouard P, Mauriat P, Malhere T, Vouhe P, Safran D. Inhaled nitric oxide as a therapy for pulmonary hypertension after operations for congenital heart defects. J Thorac Cardiovasc Surg 1994;107:1129–35
92. Kieler-Jensen N, Lundin S, Ricksten SE. Vasodilator therapy after heart transplantation: effects of inhaled nitric oxide and intravenous prostacyclin, prostaglandin E1, and sodium nitroprusside. J Heart Lung Transplant 1995;14:436–43
93. Ardehali A, Hughes K, Sadeghi A, Esmailian F, Marelli D, Moriguchi J, Hamilton MA, Kobashigawa J, Laks H. Inhaled nitric oxide for pulmonary hypertension after heart transplantation. Transplantation 2001;72:638–41
94. Jois D, Baufreton C, Mauriat P, Pouard P, Vouhe P, Safran D. Effects of inhaled nitric oxide administration on early postoperative mortality in patients operated for correction of atrioventricular canal defects. Chest 2005;128:3537–44
95. Argenziano M, Choudhri AF, Moazami N, Rose EA, Smith CR, Levin HR, Smerling AJ, Oz MC. Randomized, double-blind trial of inhaled nitric oxide in LVAD recipients with pulmonary hypertension. Ann Thorac Surg 1998;65:340–5
96. Beck JR, Mongero LB, Kroslowitz RM, Choudhri AF, Chen JM, DeRose JJ, Argenziano M, Smerling AJ, Oz MC. Inhaled nitric oxide improves hemodynamics in patients with acute pulmonary hypertension after high-risk cardiac surgery. Perfusion 1999;14:37–42
97. Pennington DG, McBride LR, Swartz MT, Kanter KR, Kaiser GC, Barner HB, Miller LW, Naunheim KS, Fiore AC, Willman VL. Use of the Pierce-Donachy ventricular assist device in patients with cardiogenic shock after cardiac operations. Ann Thorac Surg 1989;47:130–5
98. Mundth ED. Assisted circulation. In: Babiston DC, Spence WB, eds. Surgery of the chest. Philadelphia: Saunders and Co, 1990:1777–99
99. Pae WE Jr. Ventricular assist devices and total artificial hearts: a combined registry experience. Ann Thorac Surg 1993;55: 295–8
100. McGovern G. Treatment with ECMO for post cardiotomy cardiogenic shock. In: Karp RB, Laks H, eds. Advances in cardiac surgery. St. Louis, MO: Mosby Co, 1995:169–93
101. Barnard SP, Hasan A, Forty J, Hilton CJ, Dark JH. Mechanical ventricular assistance for the failing right ventricle after cardiac transplantation. Eur J Cardiothorac Surg 1995;9:297–9
102. Jacquet L, Dion R, Noirhomme P, Van DM, Goenen M. Successful bridge to retransplantation with the wearable Novacor left ventricular assist system. J Heart Lung Transplant 1996;15:620–2