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EDUCATIONAL PAPER

Epidemiology and management of right ventricular-predominant heart failure and shock in the cardiac intensive care unit

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Cardiogenic shock from left ventricular failure is a common presentation in the intensive care unit. In contrast, right ventricular (RV)-predominant heart failure (HF) causing shock is less well recognized. We review the epidemiology and mechanisms of RV-predominant HF and discuss pharmacologic and device-based approaches for the management of this challenging clinical problem.

Keywords Epidemiology • Intensive care unit • RV-predominant HF

Introduction

Cardiogenic shock (CS) from left ventricular (LV) failure is a common presentation in the intensive care unit. In contrast, right ventricular (RV)-predominant heart failure (HF) causing shock is less well recognized. The RV function is influenced by pre-load, afterload, myocardial contractility, lusitropy, and non-cardiac factors such as pericardial compliance, thoracic pressure, etc.[1–3] Generating RV output requires one-sixth the energy expenditure of the LV given the highly compliant, low-resistance pulmonic circulation.[4] This difference is exemplified by the trapezoid-shape of the RV pressure–volume (PV) loop under steady-state conditions, which lacks isovolumic phases of contraction and relaxation and has a lower peak systolic pressure, with peak ejection occurring after peak elastance is reached.[1,5] Unlike the LV which is more adapted to maintaining stroke volume despite increases in systemic afterload, the lower resistance pulmonary pathway pre-disposes the RV to be particularly sensitive to changes in afterload.[3,4] However, it is the proportional rather than absolute changes in vascular parameters in response to alterations in the ventricular afterload that determine its response. In the setting of chronic increases in pulmonary resistance, the RV has a tremendous capacity to hypertrophy and dilate. This adaptation, in turn serves to re-establish appropriate ventricular–vascular coupling in the short-term but it can eventually lead to tricuspid annular dilatation and regurgitation as well as myocardial hypertrophy and RV ischaemia.[3,6] However, in an acute setting, the RV response is much more blunted. Hence, RV-predominant HF is considered a haemodynamic problem caused by impaired function of the ventricle, the valves, or the vasculature.[7,8] Management of RV-predominant HF and shock requires not only an understanding of the anatomical and physiological particularities of the RV, but also rapid identification and treatment of the underlying causes and related pathophysiological disorders.

Epidemiology and mechanisms of right ventricular-predominant heart failure

In recent years, there has been a renewed interest in RV-predominant HF, which has in turn led to an appreciation for the incidence, diverse causes, and enhanced understanding of physiological and pathological mechanisms of right ventricular dysfunction (RVD).[8] Despite that a consensus definition of RVD or optimal diagnostic modality to identify it remains debatable. This is further compounded by the fact that RV-predominant HF remains the final common pathway in numerous disease states, which are often considered or reported in isolation. Hence, the true prevalence of RVD is probably underreported.

The PV analysis provides a helpful framework for visualizing the different haemodynamic phenotypes of RV failure.[9] Recall that the RV PV loop represents haemodynamic changes during one cardiac cycle and

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its contour is defined by two fundamental relationships—the end-systolic PV relationship (ESPVR) and the end-diastolic PV relationship (EDPVR). Load-independent evaluation of the RV's systolic or contractile function is provided by characteristics of the ESPVR, namely the slope (E_{es}, end-systolic elastance) and the volume–axis intercept (V_0). A steeper ESPVR, indicated by a higher E_{es}, and a smaller V_0, suggests increased contractile function. The ventricle's diastolic properties are relayed by the EDPVR, which is non-linear and forms the bottom boundary of the PV loop. The EDPVR can be modelled with simple equations like $P = \beta(e^{\alpha[V - V_0]} - 1)$ or $P = \beta V^{\alpha}$, where α and β are constants that relate to ventricular stiffness and are determined by specific geometric and mechanical properties of the myocytes and extracellular matrix. A steeper EDPVR indicates a stiffer ventricle that is less compliant (i.e. higher ratio of $\Delta P/\Delta V$).

When contractile dysfunction produces RV failure, the predominant abnormality is a shallower ESPVR and lower E_{es}, which in turn, results in a marked reduction in stroke volume and peak systolic pressure (*Figure 1*). In the volume-overloaded RV, the dominant pathophysiology is a right-shift of the PV loop. Until overt haemodynamic collapse occurs, RV systolic and diastolic properties are actually unchanged, and thus the ESPVR and EDPVR remain the same. However, hypervolaemia results in a significant energetic penalty: the area encapsulated by the loop, called stroke work, represents the energy required to eject blood from the RV into the pulmonary circulation, and it increases significantly as the end-diastolic pressure and volume rise with hypervolaemia. Finally, the pressure-overloaded RV can be depicted on the PV diagram by a rise in effective arterial elastance (E_a), which is the slope of a line connecting the end-systolic coordinate (V_{es}, P_{es}) with coordinates at end-diastole [V_{ed}, pulmonary capillary wedge pressure (PCWP)].[10] As E_a increases, stroke volume decreases significantly, yet the ventricle expends the same energy (i.e. stroke work) when compared with a normal RV.

Common causes of RVD can be further stratified by pathologic alterations in pre-load, afterload, lusitropy, and contractility. These include primary RV cardiomyopathies, RV ischaemia, congenital valvular pathologies, and pressure or volume overload related to left heart disease (*Table 1*). The LV failure is the most common cause of RV failure, presenting as bi-ventricular failure.[8,11] The RV-predominant failure and acute RV decompensation occur when there is an abrupt change in RV loading that precipitates RVD (*Table 1*). Primary mechanisms of acute RV failure include: (i) contractile failure secondary to myocardial ischaemia or inflammation, (ii) volume overload because of right-sided valvular insufficiency and increased venous return, and (iii) pressure overload resulting from decompensated left-sided HF, worsening pulmonary vascular resistance (PVR), or acute pulmonary embolus.[8] Indeed, the presence of pre-existing RVD is a risk factor for development of acute RV decompensation.

Though isolated RV myocardial infarction is relatively rare, ischaemic RVD has been observed in up to 40–50% of patients with acute inferior MI and associated with acute haemodynamic compromise in under half of these patients.[12] Patients with RV myocardial involvement in inferior MI are also at increased risk of death, shock, and arrhythmias.[13] In the case of acute pulmonary embolism, acute RV failure is evident in 25–60% of patients.[1] Even in the absence of haemodynamic compromise, RVD is associated with increased mortality in patients with acute pulmonary embolism.[14] In patients admitted for HF, RV systolic dysfunction is associated with overall mortality.[15,16] Estimates of in-hospital mortality in HF patients with acute RV failure range from 5 to 17%.[17]

Finally, RVD is common in patients with CS. In registries of acute myocardial infarction (AMI)-related CS, 37–45% of patients have evidence of RVD as defined by haemodynamic indices.[18] Patients with CS due to myocardial infarction or HF with right-sided congestion and RVD have higher mortality; furthermore, the severity of RVD is also associated with mortality.[19] There is growing evidence that complete haemodynamic profiling through pulmonary artery catheterization (PAC) in patients with CS may be associated with improved mortality, perhaps due to enhanced recognition of right-sided failure.[20]

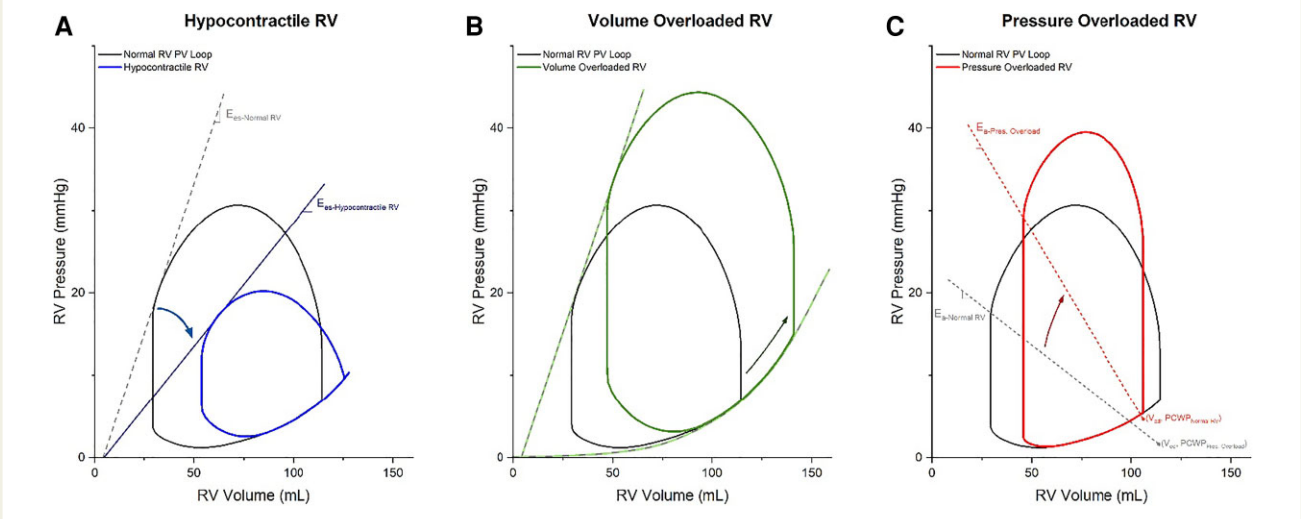

Figure 1 Changes in the pressure–volume relationship that occur with RVD precipitated by pure contractile dysfunction (*A*), hypervolaemia (*B*), and pressure overload (*C*).

Table 1 Common causes of acute and chronic RVD

	Acute RV failure	Chronic RVD
Pre-load	Acute renal failure	Atrial septal defect
	Acute valvular insufficiency	Tricuspid, pulmonic regurgitation
	Patent foramen ovale	Ventricular septal defect
		High output heart failure
		Eisenmenger syndrome
Afterload	Pulmonary thromboembolism	Pulmonic stenosis
	Hypoxia from pulmonary aetiology (e.g. acute respiratory distress syndrome, pneumonia)	Pulmonary artery stenosis
	Positive pressure ventilation	Pulmonary vascular disease
		Left heart disease
Contractility	RV myocardial infarction	RV myopathy
	Myocarditis	Arrhythmogenic RV cardiomyopathy
	Supraventricular or ventricular tachycardia; AV dys-synchrony	

Diagnosis of right ventricular-predominant heart failure and shock

Diagnosing acute RV-predominant HF and CS in the intensive care unit remains a clinical challenge. Patients with RV shock typically show signs of hypoperfusion and hypotension, including diaphoresis, cool extremities, hypotension, and tachycardia.[1,21] The clinical signs of RV-predominant HF are manifested by 'backward' failure causing systemic congestion, presenting with distension of jugular veins [elevated central venous pressure (CVP)].[22,23] Elevated CVP is the main determinant of impaired kidney and hepatic function in acute RV-predominant HF, often presenting with a cholestatic pattern and acute kidney injury.[24,25] Chronic systemic congestion from RV failure may result in hepatomegaly, abdominal distension, ascites, and peripheral edema.[26] Right upper quadrant discomfort may be caused by hepatic congestion, often presenting as an initial sign and if not recognized as a sign of RV failure, resulting in unnecessary gastroenterology-based evaluation causing further delays in management.[27] In severe forms, the right heart dilates and may shift the interventricular septum towards the left thereby compromise LV filling, reducing LV performance, and causing hypoperfusion and systemic congestion. Systemic hypoperfusion results in a sharp increase in circulating transaminases and lactic acidosis.

The most common non-invasive tool for imaging the RV, including morphology and function is echocardiography.[23,28] The indices of RV function which are most frequently used and easiest to perform are estimation of PA pressure using TR velocity, RV fractional area change, tricuspid annular plane systolic excursion, and RV end-diastolic dimension.[29] Newer imaging techniques, such as 3D-echocardiography and strain imaging, have proved to be useful and accurate imaging modalities but have limitations because they depend on good image quality and lack validation in larger cohorts. Cardiac magnetic resonance imaging and cardiac computed tomography are less helpful in the CS setting or bedside management of RV-predominant shock.

Haemodynamic assessment of RVD using a PAC remains the cornerstone of diagnostic evaluation of RV shock.[20] Different haemodynamic parameters, based on aetiology of RV shock, have been associated with outcomes. For example, a ratio of RA pressure to PCWP >0.86 is associated with pathological evidence of RV infarction and mortality risk. The PA pulsatility index (PAPi) of <1.85 is associated with a risk of RV failure after an LVAD, while a PAPi <1 portends risk of RV failure in AMI[30,31] In fact, a PAPi of <0.9 is an indication for consideration of mechanical circulatory support (MCS) for the RV in the National CS Initiative protocol for management of AMI. Similarly, RV stroke work is another important measure of RV function. Although multiple formulas to assess pulmonary haemodynamics have been developed to quantify RV afterload, including PVR, diastolic and trans-pulmonary gradient, PA elastance, compliance, or impedance, none of these formulas in isolation characterize RV failure. It is also essential to define the severity of shock while these haemodynamic measurements are performed in order to contextualize the data obtained.

Management of right ventricular-predominant heart failure and shock in intensive care unit

Principles of management

The triage and initial evaluation of patients presenting with RV-predominant HF and shock aim to assess clinical severity, with focus on rapid identification and management of the cause(s) of RV failure.

Early recognition

A critical consideration in effective management is early recognition, as unappreciated and undertreated RVD can potentiate end-organ damage caused by congestion and hypoperfusion.[1] Important in early definition of pathology is determination and correction of any potentially reversible underlying aetiologies. With these determinations in hand, a tailored management strategy can be developed utilizing the fundamental HF principles of pre-load, afterload, and contractility.

Pre-load, optimize volume status

Pre-load is the diastolic ventricular filling which ultimately imparts sarcomere stretch that sets the ventricular performance (Frank–Starling) curve. Filling is dictated by the venous return curve which relates cardiac output as the inverse of venous pressure. Volume loading has the potential to over-distend the RV and thereby increase wall tension, decrease contractility, aggravate TR, increase ventricular

interdependence, impair LV filling, and, ultimately, reduce systemic cardiac output and exacerbate organ dysfunction. Thus, an important goal in RVD and RV failure, which often occurs in a state of total body volume overload, is reduction of venous pressures to improve cardiac output and reduce systemic congestion while avoiding systemic hypotension. In addition, reducing ventricular distention also has favourable energetic effects by reducing wall stress.

Afterload, including perfusion pressure

Ventricular afterload is a principle representing ventricular wall stress during ejection which is related to the dynamic pulsatile impedance of the pulmonary circulation. Pulmonary impedance results after forward flow through the pulmonary artery interacts with multiple branch points within the pulmonary vasculature, creating a backward flow wave, which increases pulmonary pressure and reduces pulmonary blood flow.[32] The RV has long been thought to be more sensitive to changes in afterload.[3] Importantly, alterations in RV afterload are related not just to pulmonary vascular compliance but also to pulmonary parenchymal compliance and intrathoracic pressures.

Contractility, including rhythm

Molecular pathways regulating excitation–contraction coupling set the magnitude, rate, and energetics of myofibre interactions. Added to this is the unique geometry, activation pattern, and multilayered 3D-structure of myofibre architecture unique to the RV which relies on longitudinal shortening, transverse wall motion, and peristalsis.[33] Ultimately, forward flow is also related to atrioventricular synchrony and RV–LV coordination, with a portion of RV contractility augmented by contraction of the LV septum and traction of the RV free wall to insertion points at the LV. Disease states including alterations in afterload, arrhythmia, or cyanosis may also alter beta-receptor density, which can have implications on energetics and treatment responsiveness.[34–37]

Medical management of right ventricular-predominant heart failure and shock

Volume optimization

While a chronically compensated RV might physiologically be able to accommodate large variations in pre-load, patients with RV-predominant shock are pre-load dependent. In fact, a large proportion of RV failure is caused, associated with or aggravated by RV volume overload. Therefore, an essential component to pre-load management in RVD is the optimization of CVP, reduction in stressed blood volume and obviating ventricular distention, in addition to managing total body volume status (*Figure 2*).

In patients with RV failure and signs of venous congestion, diuretics are often the first option to optimize volume status. Elevated renal venous pressure often found in such patients contributes to decreased renal blood flow and reduces perfusion pressure, which decreases diuretic efficacy.[38] Hence, in RV shock patients with significant renal congestion, sufficient renal perfusion pressure (i.e. mean arterial pressure [MAP] − CVP) and an adequate plasma concentration of diuretics are crucial to achieving the desired effect.[39] Often, a continuous infusion of loop diuretics is required to maintain the decongestive effect. Early evaluation of the diuretic response by closely measuring urine output or post-diuretic spot urinary sodium content to identify patients with an inadequate diuretic response is critical.[40] If decongestion is insufficient, rapid intensification of loop diuretic dose, combining diuretics with a different mode of action or the use of ultrafiltration (UF) should be considered.[41]

Pulmonary vasodilator therapies, for afterload reduction

Pulmonary vasodilator therapies can be useful in relieving RV afterload in patients with pulmonary hypertension presenting with acute RV failure. In these patients, intravenous epoprostenol has long-term clinical benefits, including improved survival and functional capacity. However, in a patient with RV shock, systemic administration of pulmonary vasodilators may decrease systemic blood pressure, potentially reducing RV pre-load and worsening RV ischaemia. They also can worsen oxygenation by impairing ventilation–perfusion matching. Therefore, the use of short acting, inhaled nitric oxide rather than systemic pulmonary vasodilators is strongly recommended. Although multiple oral agents are available for pulmonary arterial hypertension (PAH) management, they are usually ineffective in acute RV shock given the duration of their action and need for oral absorption. Although some trials have investigated pulmonary vasodilator therapy in patients with left heart disease (WHO Group 2), these trials have not specifically targeted patients with evidence of pulmonary hypertension.

Pressors and inotropes for contractility and perfusion pressure

Restoration of coronary perfusion pressure by vasopressors is a mainstay of therapy for RV-predominant shock, since the failing RV is particularly susceptible to ischaemic injury. If the cardiac output is inadequate, inotropes should be considered to increase forward flow and possibly renal perfusion, while balancing the potential for ischaemia and arrhythmia.[1] In cases of hypotension, a drug with combined inotropic and vasopressor properties is ideal to maintain adequate perfusion. Given the inherent inotropic properties and a dose-dependent vasopressor effect from α_1 agonism, dopamine, norepinephrine, and epinephrine are useful adjuncts to augment contractility.[42] Dobutamine, levosimendan, and phosphodiesterase III inhibitors (milrinone) improve contractility and increase cardiac output and are indicated in patients with RV-predominant HF causing CS. Levosimendan and phosphodiesterase III inhibitors may favourably affect ventricular–arterial coupling by combining RV inotropy and pulmonary vasodilation and might be preferentially indicated in patients with pulmonary hypertension caused by left heart disease. However, they should be used with caution in patients with acute RV MI as these agents increase myocardial oxygen demand and arrhythmogenicity.

Vasopressors are primarily indicated to restore arterial blood pressure (target MAP of ≥65 mmHg) and improve organ perfusion. Norepinephrine can restore systemic haemodynamics without any effect on PVR or RV afterload. Arginine vasopressin causes peripheral vasoconstriction with less impact on PVR and has beneficial effects avoiding tachyarrhythmias, while supporting renal perfusion.[43] In small studies, digoxin was associated with acute increases in CO when administered to patients with pulmonary hypertension and RVD.

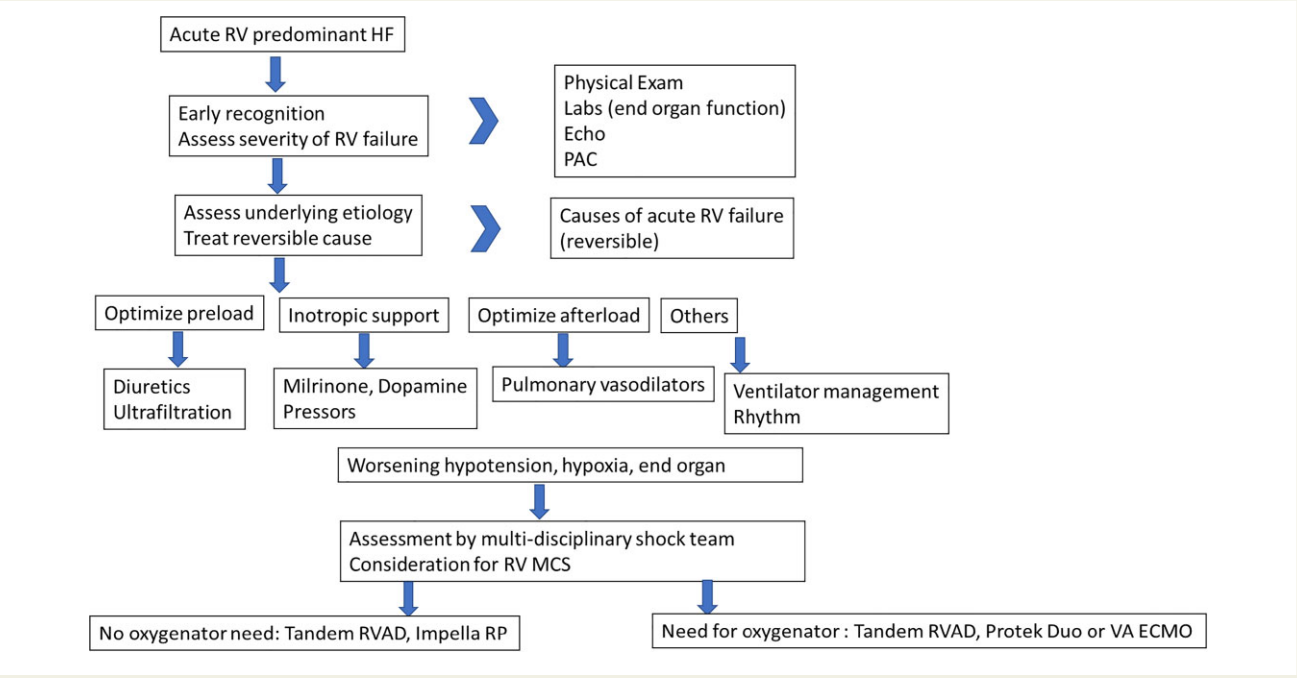

Figure 2 Approach to management of right ventricular-predominant shock in the intensive care unit.

Rhythm management

Both tachy- and brady-arrhythmias are poorly tolerated in RV-predominant shock. Brady-arrhythmias may represent RV ischaemia and often warrant inotropes or RV pacing.

Device management of right ventricular-predominant heart failure and shock

Role of ultrafiltration

As above, careful management of volume status is critical to the management of patients with RV-predominant shock. When diuretics are no longer sufficient, UF is an alternative approach to relieve congestion. In fact, as UF removes isotonic fluid, it is more effective at natriuresis than diuretics, which tend to eliminate hypotonic fluid.[44] This has led to the hypothesis that UF may be more effective than diuretics at relieving congestion in patients with HF. Clinical trials of UF in patients with decompensated HF have been limited by heterogenous inclusion criteria, unclear therapeutic targets, and high crossover rates.[45–48] While results have been mixed with regards to weight loss and rehospitalization rates, no trial has demonstrated reduction in mortality over diuretics alone. There have not been any large-scale clinical trials of UF in patients with CS, let alone RV-predominant shock, so the generalizability of these results to the higher acuity setting of CS is unknown.

Mechanical ventilation

Mechanical ventilation can negatively impact both RV pre-load and afterload, exacerbating RV-predominant shock physiology. While spontaneous inspiration results in negative intrathoracic pressure being transmitted to the right atrium (RA) and enhances venous return, positive pressure ventilation and positive end-expiratory pressure (PEEP) have the opposite effect. While some of the decreased venous return due to this rise in RA pressure is mitigated by a concomitant rise in intra-abdominal pressure, increased intra-abdominal pressure also results in narrowing of the hepatic veins and inferior vena cava, which increases venous resistance and further compromises venous return.[49] While spontaneous ventilation with normal respiratory rates has a neutral effect (i.e. effects of inspiration and counterbalanced by effects of expiration), in mechanically ventilated patients where rate and *I:E* ratios can be manipulated, the relative differences may be exaggerated. Positive pressure ventilation also shifts more of the lung into West Zones 1 and 2, where the increased airway pressure causes collapse of alveolar airways, resulting in increased PVR.[50] While there are no data supporting a particular ventilation strategy, the deleterious effects of mechanical ventilation on RV function can be mitigated by judicious use of PEEP and limiting tidal volume to avoid lung over-distention.

Interatrial shunt

In early studies of patients with PAH, the presence of a patent foramen ovale was associated with more favourable haemodynamics and improved survival, though these data have not been replicated in contemporary cohorts.[51–53] Initial human studies of iatrogenic interatrial shunt creation demonstrated high mortality due to refractory hypoxia, though this has improved with refinement of the technique and development of dedicated interatrial shunt devices that can more carefully control the degree of right to left shunting.[54] However, robust clinical trial data on hard endpoints are currently lacking and use of interatrial shunt devices for RV-predominant CS remains investigational.

Temporary mechanical circulatory support devices

The RV acute MCS now represents an important step in the management of RV failure and provides an opportunity to rapidly stabilize

patients with CS involving the RV (*Table 2*). Direct RV bypass systems source blood from the RA and delivery blood into the pulmonary artery. Direct RV bypass systems include the intra-corporeal axial flow Impella RP pump and the extracorporeal centrifugal flow pumps including the Tandem Heart RVAD or Protek Duo dual-lumen cannula. The Impella RP is a 23 French (Fr) axial flow pump mounted on a 9 Fr catheter and is placed via right femoral venous access. An updated version of the Impella RP for delivery via the internal jugular vein is currently under development. The RECOVER RIGHT trial demonstrated safety, feasibility and efficacy of the Impella RP in patients with RV failure due to acute MI or after LVAD implantation with flow rates ranging between 2 and 5 LPM and significantly improved total cardiac output and reduced CVPs.[55] The TandemHeart RVAD employs an extracorporeal centrifugal flow pump and two cannulas placed in the RA and pulmonary artery via femoral or internal jugular vein access.[56] The THRIVE registry reported improved cardiac output, reduced CVPs, and reduced pulmonary pressures with mean flows of 4.2 $\pm$ 1.3 L/min with the TandemRVAD.[57] The Protek Duo is a large bore (29 or 31 Fr) dual-lumen cannula delivered via the right internal jugular vein and employs an extracorporeal pump to simultaneously displace blood from the RA to the pulmonary artery. Several case series have illustrated the efficacy of the Protek Duo Cannula.[58,59] Indirect RV bypass with VA-ECMO displaces blood from the RA into the arterial circulation using two cannulas and an extracorporeal pump. This approach has been described in several case series but has not been prospectively evaluated.

Patient selection for acute mechanical circulatory support for right ventricular

Guidelines and widely adopted algorithms for use of RV support are lacking.[8] In the setting of AMI where RV geometry has not permanently changed due to maladaptive remodelling, any of the direct or indirect RV bypass systems work effectively. The Impella RP and TandemHeart RVAD can be rapidly deployed via the femoral vein which is readily accessible in the interventional catheterization laboratory and does not require a perfusionist. The Protek Duo requires large bore jugular vein access which can be cumbersome in the setting of acute MI but does enable ambulation. For patients with non-AMI CS or after cardiac surgery, early identification, and initiation of RV support within 48 h of shock onset is likely to be associated with improved clinical outcomes irrespective of the technology employed. If prolonged RV support is expected, then ambulatory options should be considered. If shock progresses to involve end-organ failure, then consideration for VA-ECMO or the combination of VA-ECMO with a concomitant LV decompression system may be appropriate as first-line therapy.

Timing of initiation of acute mechanical circulatory support

Recognizing when a patient is deteriorating with pharmacologic management and requires MCS is critical to optimizing patient outcomes. Pre-mature implantation may expose the patient to unnecessary risks of device-related complications while delayed implantation may not be able to reverse end-stage shock. The presence of RV failure increases the mortality risk associated with all SCAI shock stages, making timely recognition of decompensation even more important in this scenario.[11] Determining the appropriate time to initiate MCS requires careful monitoring of haemodynamic and metabolic parameters. While PAC use did not improve survival in a broad population of patients with HF, recent observational data limited to patients with CS has demonstrated a positive association with survival.[20,60] In a contemporary cohort of nearly 1500 patients with CS, presence of complete haemodynamic data (a proxy for PA catheter use) was associated with a nearly 40% lower odds of mortality compared with patients without any haemodynamic data available.[20] However, haemodynamic data alone cannot determine the adequacy of pharmacologic management as it cannot identify metabolic derangement resulting from decreased cardiac output. This transition from haemodynamic shock to haemometabolic shock is a critical turning point in a patient's disease course and is associated with a significantly increased mortality risk.[61] A recent analysis of the CULPRIT-SHOCK trial generated a biomarker risk score using cystatin C, lactate, interleukin-6, and NT-proBNP that demonstrated good discrimination in predicting mortality from AMI shock.[62] However, these markers are not routinely available in all centres in a timely fashion. Other metabolic markers such as urine output, creatinine, blood urea nitrogen, and transaminases can also indicate metabolic decompensation. It is important to monitor these metabolic parameters serially to understand the patient's clinical trajectory. In particular, the rate of lactate clearance over a period of 6–8 h has a strong association with mortality.[63] If metabolic parameters fail to improve despite aggressive pharmacologic management over the span of a few hours, MCS is indicated.

Management on device

Management of patients with RV failure on temporary MCS (tMCS) devices is similar to management of patients with left-sided MCS devices. Haemodynamic monitoring should be continued, and while there are no studies prospectively assessing specific haemodynamic targets, reasonable goals include CVP $<$14 mmHg, PCWP $<$18 mmHg, and cardiac index (CI) $>$2.2 L/min/m^2. Echocardiographic assessment, either via the transthoracic or transoesophageal approach, should be used early after MCS initiation and with clinical changes to monitor device position, ventricular size, septal position, and severity of valve disease. Markers of haemolysis, including LDH and plasma free haemoglobin, should be routinely monitored to screen for haemolysis.

All RV-MCS requires anticoagulation. Unfractionated heparin is recommended, titrated to a goal aPTT of 1.5–2$\times$ upper limit of normal, or an anti-Xa goal of 0.2–0.5 for routine cases. In the case of heparin-induced thrombocytopenia, anticoagulation should be changed to bivalirudin or argatroban according to institutional protocols. In cases where systemic anticoagulation is contraindicated (for example, intracranial haemorrhage, gastrointestinal bleeding, uncontrolled access site bleeding), MCS devices can be used without systemic anticoagulation, so long as high flows are maintained (minimum 3–4 L/min) to minimize the risk of device thrombosis. In the case of the Impella RP, heparinized purge fluid should be continued even in the absence of systemic anticoagulation.

Finally, routine critical care management should not be ignored during the period of MCS. This includes lung-protective ventilation, minimization of sedation and paralytics, and stress ulcer prophylaxis. In addition, aggressive physical therapy should be initiated whenever

Table 2 Percutaneous temporary mechanical circulatory support approaches in RVD

Author	PMID	Year	Study type	Population	Outcomes
Impella RP					
Cheung	24726682	2014	Multicentre retrospective cohort	$N = 18$ (15 Impella RD, 3 Impella RP) Aetiology • 39% post-MI • 11% myocarditis • 17% post-HT • 22% post-cardiotomy • 11% post-LVAD	30-day survival: 72% 1-year survival: 50% Haemodynamics: increased CI, decreased RAP
Anderson	26681124	2015	Multicentre prospective cohort	$N = 30$ Aetiology • 60% post-LVAD • 17% post-MI • 17% post-HT • 7% post-cardiotomy	Survival to discharge: 73% 6-month survival: 70%
Anderson	30241890	2018	Multicentre prospective cohort	$N = 60$ Aetiology • 52% post-LVAD • 22% post-cardiotomoy • 15% post-MI • 12% post-HT	30-day survival or escalation of therapy: 73% 180-day survival: 62% Haemodynamics: increased CI, decreased CVP
Jensen	29148290	2018	Single-centre retrospective cohort	$N = 6$ Aetiology • 33% post-MI • 33% cardiogenic shock • 33% post-cardiotomy	6-month survival: 33%
Elder	29514403	2018	Single-centre retrospective cohort	$N = 5$ Aetiology • 100% PE	Survival to discharge: 100% Haemodynamics: increased CI, increased SBP, decreased HR
Monteagudo-Vela	31769040	2020	Single-centre retrospective cohort	$N = 7$ Aetiology • 43% early post-LVAD • 28% late post-LVAD • 28% post-HT	30-day survival: 58% Haemodynamics: increased SBP
Qureshi	32129576	2020	Multicentre retrospective cohort	$N = 12$ adolescents Aetiology • 42% HT rejection • 25% myocarditis • 17% NICM • 8% post-cardiotomy • 8% cardiogenic shock	Survival to discharge: 83% Haemodynamics: decreased CVP
Gramegna	31866154	2020	Single-centre retrospective cohort	$N = 5$ Aetiology • 100% post-MI	30-day survival: 100% Haemodynamics: increased SBP, decreased CVP

Continued

Table 2 ***Continued***

Author	PMID	Year	Study type	Population	Outcomes
Shekiladze	32569445	2021	Single-centre retrospective cohort	*N* = 39 Aetiology • 28% post-MI • 23% acute PE • 21% post-cardiotomy • 15% post-LVAD • 13% NICM	30-day survival: 49% No haemodynamic data available
Tandem Heart RVAD					
Kapur	21868253	2011	Multicentre retrospective cohort	*N* = 9 Aetiology • 67% post-MI • 22% post-cardiotomy • 11% septic shock	Survival to discharge: 56% Haemodynamics: increased MAP, decreased CVP, increased RV stroke work
Kapur	24621838	2013	Multicentre retrospective cohort	*N* = 46 Aetiology • 33% post-valve surgery • 26% post-MI • 11% post-HT • 11% post-LVAD • 6% myocarditis • 6% chronic HF • 6% post-CABG	Survival to discharge: 43% Haemodynamics: increased CI, increased MAP, decreased CVP
Protek Duo					
Ravichandran	31986207	2018	Multicentre retrospective cohort	*N* = 17 Aetiology • 70% post-LVAD • 12% post-HT • 18% unknown	Weaned: 23% Surgical RVAD: 35% In-hospital mortality: 41%
Salna	29095736	2020	Single-centre retrospective cohort	*N* = 27 Aetiology • 100% post-LVAD	Survival to discharge: 85% 1-year survival: 81%
Rotaflow					
Joshi	34313320	2021	Single-centre retrospective cohort	*N* = 10 Aetiology • 100% post-LVAD	30-day survival: 80% 90-day survival: 60%
Natanov	34270709	2021	Single-centre retrospective cohort	*N* = 14 Aetiology • 100% post-LVAD	Survival to discharge: 86% Haemodynamics: decreased inotrope/vasopressor doses
VA-ECMO					
Taghavi	15511449	2004	Single-centre retrospective cohort	*N* = 28 (13 VA-ECMO, 15 surgical RVAD) Aetiology • 100% post-HT	ECMO vs. RVAD: • Weaned from support: 77 vs. 13% • Death on support: 15 vs. 47% Haemodynamics (both groups): increased CO, decreased CVP, decreased mPAP, decreased PVR

Continued

Table 2 *Continued*

Author	PMID	Year	Study type	Population	Outcomes
Noly	24659551	2014	Single-centre retrospective cohort	$N = 10$ Aetiology • 100% post-LVAD	Weaned from support: 80% Death on support: 20%
Riebandt	29045747	2018	Single-centre retrospective cohort	$N = 32$ Aetiology • 100% post-LVAD	30-day survival: 81% 1-year survival: 75% Haemodynamics: decreased CVP, decreased mPAP, increased CO
Pozzi	29788286	2018	Single-centre retrospective cohort	$N = 16$ Aetiology • 100% post-HT	Survival to discharge: 50%
Djordjevic	31692108	2020	Single-centre retrospective cohort	$N = 64$ Aetiology • 100% post-cardiotomy	30-day survival: 12%

possible. Devices implanted surgically or percutaneously via upper extremity vessels are compatible with patient ambulation with appropriate nursing support. However, femoral access generally precludes ambulation with Impella RP or VA-ECMO.

Weaning temporary mechanical circulatory support devices

All patients on RV-tMCS should be assessed for weaning readiness daily, as this may reduce the overall duration of MCS use. Numerous predictors of weaning readiness have been proposed, and all highlight the importance of resolution of metabolic derangement, minimal or no inotropic or vasopressor support requirements, electrical stability, and minimal or no ventilatory support requirements.[64] Once these conditions have been met, bedside weaning trials should be attempted. There are no prospectively validated weaning protocols, but published experience suggests reducing MCS support in a stepwise fashion over the course of 2–12 h, with frequent haemodynamic and echocardiographic monitoring. The exact mechanism of decreasing device support will vary by platform. For example, the Impella RP may be weaned by decreasing the performance level, while the ProTek Duo can be weaned by decreasing the pump speed or by decreasing directly measured blood flow through the circuit. Favourable signs as device support is reduced include stability of CVP, augmentation of RV systolic function without progressive RV dilation, return or augmentation of pulmonary artery pulsatility, stability of arterial blood pressure, and stability of pulmonary arterial saturation. Providers should be careful to ensure adequate anticoagulation prior to weaning to reduce the risk of device thrombosis during periods of low flow. If weaning trials are successful, initiation of low-dose inotropic support can be considered to support decannulation. It is important to remember that a successful weaning trial at low device support does not always predict successful device explant.

Failure to wean

For patients who are unable to wean from RV-tMCS, options for definitive therapy are limited.[65,66] In contrast to LV-predominant shock, there are no durable RV-MCS devices that are approved to support patients in the outpatient setting. For patients requiring biventricular MCS, bilateral durable LVAD implantation has been reported, though this strategy is not widely available due to complexity and expense.[67] For most patients, transplantation is the only available treatment approach. For patients with isolated PAH, studies have shown comparable outcomes between heart–lung transplant and bilateral lung transplant, demonstrating the ability of the RV to recover once the high afterload state has been resolved.[68] For most other aetiologies of RV failure, heart transplant (with concomitant lung transplant if pulmonary hypertension is also present) is necessary.

Conclusion

Irrespective of the underlying cause, RV failure is associated with significant morbidity and mortality. The RV is exquisitely sensitive to changes in pre-load and afterload and when impaired can significantly reduce total cardiac output by limiting left ventricular filling. RV failure also promotes systemic venous congestion, which exacerbates multi-organ hypoperfusion and can rapidly accelerate CS. Management of RV failure begins with rapid identification using either echocardiographic or invasive haemodynamic indices followed by optimization of RV pre-load and afterload using pharmacologic approaches. Temporary MCS options for the RV are growing in number; however, prospective studies and uniform guidelines for implementation of these technologies are limited.

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References

1. Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK, Kociol RD, Lewis EF, Mehra MR, Pagani FD, Raval AN, Ward C. Evaluation and management of right-sided heart failure: a scientific statement from the American Heart Association. *Circulation* 2018;**137**:e578–e622.
2. Feneley MP, Gavaghan TP, Baron DW, Branson JA, Roy PR, Morgan JJ. Contribution of left ventricular contraction to the generation of right ventricular systolic pressure in the human heart. *Circulation* 1985;**71**:473–480.
3. Pahuja M, Burkhoff D. Right ventricular afterload sensitivity has been on my mind. *Circ Heart Fail* 2019;**12**:e006345.
4. Haddad F, Hunt SA, Rosenthal DN, Murphy DJ. Right ventricular function in cardiovascular disease, part I: anatomy, physiology, aging, and functional assessment of the right ventricle. *Circulation* 2008;**117**:1436–1448.
5. Noordegraaf A V, Chin KM, Haddad F, Hassoun PM, Hemnes AR, Hopkins SR, Kawut SM, Langleben D, Lumens J, Naeije R. Pathophysiology of the right ventricle and of the pulmonary circulation in pulmonary hypertension: an update. *Eur Respir J* 2019; **53**:1801900.
6. Sanz J, Sanchez-Quintana D, Bossone E, Bogaard HJ, Naeije R. Anatomy, function, and dysfunction of the right ventricle: JACC State-of-the-Art review. *J Am Coll Cardiol* 2019;**73**:1463–1482.
7. Kanwar M, McDonnell BJ, Rosenblum H, Cockcroft JR, Stohr EJ, Cornwell WK III. Bionic women and men—part 3: right ventricular dysfunction in patients implanted with left ventricular assist devices. *Exp Physiol* 2020;**105**:759–762.
8. Kapur NK, Paruchuri V, Jagannathan A, Steinberg D, Chakrabarti AK, Pinto D, Aghili N, Najjar S, Finley J, Orr NM, Tempelhof M, Mudd JO, Kiernan MS Pham DT, DeNofrio D. Mechanical circulatory support for right ventricular failure. *JACC: Heart Failure* 2013;**1**:127–134.
9. Brener MI, Masoumi A, Ng VG, Tello K, Bastos MB, Cornwell WK III, Hsu S, Tedford RJ, Lurz P, Rommel KP, Kresoja KP, Nagueh SF, Kanwar MK, Kapur NK, Hiremath G, Sarraf M, Van Den Enden AJM, Van Mieghem NM, Heerdt PM, Hahn RT, Kodali SK, Sayer GT, Uriel N, Burkhoff D. Invasive right ventricular pressure-volume analysis: basic principles, clinical applications, and practical recommendations. *Circ Heart Fail* 2022;**15**:e009101.
10. Brener MI, Burkhoff D, Sunagawa K. Effective arterial elastance in the pulmonary arterial circulation: derivation, assumptions, and clinical applications. *Circ Heart Fail* 2020;**13**:e006591.
11. Thayer KL, Zweck E, Ayouty M, Garan AR, Hernandez-Montfort J, Mahr C, Morine KJ, Newman S, Jorde L, Haywood JL, Harwani NM, Esposito ML, Davila CD, Wencker D, Sinha SS, Vorovich E, Abraham J, O'Neill W, Udelson J, Burkhoff D, Kapur NK. Invasive hemodynamic assessment and classification of in-hospital mortality risk among patients with cardiogenic shock. *Circ Heart Fail* 2020;**13**:e007099.
12. Goldstein JA. Pathophysiology and management of right heart ischemia. *J Am Coll Cardiol* 2002;**40**:841–853.
13. Mehta SR, Eikelboom JW, Natarajan MK, Diaz R, Yi C, Gibbons RJ, Yusuf S. Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. *J Am Coll Cardiol* 2001;**37**:37–43.
14. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, Gibbs JS, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Vonk Noordegraaf A, Zamorano JL, Zompatori M, Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014;**35**:3033–3069, 3069a-3069.
15. Iglesias-Garriz I, Olalla-Gomez C, Garrote C, Lopez-Benito M, Martin J, Alonso D, Rodríguez MAR. Contribution of right ventricular dysfunction to heart failure mortality: a meta-analysis. *Rev Cardiovasc Med* 2012;**13**:e62–e69.
16. Lewis JF, Webber JD, Sutton LL, Chesoni S, Curry CL. Discordance in degree of right and left ventricular dilation in patients with dilated cardiomyopathy: recognition and clinical implications. *J Am Coll Cardiol* 1993;**21**:649–654.
17. Harjola VP, Mebazaa A, Celutkiene J, Bettex D, Bueno H, Chioncel O, Crespo-Leiro MG, Falk V, Filippatos G, Gibbs S, Leite-Moreira A, Lassus J, Masip J, Mueller C, Mullens W, Naeije R, Nordegraaf AV, Parissis J, Riley JP, Ristic A, Rosano G, Rudiger A, Ruschitzka F, Seferovic P, Sztrymf B, Vieillard-Baron A, Yilmaz MB, Konstantinides S. 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**:226–241.
18. Lala A, Guo Y, Xu J, Esposito M, Morine K, Karas R, Katz SD, Hochman JS, Burkhoff D, Kapur NK. Right ventricular dysfunction in acute myocardial infarction complicated by cardiogenic shock: a hemodynamic analysis of the should we emergently revascularize occluded coronaries for cardiogenic shock (SHOCK) Trial and Registry. *J Card Fail* 2018;**24**:148–156.
19. Jain P, Thayer KL, Abraham J, Everett KD, Pahuja M, Whitehead EH, Schwartz BP, Lala A, Sinha SS, Kanwar MK, Garan AR, Hernandez-Monfort JA, Mahr C, Vorovich E, Wencker D, Mccabe JM, Jones T, Goud M, Baca P, Harwani N, Burkhoff D, Kapur NK. Right ventricular dysfunction is common and identifies patients at risk of dying in cardiogenic shock. *J Card Fail* 2021;**27**:1061–1072.
20. Garan AR, Kanwar M, Thayer KL, Whitehead E, Zweck E, Hernandez-Montfort J, Mahr C, Haywood JL, Harwani NM, Wencker D, Sinha SS, Vorovich E, Abraham J, O'Neill W, Burkhoff D, Kapur N. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. *JACC Heart fail* 2020;**8**:903–913.
21. Zochios V, Jones N. Acute right heart syndrome in the critically ill patient. *Heart Lung Vessel* 2014;**6**:157–170.
22. Piazza G, Goldhaber SZ. The acutely decompensated right ventricle: pathways for diagnosis and management. *Chest* 2005;**128**:1836–1852.
23. Ryan JJ, Tedford RJ. Diagnosing and treating the failing right heart. *Curr Opin Cardiol* 2015;**30**:292–300.
24. Damman K, van Deursen VM, Navis G, Voors AA, van Veldhuisen DJ, Hillege HL. Increased central venous pressure is associated with impaired renal function and mortality in a broad spectrum of patients with cardiovascular disease. *J Am Coll Cardiol* 2009;**53**:582–588.
25. Sundaram V, Fang JC. Gastrointestinal and liver issues in heart failure. *Circulation* 2016;**133**:1696–1703.
26. Poelzl G, Ess M, Mussner-Seeber C, Pachinger O, Frick M, Ulmer H. Liver dysfunction in chronic heart failure: prevalence, characteristics and prognostic significance. *Eur J Clin Invest* 2012;**42**:153–163.
27. Sandek A, Bauditz J, Swidsinski A, Buhner S, Weber-Eibel J, von Haehling S, Schroedl W, Karhausen T Doehner W, Rauchhaus M, Poole-Wilson P, Volk HD, Lochs H, Anker SD. Altered intestinal function in patients with chronic heart failure. *J Am Coll Cardiol* 2007;**50**:1561–1569.
28. Portnoy SG, Rudski LG. Echocardiographic evaluation of the right ventricle: a 2014 perspective. *Curr Cardiol Rep* 2015;**17**:21.
29. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;**23**:685–713.
30. Korabathina R, Heffernan KS, Paruchuri V, Patel AR, Mudd JO, Prutkin JM, Orr NM, Weintraub A, Kimmelstiel CD, Kapur NK. The pulmonary artery pulsatility index identifies severe right ventricular dysfunction in acute inferior myocardial infarction. *Catheter Cardiovasc Interv* 2012;**80**:593–600.
31. Morine KJ, Kiernan MS, Pham DT, Paruchuri V, Denofrio D, Kapur NK. Pulmonary artery pulsatility index is associated with right ventricular failure after left ventricular assist device surgery. *J Card Fail* 2016;**22**:110–116.
32. Kapur NK, Esposito ML, Bader Y, Morine KJ, Kiernan MS, Pham DT, Burkhoff D. Mechanical circulatory support devices for acute right ventricular failure. *Circulation* 2017;**136**:314–326.
33. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. *Circulation* 2008;**117**:1717–1731.
34. Shah AS, Atkins BZ, Hata JA, Tai O, Kypson AP, Lilly RE, Koch WJ, Glower DD. Early effects of right ventricular volume overload on ventricular performance and beta-adrenergic signaling. *J Thorac Cardiovasc Surg* 2000;**120**:342–349.
35. Wichter T, Schafers M, Rhodes CG, Borggrefe M, Lerch H, Lammertsma AA, Hermansen F, Schober O, Breithardt G, Camici PG. Abnormalities of cardiac sympathetic innervation in arrhythmogenic right ventricular cardiomyopathy: quantitative assessment of presynaptic norepinephrine reuptake and postsynaptic beta-adrenergic receptor density with positron emission tomography. *Circulation* 2000;**101**:1552–1558.
36. Pela G, Raddino R, Missale C, Condorelli E, Spano PF, Visioli O. The adrenergic beta system in an experimental model of heart failure. *Cardiologia* 1990;**35**:543–550.
37. Bristow MR, Ginsburg R, Minobe W, Cubicciotti RS, Sageman WS, Lurie K, Billingham ME, Harrison DC, Stinson EB. Decreased catecholamine sensitivity and beta-adrenergic-receptor density in failing human hearts. *N Engl J Med* 1982;**307**: 205–211.
38. Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, Young JB, Tang WHW. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol* 2009;**53**:589–596.
39. Testani JM, Khera AV, St John Sutton MG, Keane MG, Wiegers SE, Shannon RP, Kirkpatrick JN. Effect of right ventricular function and venous congestion on cardiorenal interactions during the treatment of decompensated heart failure. *Am J Cardiol* 2010;**105**:511–516.
40. Arrigo M, Huber LC, Winnik S, Mikulicic F, Guidetti F, Frank M, Flammer AJ, Ruschitzka F. Right ventricular failure: pathophysiology, diagnosis and treatment. *Card Fail Rev* 2019;**5**:140–146.
41. Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WHW, Orso F, Rossignol P, Metra M, Filippatos G, Seferovic PM, Ruschitzka F, Coats AJ. The use of diuretics in heart failure with congestion—

a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2019;**21**:137–155.
42. Murphy MB, Elliott WJ. Dopamine and dopamine receptor agonists in cardiovascular therapy. *Crit Care Med* 1990;**18**:S14–S18.
43. Edwards RM, Trizna W, Kinter LB. Renal microvascular effects of vasopressin and vasopressin antagonists. *Am J Physiol* 1989;**256**:F274–F278.
44. Costanzo MR, Jessup M. Treatment of congestion in heart failure with diuretics and extracorporeal therapies: effects on symptoms, renal function, and prognosis. *Heart Fail Rev* 2012;**17**:313–324.
45. Marenzi G, Muratori M, Cosentino ER, Rinaldi ER, Donghi V, Milazzo V, Ferramosca E, Borghi C, Santoro A, Agostoni P. Continuous ultrafiltration for congestive heart failure: the CUORE trial. *J Card Fail* 2014;**20**:9–17.
46. Bart BA, Goldsmith SR, Lee KL, Redfield MM, Felker GM, O'Connor CM, Chen HH, Rouleau JL, Givertz MM, Semigran MJ, Mann D, Deswal A, Bull DA, Lewinter MM, Braunwald E. Cardiorenal rescue study in acute decompensated heart failure: rationale and design of CARRESS-HF, for the Heart Failure Clinical Research Network. *J Cardiac Fail* 2012;**18**:176–182.
47. Costanzo MR, Guglin ME, Saltzberg MT, Jessup ML, Bart BA, Teerlink JR, Jaski BE, Fang JC, Feller ED, Haas GJ, Anderson AS, Schollmeyer MP, Sobotka PA. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol* 2007;**49**:675–683.
48. Bart BA, Goldsmith SR, Lee KL, Givertz MM, O'Connor CM, Bull DA, Redfield MM, Deswal A, Rouleau JL, LeWinter MM, Ofili EO, Stevenson LW, Semigran MJ, Felker GM, Chen HH, Hernandez AF, Anstrom KJ, McNulty SE, Velazquez EJ, Ibarra JC, Mascette AM, Braunwald E. Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *N Engl J Med* 2012;**367**:2296–2304.
49. Disselkamp M, Adkins D, Pandey S, Coz Yataco AO. Physiologic approach to mechanical ventilation in right ventricular failure. *Ann Am Thorac Soc* 2018;**15**:383–389.
50. Tavazzi G. Mechanical ventilation in cardiogenic shock. *Curr Opin Crit Care* 2021;**27**:447–453.
51. Sharan L, Stackhouse K, Awerbach JD, Bashore TM, Krasuski RA. Effect of patent foramen ovale in patients with pulmonary hypertension. *Am J Cardiol* 2018;**122**:505–510.
52. Glanville AR, Burke CM, Theodore J, Robin ED. Primary pulmonary hypertension. Length of survival in patients referred for heart-lung transplantation. *Chest* 1987;**91**:675–681.
53. Rozkovec A, Montanes P, Oakley CM. Factors that influence the outcome of primary pulmonary hypertension. *Br Heart J* 1986;**55**:449–458.
54. Lehner A, Schulze-Neick I, Fischer M, Fernandez-Rodriguez S, Ulrich S, Haas NA, Jakob A. The creation of an interatrial right-to-left shunt in patients with severe, irreversible pulmonary hypertension: rationale, devices, outcomes. *Curr Cardiol Rep* 2019;**21**:31.
55. Anderson MB, Goldstein J, Milano C, Morris LD, Kormos RL, Bhama J, Kapur NK, Bansal A, Garcia J, Baker JN, Silvestry S, Holman WL, Douglas PS, O'Neill W. Benefits of a novel percutaneous ventricular assist device for right heart failure: the prospective RECOVER RIGHT study of the Impella RP device. *J Heart Lung Transplant* 2015;**34**:1549–1560.
56. Kiernan MS, Grandin EW, Brinkley MJR, Kapur NK, Pham DT, Ruthazer R, Rame JE, Atluri P, Birati EY, Oliveira GH, Pagani FD, Kirklin JK, Naftel D, Kormos RL, Teuteberg JJ, DeNofrio D. Early right ventricular assist device use in patients undergoing continuous-flow left ventricular assist device implantation: incidence and risk factors from the interagency registry for mechanically assisted circulatory support. *Circ Heart Fail* 2017;**10**:e003863.
57. Kapur NK, Paruchuri V, Jagannathan A, Steinberg D, Chakrabarti AK, Pinto D, Aghili N, Najjar S, Finley J, Orr NM, Tempelhof M, Mudd JO, Kiernan MS, Pham DT, DeNofrio D. Mechanical circulatory support for right ventricular failure. *JACC Heart Fail* 2013;**1**:127–134.
58. Aggarwal V, Einhorn BN, Cohen HA. Current status of percutaneous right ventricular assist devices: first-in-man use of a novel dual lumen cannula. *Catheter Cardiovasc Interv* 2016;**88**:390–396.
59. Bermudez CA, Lagazzi L, Crespo MM. Prolonged support using a percutaneous OxyRVAD in a patient with end-stage lung disease, pulmonary hypertension, and right cardiac failure. *ASAIO J* 2016;**62**:e37–e40.
60. Binanay C, Califf RM, Hasselblad V, O'Connor CM, Shah MR, Sopko G, Stevenson LW, Francis GS, Leier CV, Miller LW; ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA* 2005;**294**:1625–1633.
61. Zweck E, Thayer KL, Helgestad OKL, Kanwar M, Ayouty M, Garan AR, Hernandez-Montfort J, Mahr C, Wencker D, Sinha SS, Vorovich E, Abraham J, O'Neill W, Li S, Hickey GW, Josiassen J, Hassager Cn, Jensen LO, Holmvang L, Schmidt H, Ravn HB, Møller JE, Burkhoff D, Kapur NK. Phenotyping cardiogenic shock. *J Am Heart Assoc* 2021;**10**:e020085.
62. Ceglarek U, Schellong P, Rosolowski M, Scholz M, Willenberg A, Kratzsch J, Zeymer U, Fuernau G, de Waha-Thiele S, Büttner P, Jobs A, Freund A, Desch S, Feistritzer HJ, Isermann B, Thiery J, Pöss J, Thiele H. The novel cystatin C, lactate, interleukin-6, and N-terminal pro-B-type natriuretic peptide (CLIP)-based mortality risk score in cardiogenic shock after acute myocardial infarction. *Eur Heart J* 2021;**42**:2344–2352.
63. Marbach JA, Stone S, Schwartz B, Pahuja M, Thayer KL, Faugno AJ, Chweich H, Rabinowitz JB, Kapur NK. Lactate clearance is associated with improved survival in cardiogenic shock: a systematic review and meta-analysis of prognostic factor studies. *J Card Fail* 2021;**27**:1082–1089.
64. Randhawa VK, Al-Fares A, Tong MZY, Soltesz EG, Hernandez-Montfort J, Taimeh Z, Weiss AJ, Menon V Campbell J, Cremer P, Estep JD. A pragmatic approach to weaning temporary mechanical circulatory support: a state-of-the-art review. *JACC Heart Fail* 2021;**9**:664–673.
65. Bernhardt AM, De By TM, Reichenspurner H, Deuse T. Isolated permanent right ventricular assist device implantation with the HeartWare continuous-flow ventricular assist device: first results from the European Registry for Patients with Mechanical Circulatory Support. *Eur J Cardiothorac Surg* 2015;**48**:158–162.
66. Vullaganti S, Tibrewala A, Rich JD, Pham DT, Rich S. The use of a durable right ventricular assist device for isolated right ventricular failure due to combined pre- and postcapillary pulmonary hypertension. *Pulm Circ* 2019;**9**:2045894019831222.
67. Maltais S, Womack S, Davis ME, Danter MR, Kushwaha SS, Stulak JM, Haglund N. Surgical considerations and challenges for bilateral continuous-flow durable device implantation. *ASAIO J* 2016;**62**:e18–e21.
68. Brouckaert J, Verleden SE, Verbelen T, Coosemans W, Decaluwe H, De Leyn P, Depypere L, Nafteux P, Van Veer H, Meyns B, Rega F, Van De Velde M, Poortmans G, Rex S, Neyrinck A, Van den Berghe G, Vlasselaers D, Van Cleemput J, Budts W, Vos R, Quarck R, Belge C, Delcroix M, Verleden GM, Van Raemdonck D. Double-lung versus heart-lung transplantation for precapillary pulmonary arterial hypertension: a 24-year single-center retrospective study. *Transpl Int* 2019;**32**:717–729.