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JACC REVIEW TOPIC OF THE WEEK

Managing Patients With Short-Term Mechanical Circulatory Support

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Tim Balthazar, MD,[a] Christophe Vandenbriele, MD, PhD,[a,b] Frederik H. Verbrugge, MD, PhD,[c,d] Corstiaan Den Uil, MD, PhD,[e,f] Annemarie Engström, MD, PhD,[e,f] Stefan Janssens, MD, PhD,[a] Steffen Rex, MD, PhD,[g] Bart Meyns, MD, PhD,[h] Nicolas Van Mieghem, MD, PhD,[f] Susanna Price, MD, PhD,[b] Tom Adriaenssens, MD, PhD[a]

ABSTRACT

The use of mechanical circulatory support for patients presenting with cardiogenic shock is rapidly increasing. Currently, there is only limited and conflicting evidence available regarding the role of the Impella (a microaxial, continuous-flow, short-term, left or right ventricular assist device) in cardiogenic shock; further randomized trials are needed. Patient selection, timing of implantation, and post-implantation management in the cardiac intensive care unit are crucial elements for success. Particular challenges at the bedside include the practical management of anticoagulation, evaluation of correct device position, and the approach to use in a patient with signs of insufficient hemodynamic support. Profound knowledge of these issues is required to enable the maximal potential of the device. This review provides a comprehensive overview of the short-term assist device and describes a practical approach to optimize care for patients supported with the device. (J Am Coll Cardiol 2021;77:1243–56) © 2021 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Cardiogenic shock (CS) is the most severe manifestation of acute heart failure. Although a uniform definition is lacking, CS basically represents the situation whereby cardiac output is insufficient to meet the basic metabolic requirements needed to ensure proper organ function and tissue integrity (1,2). A deleterious downward spiral of systemic inflammatory response syndrome (SIRS) and multiple organ failure rapidly ensues, making quick restoration of tissue perfusion the first priority (3). Mechanical circulatory support (MCS) allows immediate restoration of tissue perfusion and is increasingly used in CS (4). The Impella (Abiomed, Danvers, Massachusetts) is an emerging percutaneous ventricular assist device (pVAD). It is a microaxial, continuous-flow pump, placed over the aortic or pulmonary valve to support the failing ventricle, with blood flows up to 5.5 l/min. Over the 2004 to 2016 period, uptake of pVADs in the United States steadily increased from 10% to 32% among patients with CS after percutaneous coronary intervention (5).

The goal of the current review was to discuss the particular challenges that come with managing patients in the cardiac intensive care unit (CICU) with a pVAD and to offer a comprehensive practical approach.

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From the [a]Department of Cardiovascular Diseases, University Hospitals Leuven, Leuven, Belgium; [b]Department of Adult Intensive Care, Royal Brompton & Harefield NHS Foundation Trust, London, United Kingdom; [c]Department of Cardiovascular Diseases, University Hospitals Brussels, Brussels, Belgium; [d]Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium; [e]Department of Intensive Care Medicine, Erasmus Medical Centre, Rotterdam, the Netherlands; [f]Department of Cardiology, Erasmus Medical Centre, Rotterdam, the Netherlands; [g]Department of Anaesthesiology, University Hospitals Leuven, Leuven, Belgium; and the [h]Department of Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium.
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ABBREVIATIONS AND ACRONYMS

CICU = cardiac intensive care unit

CP = cardiac power

CS = cardiogenic shock

CVP = central venous pressure

IABP = intra-aortic balloon pump

LV = left ventricular

MCS = mechanical circulatory support

PAPi = pulmonary artery pulsatility index

$PvaCO_2$ gap = mixed venous partial pressure of carbon dioxide (Pco_2) minus arterial Pco_2

pVAD = percutaneous ventricular assist device

RP = right percutaneous

RV = right ventricular

SIRS = systemic inflammatory response syndrome

SvO_2 = mixed venous oxygen saturation

UFH = unfractionated heparin

VA-ECMO = veno-arterial extracorporeal membrane oxygenation

CURRENT EVIDENCE

Despite increasing left ventricular (LV) pVAD uptake, only 2 randomized clinical trials have been performed, both neutral with respect to survival (**Table 1**). However, both trials were underpowered and had different designs. The ISAR-SHOCK (Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock; NCT00417378) trial of the Impella 2.5 versus an intra-aortic balloon pump (IABP) was actually a feasibility study targeting hemodynamic improvements (6). An important limitation of the IMPRESS in Severe Shock (Impella Versus IABP Reduces Mortality in STEMI Patients Treated With Primary PCI in Severe Cardiogenic Shock; NTR3450) trial, which aimed to investigate the effect of pVAD versus IABP support on mortality in CS, was that outcomes were mainly driven by hypoxic encephalopathy due to the high proportion of patients with out-of-hospital cardiac arrest (92%) (7). In recent propensity-matched registries, compared with the IABP, LV pVAD use has been associated with higher risks of bleeding, stroke, and death, as well as higher costs (5,8,9). However, residual confounding because of indication bias with use in sicker patients cannot be excluded (9). Some centers have reported better survival rates in CS after implementation of a comprehensive shock protocol using LV pVADs (10,11). Studies comparing outcomes between patients supported by LV pVAD versus veno-arterial extracorporeal membrane oxygenation (VA-ECMO) suggest a lower incidence of major complications, such as bleeding, with pVAD use, although selection bias can be expected (12).

Even more limited evidence is available for right ventricular (RV) pVAD use. The RECOVER RIGHT (The Use of Impella RP Support System in Patients With Right Heart Failure; NCT01777607) study was the first to suggest the feasibility and safety of the right percutaneous (RP) device (13). A subsequent cohort study seemed to confirm these results, but in 2019, the U.S. Food and Drug Administration issued a warning because post-approval study data showed lower survival rates, creating controversy regarding the timing of implantation and patient selection criteria (14).

The large variability in patient outcomes between pVAD centers suggests that differences in patient selection (e.g., individual hemodynamics), timing of implantation (e.g., before revascularization), and post-intervention management in the CICU likely account for this heterogeneity (5,15).

HIGHLIGHTS

- Randomized trials are needed to guide optimum patient selection for MCS.
- Despite conflicting evidence, MCS is commonly used to manage patients in CS.
- Safer anticoagulation strategies are under investigation to reduce the incidence of bleeding, the most frequent complication of MCS.
- Multimodality approaches should be taken to evaluate the positioning of MCS devices.

PHYSIOLOGICAL BACKGROUND FOR SUPPORT WITH THE LV pVAD DEVICE

The Impella device family comprises an assortment of different micro-axial, continuous-flow pumps, all based on the same principle but with different support capacities (2.5 to 5.5 l/min) and designs (left- vs. right-sided support). The pump draws blood from its inlet inside the ventricle, pumping toward the outlet in the ascending aorta (or pulmonary artery). Because the device is continuously emptying the ventricle during systole and diastole, it reduces both afterload and preload. Pressure volume loops under LV pVAD support therefore exhibit a leftward shift and triangular shape with markedly reduced pressure volume area, representing less stroke work performed by the ventricle, and consequently reduced myocardial oxygen consumption (**Figure 1A**) (16). In contrast, VA-ECMO only decreases preload but at the same time substantially increases afterload, with no favorable impact on myocardial oxygen consumption (**Figure 1B**). Because of these opposing effects on ventricular filling pressures, the pVAD is increasingly used to unload the left heart during VA-ECMO (17).

INDICATION AND TIMING

Patients are ideally selected based on their individual hemodynamic phenotypes (**Figure 2**), need for oxygenation, and relevant comorbidities (**Central Illustration**). Most available studies (**Table 1**) have focused on CS in the setting of acute myocardial infarction. However, LV pVADs are now being used for a broad range of indications (18). The RP device

TABLE 1 Overview of the Most Important Studies on Impella

First Author (Ref. #)	Year	Population	Design	Key Outcomes	Limitations
Seyfarth et al. (6)	2008	AMI-CS N = 26	RCT pVAD vs. IABP	Higher increase in cardiac index with pVAD No difference in 30-day survival for pVAD (54%) vs. IABP (54%)	Underpowered for survival analysis Single-center
Ouweneel et al. (7)	2017	AMI-CS Impella: N = 24 IABP: N = 24	RCT pVAD vs. IABP	No difference in 30-day survival for pVAD (56%) vs IABP (50%)	Underpowered Survival driven by neurological outcome
Anderson et al. (13)	2015	Right heart failure N = 30	Prospective cohort study	Improved hemodynamics 30-day survival 73.3%	No control group
O'Neill et al. (15)	2018	AMI-CS N = 15,259	Retrospective analysis	51% survival to explantation Large variability in survival between centers Higher survival when RHC was used Higher survival in pre-PCI pVAD group	Retrospective No control group
Ogunbayo et al. (44)	2018	Non-AMI-CS pVAD: N = 1,414; IABP: N = 16,619	Retrospective analysis	pVAD associated with lower survival than IABP	Retrospective Indication bias
Anderson et al. (14)	2018	Right heart failure N = 60	Retrospective analysis	30-day survival: 72%	Retrospective No control group
Basir et al. (10)	2019	AMI-CS N = 171	Retrospective analysis	Survival to explant: 72% High adherence to specific shock protocol	Retrospective No control group
Schrage et al. (8)	2019	AMI-CS N = 237 (matched pairs)	Retrospective analysis with patient matching to IABP-Shock trial population	No difference in 30-day survival for pVAD (51.5%) vs. IABP (53.6%) More bleeding, vascular complications, and sepsis in pVAD patients	Retrospective
Amin et al. (5)	2019	Impella-supported PCI Impella and shock: N = 1,792; IABP and shock: N = 22,558	Retrospective analysis with propensity matching	Higher costs and more bleeding associated with pVAD use Significant variation in costs and outcome between centers	Not specifically investigating cardiogenic shock
Tehrani et al. (11)	2019	Mixed etiology N = 204	Retrospective before/after study investigating effect of team-based approach including Impella	Significant increase in 30-day survival after implementation of protocol (47% to 58% to 77%)	Not study on pVAD device as such Retrospective Indication bias
Karami (12)	2020	Mixed etiology pVAD: N = 90; ECMO: N = 38	Retrospective analysis	No difference in 30-day survival for pVAD (47%) vs. ECMO (51%) Lower complication rate in pVAD group	Retrospective Indication bias
Dhruva et al. (9)	2020	AMI-CS N = 1680 (matched pairs)	Retrospective analysis with propensity matching	Lower in-hospital survival in pVAD group (55%) vs. IABP (65.9%)	Retrospective High survival IABP group suggests selection bias
Helgestad et al. (45)	2020	AMI-CS Impella: N = 40 (matched pairs); IABP: N = 40 (matched pairs)	Retrospective analysis with propensity matching	Higher 30-day survival in pVAD group (60%) vs. control (32.5%) No difference in survival in IABP group vs. control	Retrospective IABP and Impella not directly compared

AMI-CS = acute myocardial infarction-induced cardiogenic shock; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; IABP-SHOCK = Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock; PCI = percutaneous coronary intervention; pVAD = percutaneous ventricular assist device; RCT = randomized controlled trial; RHC = right heart catheterization.

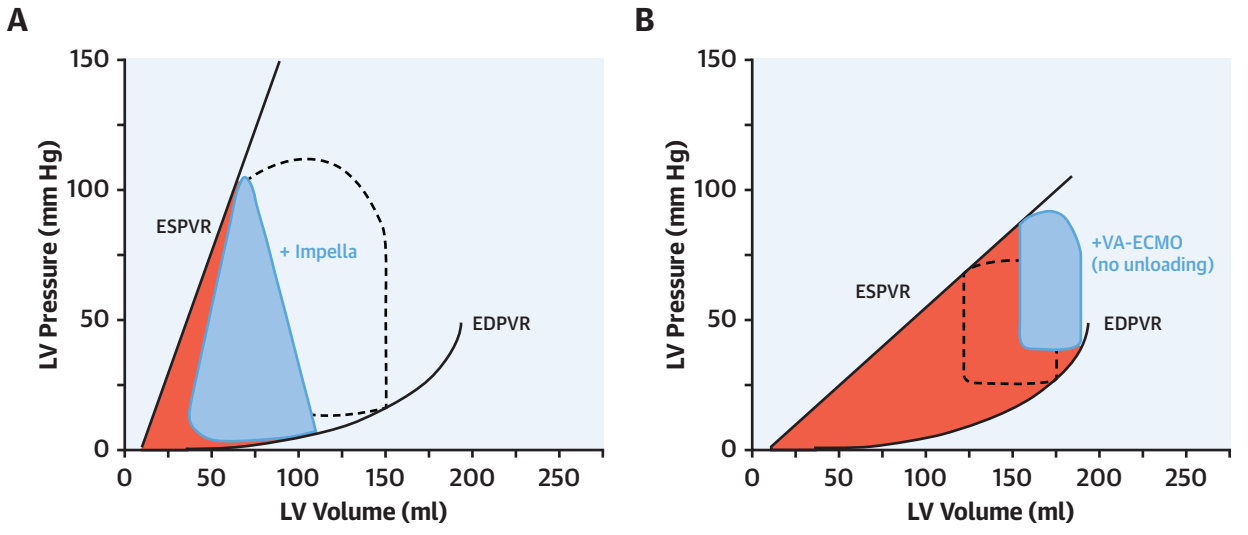
has mainly been studied in RV failure after durable VAD implantation or after cardiac surgery, but it has also been used in patients with myocardial ischemia, myocarditis, and even pulmonary embolism (either combined with an LV pVAD or in isolation) (19,20).

Current data suggest that implantation before revascularization maximizes the potential benefit (15) and that survival decreases by 9.9% for every 60 min of delay in MCS, stressing the importance of timely intervention (11). The stages of shock according to the Society for Cardiovascular Angiography and Interventions could also be useful in selecting the optimal time window for MCS, with preliminary data suggesting that stages C and D qualify most for pVAD use (21). Ideally, future studies will randomize patients based on such classification.

HEMOCOMPATIBILITY

Hemocompatibility is a major challenge for any MCS device (**Central Illustration**). Pump thrombosis is rare but has been reported, resulting in a strong case for routine systemic anticoagulation (22). Unsurprisingly, bleeding is the most frequent adverse event under pVAD support, with an incidence of ~30%, which is double the risk of an IABP but less than has been

FIGURE 1 Pressure-Volume Relationships in CS



(A) The pressure-volume relationship before **(dashed line)** and during **(blue line)** support with a percutaneous ventricular assist device (pVAD). **(B)** The evolution of the pressure-volume relationship before **(dashed line)** and during **(blue line)** support with veno-arterial extracorporeal membrane oxygenation (VA-ECMO). The pressure-volume area represents total ventricular energy expenditure, with ventricular stroke work represented as the **blue area** inside the loop and potential energy represented as the **red area** beneath the loop. Only with a pVAD is the pressure-volume area reduced, and thus energy expenditure decreases. CS = cardiogenic shock; EDPVR = end-diastolic pressure-volume relationship; ESPVR = end-systolic pressure-volume relationship; LV = left ventricular.

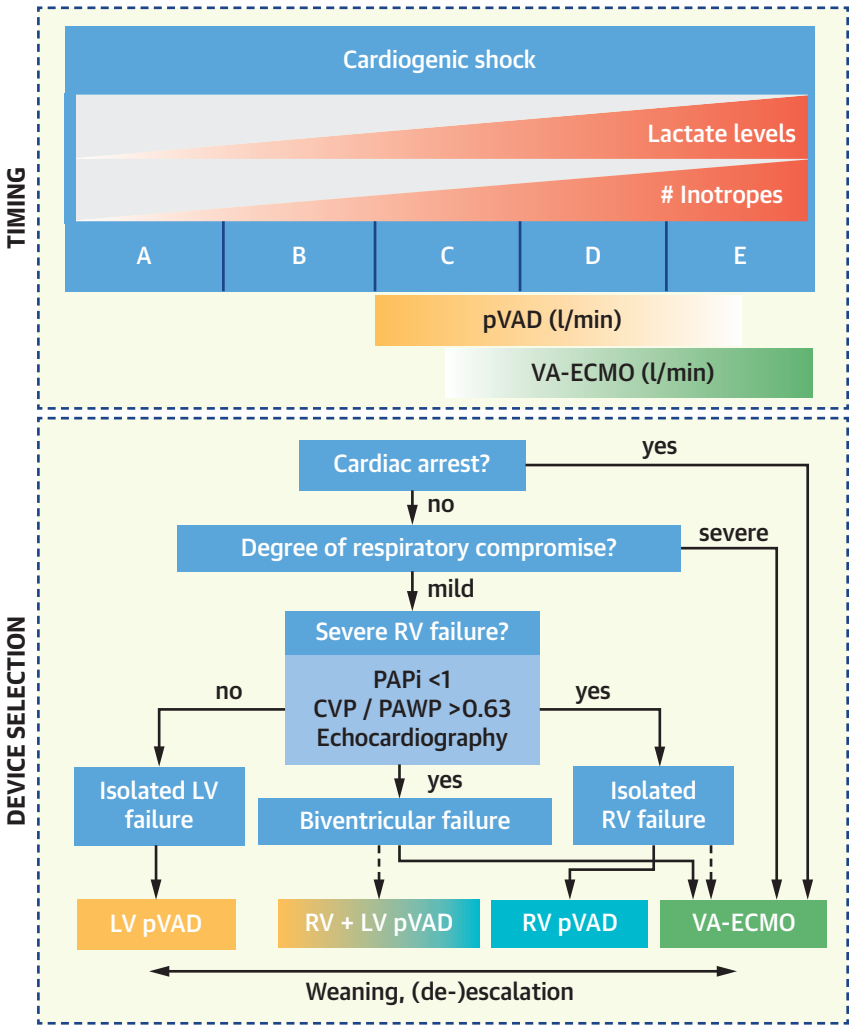
observed with VA-ECMO (9,12). There are no clear data regarding the optimal antithrombotic regimen.

An important characteristic of the pump system is the protection of its motor from direct contact with the blood through a heparinized dextrose solution that runs in the opposite direction of blood flow (**Figure 3**). This fluid, called purge solution, is administered at a variable flow rate by the controller to keep the purge pressure above the systolic blood pressure. Purge solution usually contains unfractionated heparin (UFH) at a concentration of 25 to 50 U/ml. Consequently, a variable UFH dose is administered by the pump into the systemic circulation (~8 to 10 U/kg/h for an average-sized individual). In case of bleeding (**Table 2**), the volume of purge fluid and hence the UFH dose administered can be reduced by increasing the viscosity of the solution (i.e., 10% dextrose instead of 5%), which according to Poiseuille's law, increases the resistance to purge flow. Because the device controller aims to keep purge pressure within range, flow automatically drops. The next step is to decrease the UFH heparin concentration in the purge solution.

In addition, low-grade systemic anticoagulation that is intrinsically provided through the pVAD design may offer opportunities for less intensive anticoagulation regimens. Preliminary results suggest the safe application of an intermediate anticoagulation target (anti-factor Xa, 0.2 to 0.3 U/ml or an activated partial thromboplastin time of 40 to 50 s), with a decreased bleeding risk compared with a classic therapeutic target (anti-factor Xa 0.3 to 0.5 U/ml or an activated thromboplastin time of 60 s) (23). Randomized studies on the appropriate level of anticoagulation are thus needed in patients supported by a pVAD.

Hemolysis is a feared complication of this pVAD, but its incidence has decreased over time with technical improvements. Nevertheless, hemolysis is still reported at meaningful frequencies of 8% to 63%, with large variations possibly related to differences in device management (7,24). Ideally, plasma-free hemoglobin should be measured on a daily basis. Significant hemolysis is defined as a free hemoglobin level >40 mg/dl or a sudden increase >27 mg/dl (25). Because hemolysis is most often caused by subtle abnormalities in device position or hypovolemia, the first step is to check volume status and device position (**Table 2**). In most cases, hemolysis can be eliminated by repositioning or optimizing cardiac preload (25). Alternatively, this may indicate pump thrombosis.

FIGURE 2 Algorithm for Device Selection in CS



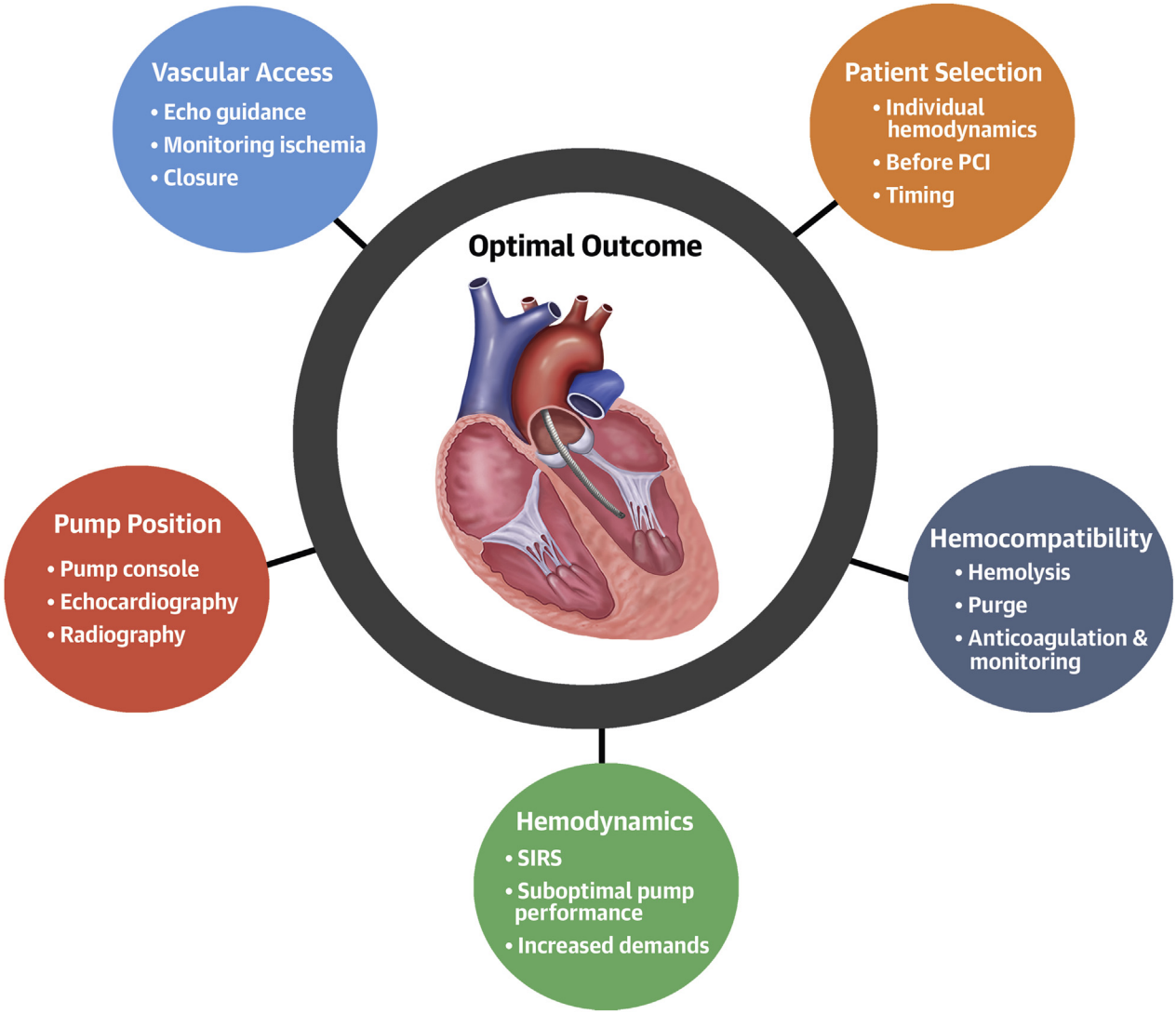
The **upper panel** illustrates a possible timeline for initiation of mechanical circulatory support. Lactate as well as inotropic support increase when the patient progresses through the shock stages according to the Society for Cardiovascular Angiography and Interventions. When shock severity increases, higher device flows are expected to be needed. The **lower panel** illustrates device selection based on individual hemodynamics and respiratory compromise. CS = cardiogenic shock; CVP = central venous pressure; PAPi = pulmonary artery pulsatility index; PAWP = pulmonary artery wedge pressure; RV = right ventricular; other abbreviations as in Figure 1.

pVAD POSITION AND REPOSITIONING

Adequate device position is key to obtaining optimal circulatory support, and susceptibility to dislocation is one of the most important pitfalls of pVAD use (Central Illustration). The ventricular inlet opening of a left-sided pump should typically be positioned at the midventricular level of the papillary muscles (3.5 to 4 cm from the aortic valve). For right-sided devices, the outflow opening should reside 2 to 4 cm into the pulmonary trunk and preferably into the left pulmonary artery. A position too deep within the ventricle results in frequent suction alarms, hemolysis, or ventricular arrhythmias. In contrast, a too distal position may result in the inlet being (partly) outside of the ventricle, resulting in inefficient support.

THE pVAD CONSOLE. The console provides a placement signal based on a pressure measurement at the outflow opening of the catheter (Figure 3). In addition, the electrical current used by the motor is continuously displayed in green (i.e., the motor current). As long as there is significant ventricular activity, the motor current should be pulsatile because

CENTRAL ILLUSTRATION **Optimizing Management of the Percutaneous Ventricular Assist Device–Supported Patient**

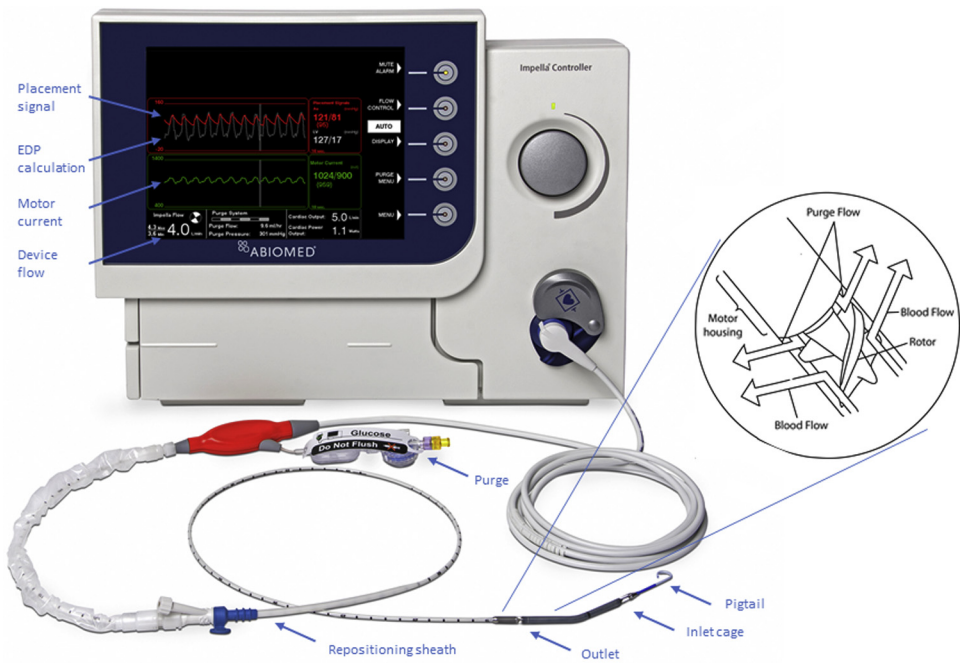


Balthazar, T. et al. J Am Coll Cardiol. 2021;77(9):1243–56.

The most important aspects of patient management are represented as pieces of a puzzle that fit together to result in an optimal outcome during percutaneous ventricular assist device support. All of these items are discussed throughout this review, from initial patient selection and access site management to issues that arise during further intensive care treatment such as hemocompatibility, device positioning, and optimizing hemodynamics. Echo = vascular ultrasound; PCI = percutaneous coronary intervention; SIRS = systemic inflammatory response syndrome.

the pressure difference between the inlet and outlet cannulas changes from systole (minimum) to diastole (maximum), resulting in variations of flow and energy consumed by the device. If the device dislocates and the inlet and outlet openings move toward the same compartment (aorta/pulmonic artery or ventricle), the motor current flattens. For the cardiac power (CP) device, the placement signal waveform (ventricular vs. aortic) can indicate the direction of dislocation. Recent technological improvements (the addition of an optical pressure sensor below the outlet) will enable the position of the device to be to even more precisely interpreted in the future. Importantly, in the case of significant ventriculoarterial uncoupling, arterial blood pressure is entirely dependent on blood flow through the pump. In such situations, both the

FIGURE 3 Setup of the CP Pump and Purge System



The most important elements of the system are highlighted in **blue**. The purge principle is illustrated by the drawing of the impeller showing the purge solution that runs in the opposite direction of blood flow, pushing blood away from the motor housing. CP = cardiac power; EDP = end-diastolic pressure. Adapted and reproduced with permission from Abiomed, Danvers, Massachusetts.

motor current and placement signal lack pulsatility, regardless of position (26).

CHEST RADIOGRAPHS. Chest radiographs are not routinely indicated for the evaluation of a left-sided pVAD. Nevertheless, it has been shown that the distance between the aortic valve and carina is relatively constant at 0.25 ± 0.05 times the thoracic width in men and 0.28 ± 0.05 times the thoracic width in women, allowing the insertion depth of a left-sided pVAD to be estimated on chest radiograph (27). In contrast, a chest radiograph is the preferred modality for evaluating the position of the RP. Ideally, the pigtail of the RP should be in the left pulmonary artery, with a distance >2 cm between the outflow opening and pulmonary valve. Because of its specific design, RP insertion too deep into the pulmonary artery is highly unlikely, and a malpositioned device is most often due to fallback into the right ventricle.

ECHOCARDIOGRAPHY. Echocardiography plays an important role in confirming adequate positioning of left-sided devices. In most situations, transthoracic echocardiography offers sufficient image quality, but sometimes a transesophageal view is needed. **Figure 4** presents typical examples of position images. The ideal distance between the aortic valve and the cage of the inflow opening (referred to as the teardrop because of its shape on echocardiography) is ~3.5 cm. It is important not to include the pigtail in this measurement. This is a classic mistake that may lead to erroneous pullback of a correctly positioned device. Measurements should be made in more than one plane because the catheter is curved. On transesophageal echocardiography, the most useful window is the long-axis view of the aortic valve at 120° to 145°. The artifact that arises when color Doppler is used can be very helpful. This color mosaic artifact locates the outflow opening of the device. The inflow opening can be visualized as well, at the point where the color flow converges. Even transesophageal echocardiography-guided insertion at the bedside is possible, although it requires a great deal of expertise (28).

FLUOROSCOPY. When the position of a pVAD is uncertain using the modalities described in the preceding text, it is recommended to confirm it with fluoroscopy. Looping a wire or catheter at the level of the aortic cusps may help to delineate the aortic valve for left-sided devices, whereas a pulmonary artery catheter is useful with the RP.

TABLE 2 Case Vignettes, Illustrating Common Clinical Scenarios

Case vignette: hemolysis	
Case presentation	Patient supported with a CP device for CS after out-of-hospital cardiac arrest develops increasing levels of plasma-free hemoglobin and dark urine during the night shift.
Diagnostic approach	1. Evaluation of device position 2. Evaluation of ventricular preload. RHC can be helpful: • Low PAWP plus low CVP suggests hypovolemia • Low to normal PAWP with disproportionately high CVP suggests RV failure
Treatment	1. Pump repositioning (most often pullback under echo guidance). 2. Increasing ventricular preload (see case vignette on preload).
Future perspectives	1. New technological improvements will allow faster detection of subtle suction events that currently go unnoticed by the controller and may improve stable device positioning. 2. Future studies could include protocols for hemolysis detection, allowing early intervention.
Case vignette: bleeding	
Case presentation	Patient on dual antiplatelet therapy after coronary stent implantation, supported with a CP device for CS, suddenly becomes pale. Hemoglobin levels are decreasing and cardiac filling pressures are low, despite reducing the support level because of a suction alarm with adequate CPO of 0.6 W but decreasing SvO_2.
Diagnostic approach	1. Search source of active bleeding. 2. Check coagulation status: platelets, activated partial thromboplastin time, prothrombin time, anti-factor Xa levels, fibrinogen. 3. SvO_2 is lower because hemoglobin is decreasing.
Treatment	1. Stop active bleeding (source control). 2. Reduce anticoagulation targets, especially because antiplatelet therapy cannot be discontinued due to the recent stent. Systemic unfractionated heparin should first be discontinued. Second, purge viscosity may be increased or heparin concentration in the purge fluid reduced (to 12.5 U/ml).
Future perspectives	1. Optimal anticoagulation targets are not known but rather based on experience with ECMO. Future studies could compare less intensive protocols vs. full therapeutic anticoagulation. 2. Future studies could compare targets in patients on antiplatelet therapy vs. those without antiplatelet therapy.
Case vignette: insufficient preload	
Case presentation	A patient is transferred from the operating room to the CICU supported with a 5.0 device for post-cardiotomy shock. He progressively becomes more hypotensive. Lactate levels increase and SvO_2 is dropping to 50%, with low cardiac output (3.2 l/min) and CPO to 0.5 W. Pump flow is lower than expected for the level of support chosen on the controller. Intermittently, suction alarms are observed.
Diagnostic approach	1. Always evaluate device position first with echocardiography. Abnormal device position may reduce flow, leading to insufficient support. 2. Invasive hemodynamics are helpful in differentiating hypovolemia (low PAWP and CVP) from tamponade (high CVP) or RV failure (high CVP). 3. In case of high CVP, PAPi <1 and echocardiography (RV dilation, D-shaping vs. pericardial fluid) can help in making a final diagnosis.
Cause	Insufficient pump preload, mainly caused by: 1. Hypovolemia 2. RV failure 3. Tamponade
Treatment	1. Empirical fluid challenge may be considered when filling pressures are not elevated. The CVP response may be helpful. In case of hypovolemia, the increase in CVP will be limited (e.g., 1 mm Hg), and cardiac output will increase >10%. In case of RV failure, CVP will increase rapidly (e.g., 3 mm Hg), and cardiac output will increase minimally (<10%). Also, CVP will increase more than PAWP in RV failure, leading to an increase in CVP/PAWP >0.6–0.7 in most cases. 2. For RV failure, a pulmonary vasodilator (e.g., inhaled nitrous oxide) can be initiated. Also, ventilation settings should be optimal to lower RV afterload (optimal PEEP, low tidal volume). An inotrope at low/moderate dose may be considered before providing mechanical circulatory support to the right ventricle (e.g., RP device). Current evidence is inconclusive as to which strategy provides the best outcome, but the right ventricle often recuperates when the left-sided problem can be fixed. 3. Tamponade needs surgical intervention in this case.
Future perspectives	Future studies may include management protocols to optimize adequacy of mechanical support and strategies for escalation in case of RV failure.

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REPOSITIONING. Hemolysis can quickly become problematic in the case of pump dislocation, which requires swift repositioning. In such cases, the support level first needs to be decreased to minimize the risk of damaging cardiac structures. When the device has migrated too deeply, it can easily be withdrawn under real-time ultrasound guidance. However, when the device inlet has dislocated completely into the aorta, it can be difficult to safely cross the aortic valve without reinsertion of a wire. In urgent cases, it is possible to (re-)insert the pump under transesophageal echocardiography guidance (28). Alternatively, a snare/direct-push technique has been used in the catheterization laboratory to reposition the device (29).

MANAGING THE PATIENT WITH SIGNS OF INSUFFICIENT CIRCULATORY SUPPORT

Signs of end-organ hypoperfusion despite adequate pVAD flow may indicate that the maximally achieved circulatory flow remains inadequate, and an upgrade to a higher flow device is required (i.e., a larger pVAD, VA-ECMO, or durable VAD) (**Table 2**). No randomized data are currently available to guide this decision. In

TABLE 2 Continued

Case vignette: vasoplegia	
Case presentation	A patient with myocarditis was stable on a CP device for days. Now he becomes progressively hypotensive and lactate is slightly elevated. Mixed venous oxygen saturation is 63%. CPO is 0.58 W. The device controller indicates maximal flow levels of 3.5 l/min.
Diagnostic approach	1. The device is performing optimally. The SVR and SvO_2 are helpful to differentiate vasoplegia from insufficient support, although SvO_2 may be falsely elevated in case of sepsis. 2. In this case, the $PvaCO_2$ gap can be helpful. When lactic acidosis persists after restoring SVR, an elevated $PvaCO_2$ gap (>6 mm Hg) can be indicative of insufficient blood flow to the tissues and could support a decision to either optimize native heart output (e.g., fluid challenge) or escalate in support, especially at low-normal SvO_2 values in this context.
Cause	Sepsis with vasoplegia
Treatment	1. Treat the cause of the vasoplegia, in this case with appropriate empirical antibiotic therapy. 2. A vasopressor (norepinephrine) should be started/increased when SVR is low. This might also increase venous return and flow. 3. Consider a fluid challenge when filling pressures are not elevated, especially when abnormal SvO_2, the $PvaCO_2$ gap, and lactate indicate insufficient flow despite restoring SVR. 4. Escalation is a rescue option in refractory cases but only useful when low SvO_2 and/or a high $PvaCO_2$ gap as well as low cardiac output indicate insufficient flow.
Future perspectives	Future studies should investigate the role of mechanical circulatory support in patients with an important systemic inflammatory response. Benefits in those patients are less certain as resulting multiorgan failure is not easily reversed by solely supporting the heart.
Case vignette: escalation	
Case presentation	An obese patient arrives from the catheterization laboratory after successful revascularization, supported with a CP device for CS. His skin is mottled. SvO_2 is 50% and lactate remains elevated despite normal blood pressure (with norepinephrine). Cardiac output is 3.8 l/min and CPO is 0.6 W. The device is delivering 3.5 l/min of flow without suction alarms.
Diagnostic approach	1. Despite the maximal flow level of the device, the patient is not receiving sufficient support. 2. Invasive hemodynamic assessment is helpful to evaluate whether increasing preload or decreasing afterload may be helpful by increasing native heart cardiac output and pump flow.
Cause	Insufficient support
Treatment	1. Either escalation of support to a higher flow device (e.g., a larger pVAD or VA-ECMO), especially when cardiac filling pressures are elevated. One should take into account CVP and PAPi in the decision between VA-ECMO and a higher flow pVAD. In case of poor RV function, biventricular support is needed. 2. When cardiac filling pressures are low/normal, a fluid challenge may be considered. Sometimes, native heart cardiac output can be increased this way to provide enough total forward flow. Importantly, in those cases, device flow is often also slightly lower than expected. The patient in this case vignette has a large body surface area and high metabolic needs, which may contribute to the lack of adequate support. 3. One may also consider addition of an inotrope in case filling pressures are elevated. Data are lacking to compare this strategy with escalation, but a progressively increasing need for inotropic support should likely trigger timely escalation.
Future perspectives	Future trials might include a dedicated algorithm to decide on escalation of support, which could not only use cardiac output or CPO but also parameters that reflect the metabolic needs of the tissues (e.g., SvO_2).

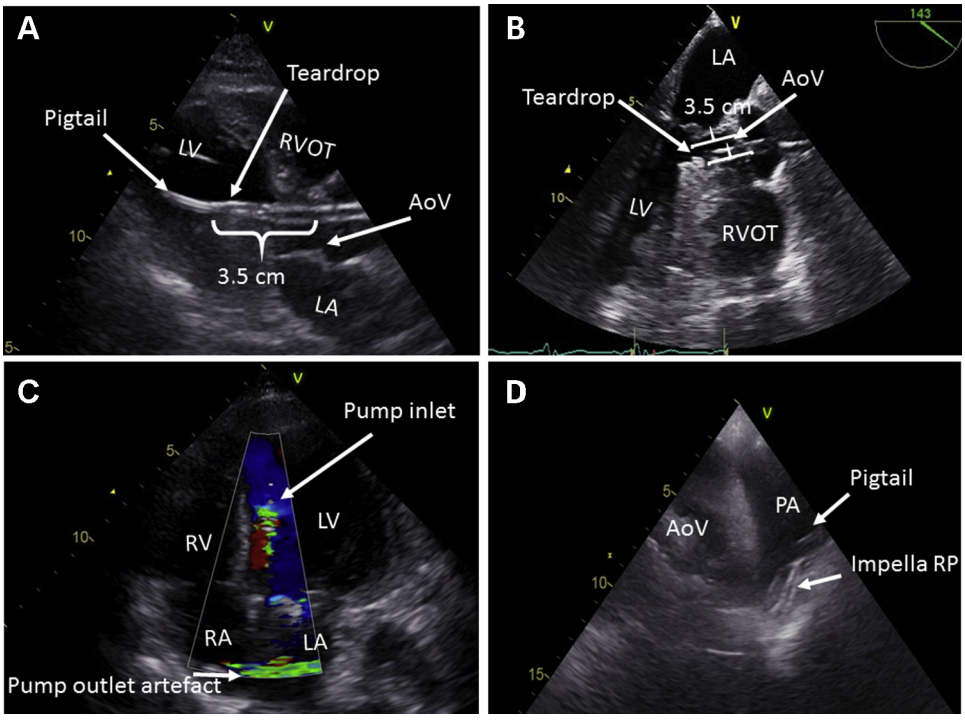
CICU = cardiac intensive care unit; CP = cardiac power; CPO = cardiac power output; CS = cardiogenic shock; CVP = central venous pressure; Echo = echocardiography; PAPi = pulmonary artery pulsatility index; PAWP = pulmonary artery wedge pressure; PEEP = positive end-expiratory pressure; $PvaCO_2$ gap = mixed venous partial pressure of carbon dioxide (P_{CO_2}) minus arterial P_{CO_2}; RP = right percutaneous; RV = right ventricular; SvO_2 = mixed venous oxygen saturation; SVR = system vascular resistance; VA-ECMO = veno-arterial extracorporeal membrane oxygenation; other abbreviations as in Table 1.

the absence of guidance from randomized data, the choice is dependent on many factors, including the need for pulmonary support, underlying disease and potential for recovery, local expertise, availability, and costs. However, this scenario is unlikely with current high-flow devices (5.0 and 5.5 l/min) that provide flow rates not much short of VA-ECMO. More frequently, hypoperfusion is the consequence of increased tissue oxygen demands, SIRS with vasoplegia, or suboptimal pVAD performance. Those situations each require a specific approach (**Figure 5, Central Illustration**).

SIRS AND VASOPLEGIA. CS in the CICU is frequently complicated by SIRS, causing vasoplegia and microcirculatory dysfunction (30). During SIRS, it might be difficult to evaluate whether increasing circulatory flow might benefit tissue perfusion because microvascular shunts increase mixed venous oxygen saturation (SvO_2) independently of oxygen delivery. The $PvaCO_2$ gap (mixed venous partial pressure of carbon dioxide [P_{CO_2}] minus arterial P_{CO_2}) is an interesting parameter in this scenario. Because carbon dioxide is continuously produced by the tissues (even in anaerobic conditions) and diffuses more easily toward the venous bed, one may apply the Fick principle to carbon dioxide. A $PvaCO_2$ gap >6 mm Hg reflects insufficient flow through the microcirculation and might suggest benefit from increasing cardiac output. An elevated $PvaCO_2$ gap is also an independent predictor of mortality in CS (31). The PvaCO2 gap could be used to decide whether increasing cardiac output (e.g., escalation in MCS) is useful in resolving the clinical problem (e.g., lactic acidosis) in a CS patient with SIRS and low-normal SvO2 (**Table 2**).

SUBOPTIMAL pVAD PERFORMANCE. Low SvO_2 with reduced pVAD flow indicates that the device is not functioning at its full capacity. Importantly, suboptimal pVAD performance often manifests as suction alarms at maximal pump speeds. However, it may be more subtle, with pump flow only slightly lower than

FIGURE 4 Optimal Device Position on Echocardiography



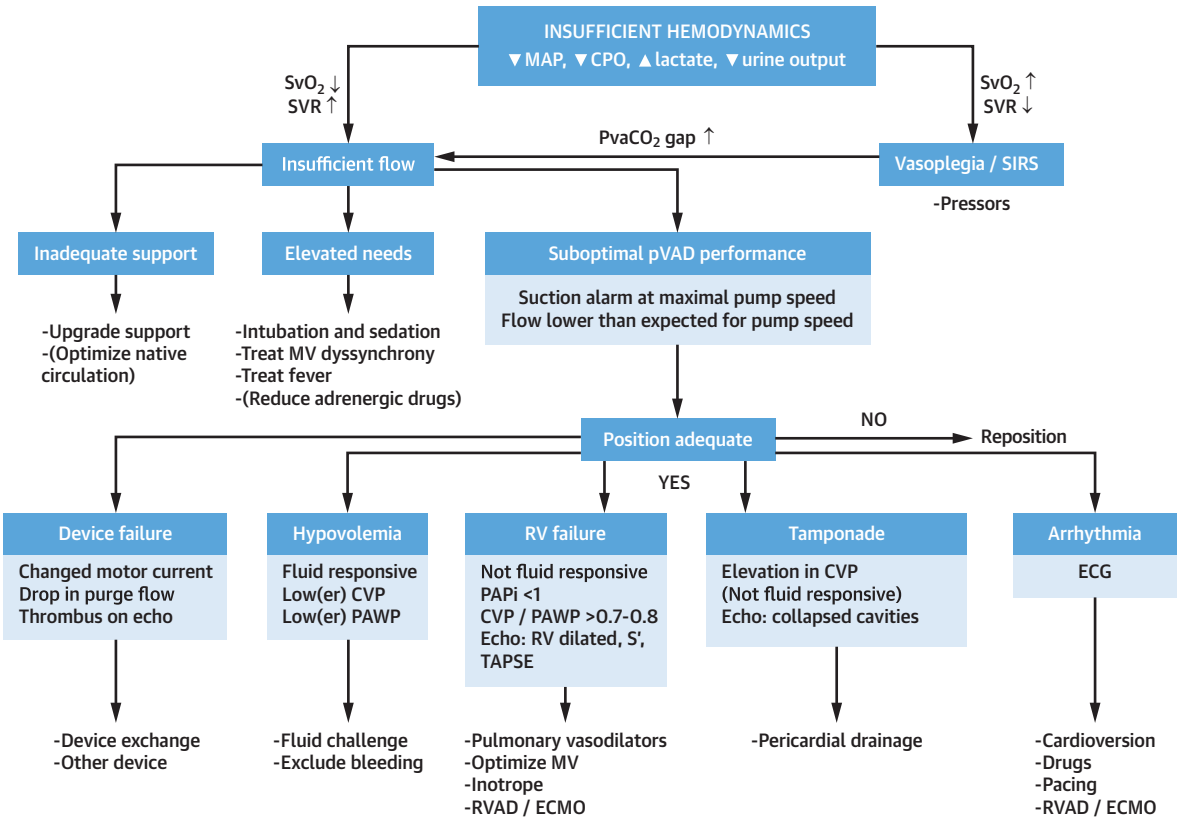
(A) Transthoracic parasternal long-axis view with the "teardrop" at 3.5 cm below the aortic valve. **(B)** Transesophageal echocardiography at 143° confirming correct position. **(C)** Modified apical 4-chamber view with color Doppler signaling to identify the pump inlet (flow convergence) and outlet (mosaic artifact). **(D)** Transesophageal echocardiography view of a right percutaneous (RP) device in the pulmonary artery (PA), with pigtail in the left branch. AoV = aortic valve; LA = left atrium; LV = left ventricle; RA = right atrium; RVOT = right ventricular outflow tract.

expected. Suction should not automatically result in decreasing the level of support with the aim of preventing new suction events. After incorrect device position has been excluded, insufficient LV filling with impaired preload volume offered to the pVAD is the most frequent cause (Table 2). For LV pVADs, this is caused by hypovolemia, RV failure, tamponade, and arrhythmia. It is important to recognize and distinguish these conditions, as they each require a specific approach. Although rare, pump failure or thrombosis is also possible.

Hypovolemia. In these patients, hypovolemia is best assessed with a dynamic test (i.e., passive leg raise or fluid bolus). Predictors of fluid responsiveness, such as pulse pressure or stroke volume variation, must be used with caution and only when the patient is intubated and in sinus rhythm (32). It is important to appreciate that RV dysfunction may increase these parameters as well. Pulse pressure and stroke volume variation are based on a decreased stroke volume during ventilator inspiration, caused by increased intrathoracic pressure impeding venous return. This phenomenon is more pronounced in hypovolemia. However, ventilatory inspiration increases RV afterload as well, which can be the dominant mechanism reducing the stroke volume in the case of RV dysfunction (33). It is safe to titrate fluids by administering small amounts over a short period of time (fluid challenge). A quick rise in central venous pressure (CVP) >2 to 4 mm Hg may serve as a warning sign that the right ventricle is not coping well with the increased venous return (34).

RV failure. The right ventricle is especially vulnerable in the patient supported by a left-sided pVAD. It is responsible for the transmission of venous return to the left side of the heart and secure enough preload to the pump. There is no clear definition of RV failure in a patient on MCS. In patients with a left-sided pVAD, RV failure most often manifests as suction alarms when the pump speed is increased. Hemodynamically, this condition manifests as high CVP and increased CVP/pulmonary arterial wedge pressure (35). Alternatively, the pulmonary artery pulsatility index (PAPi) can be calculated, as it was validated in patients with RV

FIGURE 5 Algorithm to Approach Deteriorating Hemodynamics During LV pVAD Support



First, vasoplegia is differentiated from insufficient flow based on mixed venous oxygen saturation (SvO_2) and systemic vascular resistance (SVR). The specific hemodynamic culprit is then identified by using a structured approach. CPO = cardiac power output; CVP = central venous pressure; ECG = electrocardiogram; MV = mechanical ventilation; PAPi = pulmonary artery pulsatility index; $PvaCO_2$ gap = mixed venous partial pressure of carbon dioxide (P_{CO_2}) minus arterial P_{CO_2}; RVAD = right ventricular assist device; SIRS = systemic inflammatory response syndrome; TAPSE = tricuspid annular plane systolic excursion; other abbreviations as in Figures 1, 2, and 4.

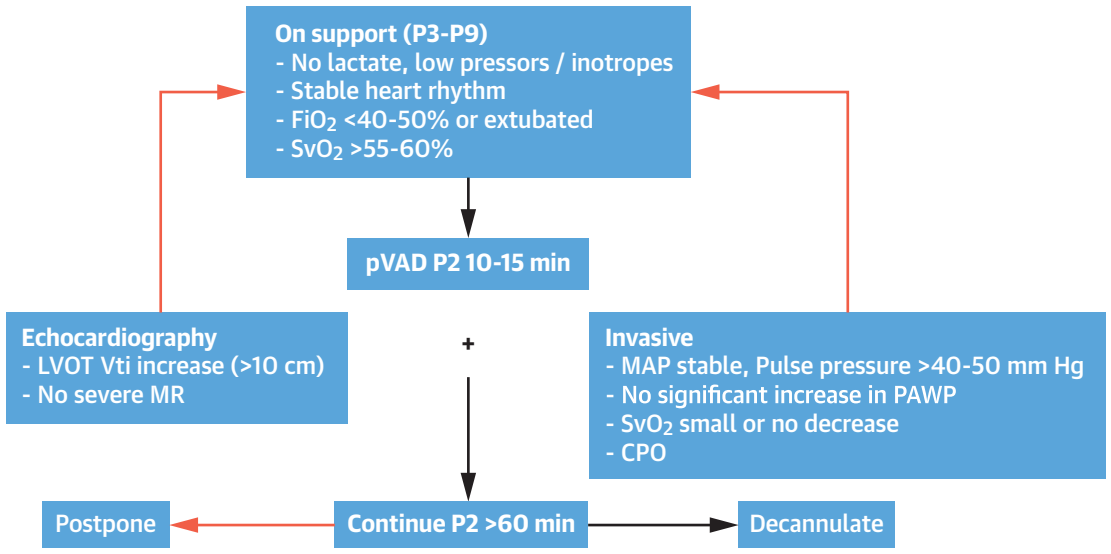
failure after durable VAD implantation (36). PAPi equals systolic minus diastolic pulmonary arterial pressure over CVP, with PAPi <1 indicating RV failure. On echocardiography, a dilated right ventricle (RV-to-LV ratio), with typical bulging of the interatrial and/or interventricular septum to the left, is seen (35).

The device starts in auto mode after implantation. This indicates that the pump searches for the maximum achievable flow. In the case of (high risk for) RV dysfunction, it may be helpful to start immediately in the manual configuration with lower flows that are gradually increased, allowing the right ventricle time to adapt to increased venous return. Further treatment should integrate all aspects of the critically ill patient, including optimal ventilator settings, consideration of pulmonary vasodilators (i.e., inhaled nitrous oxide), and a negative fluid balance when possible (35). An inotrope can be helpful in avoiding the need for RV mechanical support. The latter can be provided with an RP, PROTEK Duo cannula with pump (LivaNova, London, United Kingdom), or with VA-ECMO (37).

Tamponade. Pericardial tamponade may have an atypical presentation under pVAD support. As the device continuously removes blood from the left ventricle, pulmonary arterial wedge pressure is often normal, and no equalization of left- and right-sided filling pressures is observed. In contrast, pVAD flow typically decreases, resulting in suction events when the device is maintained at maximal performance level. Invasive hemodynamics may provide a clue, mainly when a sudden increase in CVP is observed.

Arrhythmia. The pVAD depends on sufficient preload volume provided by the right ventricle. In the case of an arrhythmia, RV function is frequently impaired, with ventricular fibrillation the extreme

FIGURE 6 Example of a Weaning Algorithm for a Left-Sided pVAD



Once the patient is stable on support, a brief reduction in device flow is proposed to evaluate hemodynamics invasively and with echocardiography. When cardiac output can be maintained without excessive rise in filling pressures and mitral regurgitation, the weaning trial can be prolonged to make sure stability is maintained before proceeding to decannulation. FiO_2 = fraction of inspired oxygen; LVOT = left ventricular outflow tract; MAP = mean arterial pressure; MR = mitral regurgitation; Vti = velocity time integral; other abbreviations as in Figures 1, 2, and 5.

example. Insufficient preload for a left-sided pVAD can lead to device suction and patient instability. During chest compressions, the device can dislocate, and temporary reduction of the pump flow until successful defibrillation is advised. Sometimes, escalation to VA-ECMO is needed in this situation. Ventricular arrhythmia can also be the consequence of the device sucking into ventricular structures but should disappear when pump flow is reduced.

Device failure. Device failure is most often caused by a thrombus being sucked into the impeller. Classically, this results in a spike in the motor current, followed by an unstable motor current and hemolysis. A sudden pump stop is possible (22). Sometimes purge outflow can become blocked, resulting in progressively decreasing purge flows. For selective purge lumen thrombosis, local thrombolysis is an option, although data are scarce (38). The new CP has a side port on the repositioning sheath that can be used to maintain access during pump exchange.

MANAGING VASCULAR ACCESS AND COMPLICATIONS

The larger (5.0 and 5.5) devices are implanted surgically, whereas the 2.5, CP, and RP are implanted percutaneously. Most centers still prefer a femoral approach for percutaneous access and the axillary approach for surgical implantation. Percutaneous axillary implantation might be an interesting option, allowing improved patient mobility (39). Vascular ultrasound-guided access with use of a micropuncture needle and confirmation of central vessel wall puncture is advisable (**Central Illustration**) (40). Access site bleeding is one of the most frequent pVAD complications but can be managed in most cases by optimizing device-skin angle, reduction of systemic UFH, application of tranexamic acid gauze, and compression (9,41). Leg ischemia is reported in up to 12.5% of cases, strongly dependent on local practices (18). Monitoring the limbs with near-infrared spectroscopy is an interesting option that allows for early diagnosis (41). Percutaneous femoral-to-femoral crossover by retrograde puncture can be a limb-saving salvage strategy, although surgery is sometimes preferred (42). Closure devices can be used after removal of percutaneously implanted devices but require local expertise.

WEANING FROM THE pVAD

Once the patient shows signs of improved perfusion, an early weaning strategy is warranted, as adverse events and bleeding may quickly offset the initial gains with MCS. A daily turndown of the pVAD flow with a hemodynamic evaluation can be attempted

when the patient meets the criteria for weaning (**Figure 6**). In most patients, the increase in ventricular volume and pressure via the Frank-Starling and Anrep effects results in increased contractility and stroke volume. Sometimes, weaning can be facilitated by using alternative unloading strategies (i.e., angiotensin-converting enzyme inhibitors when kidney function has recovered or, alternatively, nitroprusside to reduce afterload, or diuretic agents to reduce preload). If no further myocardial recovery can be expected, a decision should be made regarding the implantation of a durable VAD. Low-dose inotropes to facilitate the weaning process might be considered. Sometimes, a decision for palliative continuous inotrope therapy can be made in patients who are no longer candidates for durable VADs (43). If the increase in native cardiac output after withdrawal of support meets the patient's metabolic needs and does not result in important increases in ventricular pressures, the device can be removed.

CONCLUSIONS

MCS with a pVAD is an emerging treatment option for CS, although randomized evidence to support its routine clinical use remains scarce. Post-implantation management of these patients at the CICU comes with particular challenges and is crucial to enable the maximal potential of the device and ensure acceptable outcomes. Profound knowledge of specific issues, such as hemocompatibility and its implications for anticoagulation therapy, correct device position, and management of the patient with insufficient hemodynamic support, is indispensable to solve problems encountered frequently at the bedside. Early weaning trials should be attempted to reduce device-related complications. This might have important implications for the design and successful execution of future randomized studies and trials.

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ADDRESS FOR CORRESPONDENCE: Dr. Tim Balthazar, Department of Cardiovascular Diseases, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium. E-mail: tim.balthazar@uzleuven.be. Twitter: @UZLeuven.

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