

# Temporary mechanical circulatory support devices: practical considerations for all stakeholders

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### Abstract

Originally intended for life-saving salvage therapy, the use of temporary mechanical circulatory support (MCS) devices has become increasingly widespread in a variety of clinical settings in the contemporary era. Their use as a short-term, prophylactic support vehicle has expanded to include procedures in the catheterization laboratory, electrophysiology suite, operating room and intensive care unit. Accordingly, MCS device design and technology continue to develop at a rapid pace. In this Review, we describe the functionality, indications, management and complications associated with temporary MCS, together with scenario-specific utilization, goal-directed development and bioengineering of future devices. We address various considerations for the use of temporary MCS devices in both prophylactic and rescue scenarios, with input from stakeholders from various cardiovascular specialties, including interventional and heart failure cardiology, electrophysiology, cardiothoracic anaesthesiology, critical care and cardiac surgery.

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# **Key points**

- The use of mechanical circulatory support (MCS) devices involves several different stakeholders and requires a multidisciplinary approach to consideration and management.
- Choosing the appropriate MCS device involves a thorough evaluation
  of the patient's phenotype, history, physical condition, laboratory data,
  haemodynamic deficit (univentricular or biventricular compromise)
  and echocardiographic findings and the objectives of care.
- Optimal patient outcome is continually reassessed and is based on a balanced intersection between the objectives and level of support, the risk of complications, timing and the available resources.
- Important opportunities for MCS innovation include challenges related to pump size, vascular access, biocompatibility and use in the ambulatory setting.

# Introduction

The use of temporary mechanical circulatory support (MCS) devices has evolved from exclusive use as a rescue strategy for cardiogenic shock to functioning as an integral tool in various aspects of cardiovascular care. Indeed, temporary MCS is now routinely relied on for procedures in the catheterization laboratory, electrophysiology suite, operating room and intensive care unit. Expanded indications have led to rapid innovation in MCS device design and technology, with several devices and variations from which to choose, depending on the clinical scenario. The use of MCS devices involves several different stakeholders and requires a multidisciplinary approach to consideration and management. Various aspects of temporary MCS care must be considered holistically for an integrated effort from specialists in intensive care, cardiothoracic surgery, anaesthesiology, heart failure. electrophysiology and interventional cardiology, and from nursing and other support staff. Although a comprehensive review of the indications, design, technology, management and pitfalls of temporary MCS devices is a moving target, the incremental value of this Review lies in its multidisciplinary authorship and perspectives on how temporary MCS devices can be considered in a variety of prophylactic and rescue scenarios.

# **Current devices**

Temporary MCS devices differ according to the level of support provided, haemodynamic effects, contraindications for use, site of vascular access and placement, sheath size required for delivery and associated complications, some of which are summarized in Table 1. Device selection involves a thorough evaluation of the patient's phenotype, history, physical examination, laboratory data, imaging findings and goals of care. Although operator experience and institutional resources must also be considered, specific device selection is ultimately contingent on the degree of univentricular or biventricular haemodynamic support required. Optimal patient outcome is based on a balance between the goals and level of haemodynamic support as well as the risk of complications, timing and available resources, all of which are reassessed on a continual basis (Box 1). A brief summary of available temporary MCS devices is given below and in Figs. 1 and 2, followed by their practical applications according to indication and subspecialty.

### Intra-aortic balloon pump

The intra-aortic balloon pump (IABP), commonly inserted via the axillary or femoral artery, uses counterpulsation to increase mean arterial blood pressure, coronary perfusion pressure and cardiac output (by approximately 1 l/min), resulting in a decrease in left ventricular (LV) end-diastolic pressure (LVEDP), LV wall stress and myocardial oxygen demand<sup>1-4</sup>. The quality of support provided by an IABP is dependent on several factors, including heart rate, heart rhythm and systemic vascular resistance. IABP counterpulsation is synchronized with the cardiac cycle and, therefore, disturbances in heart rate and rhythm can compromise device function. Tachycardia reduces the time spent in diastole, limiting IABP inflation and, consequently, the intended increases in coronary perfusion pressure, whereas arrhythmias lead to dyssynchrony between balloon inflation and deflation<sup>5</sup>. Contraindications to IABP use include severe peripheral vascular disease and aortic dissection, tortuosity and aneurysm. In addition, counterpulsation in the setting of clinically significant aortic valve regurgitation is counterproductive, leading to increased LV wall stress, rather than producing the desired cardioprotective effects<sup>2</sup>.

## Percutaneous left ventricular devices

The two major classes of percutaneous LV support devices are microaxial flow pumps (such as the Impella (Abiomed)) and extracorporeal centrifugal devices. Both devices allow increases in cardiac output, cardiac power and mean arterial blood pressure, with corresponding increases in coronary and systemic perfusion pressures. Effective LV 'unloading' reduces LVEDP, leading to decreased wall tension and, therefore, myocardial oxygen demand<sup>4,6-9</sup>. Microaxial flow devices traverse the aortic valve and continuously remove blood from the LV cavity to achieve unloading. The left-sided Impella comes in various sizes and can deliver 2.5–5.5 l/min of flow, depending on the device. The Impella 2.5 and Impella CP can be inserted percutaneously via the femoral artery. The Impella 5 and Impella 5.5 use a larger introducer sheath, requiring a surgical cut down for insertion, and are most often placed via the axillary artery. Pump flow is determined by the pressure difference between the aorta and left ventricle and the pump support level (P-level). The Impella CP with SmartAssist additionally provides measurements of LVEDP, mean arterial blood pressure and cardiac power output in real-time to support optimization and weaning<sup>6</sup>. Several important contraindications exist to the placement of leftsided microaxial flow pumps, including severe aortic valve stenosis  $(\leq 0.6 \text{ cm}^2)$ , moderate-to-severe a ortic valve regurgitation, clinically significant peripheral arterial disease, and the presence of a mechanical aortic valve or LV thrombus<sup>6,7</sup>. Lastly, ideal positioning of the Impella device is approximately 3.5 cm below the aortic valve, into the middle of the left ventricle, as seen on echocardiography<sup>7</sup>. Device migration and malpositioning can lead to ineffective circulatory support and unloading, as well as haemolysis and arrhythmias. Algorithms incorporated into controllers can detect suction and automatically adjust pump speed to compensate, if these events occur.

The TandemHeart (LivaNova) percutaneous assist device is a continuous flow, centrifugal pump, left atrium to femoral artery system. A 21F transseptal inflow cannula is inserted via the femoral vein into the left atrium, while an outflow cannula (15F–19F) is placed into the descending aorta, thereby bypassing the left ventricle. The device is powered by an extracorporeal electromagnetic motor that drives a plastic impeller at a speed of 3,000–7,500 rpm and can deliver flows of up to 5 l/min $^{8,9}$ . Despite the haemodynamic benefits observed with the use of TandemHeart, more widespread implementation is limited

Table 1 | Comparison of temporary mechanical circulatory support devices

Device (examples)	Circuit	Level of cardiac output support	Contraindications	Device-specific complications
Intra-aortic balloon pump	Aorta	+/-	Moderate-to-severe aortic valve insufficiency, severe peripheral vascular disease, aortic dissection, aortic aneurysm	Renal or gut ischaemia, balloon rupture, aortic plaque embolism, limb ischaemia
Microaxial flow pump (Impella)	Left ventricle to aorta	++	Moderate-to-severe aortic valve insufficiency, left ventricular thrombus, mechanical aortic valve, severe peripheral vascular disease, aortic dissection	Malignant ventricular arrhythmias, cardiac or vascular injury, haemolysis, limb ischaemia (left)
	Right atrium to pulmonary artery		Mechanical tricuspid or pulmonary valve, severe tricuspid valve stenosis, severe pulmonary valve stenosis or insufficiency, thrombosis in the vena cava or right atrium or ventricle	
Percutaneous centrifugal (TandemHeart; right percutaneous CentriMag, dual-lumen devices)	Left atrium to femoral artery (TandemHeart)	+++	Moderate-to-severe aortic valve insufficiency, severe peripheral vascular disease	Air embolism, limb ischaemia, stroke
	Right atrium or ventricle to pulmonary artery		Mechanical tricuspid or pulmonary valve, severe tricuspid valve stenosis, severe pulmonary valve stenosis or insufficiency, thrombosis in the vena cava or right atrium or ventricle, superior vena cava or internal jugular vein stenosis or occlusion	Cardiac injury, tamponade
Peripheral venoarterial extracorporeal membrane oxygenation	Right atrium to femoral (or axillary) artery	++++	Severe aortic valve insufficiency, severe peripheral vascular disease	Limb ischaemia, pulmonary oedema, intracardiac thrombus, stroke
Surgical centrifugal	Left atrium or ventricle to aorta; right atrium or ventricle to pulmonary artery	++++	Patient not a surgical candidate	Complications of sternotomy or thoracotomy, bleeding, stroke

by the challenges of device insertion (that is, the need for transseptal puncture), especially in emergency situations. Improper placement or device dislodgement into the right atrium can precipitate substantial right-to-left shunting of deoxygenated blood. Device fixation is therefore paramount, as minor changes in position can compromise the intended circulatory support.

# Percutaneous right ventricular devices

Like the temporary LV support options discussed above, options for percutaneous right ventricular (RV) support similarly include microaxial and extracorporeal centrifugal devices. These devices directly reduce right atrial and RV pressures and increase blood flow across the pulmonary artery, leading to increases in mean pulmonary arterial pressure, LV preload and, in turn, cardiac output in the setting of preserved or assisted LV function<sup>10,11</sup>.

The Impella RP system is a percutaneous microaxial RV assist device that operates on the same principles as the other Impella devices. A 22F catheter sits in the inferior vena cava and delivers blood from the inlet area to the outlet opening in the pulmonary artery<sup>12</sup>. Although data to support the ubiquitous or routine use of the Impella RP in the setting of RV failure are lacking, emergency use authorization was granted specifically to treat RV failure related to coronavirus disease 2019 (COVID-19), including patients with pulmonary emboli<sup>13</sup>. The ProtekDuo (LivaNova) differs from the Impella RP in design and is a dual-lumen, percutaneous RV assist device that directs blood from the right atrium into the pulmonary artery and is connected to an external continuous centrifugal pump. The system supports up to 5 l/min of blood flow, and an oxygenator can be inserted for extracorporeal membrane oxygenation (ECMO). The ProtekDuo is manufactured in two sizes (29F and 31F) and is typically inserted via the right internal jugular vein<sup>14</sup>.

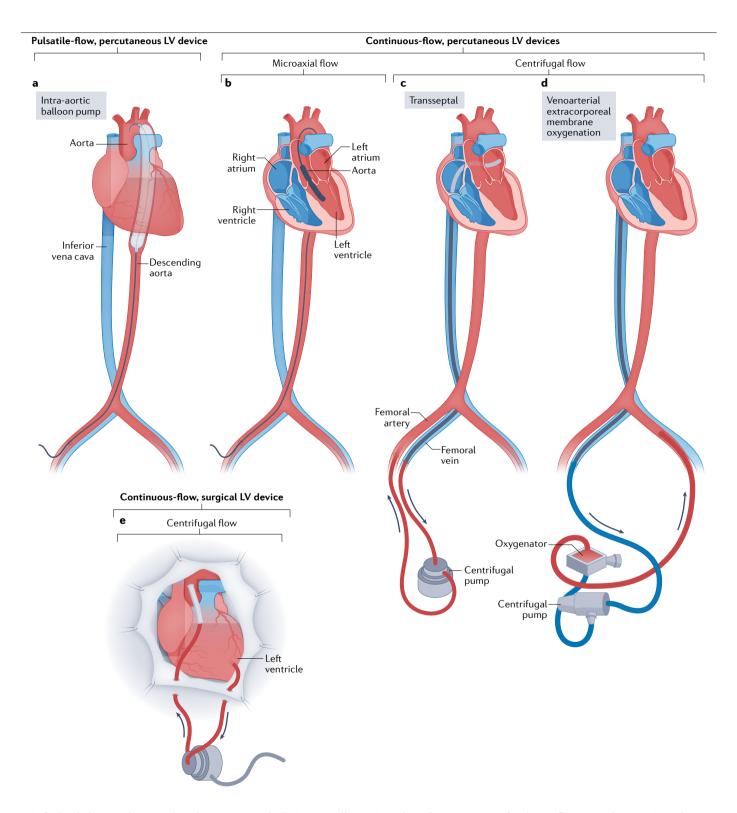
The Dual Lumen Cannula (Spectrum Medical) is another advanced, dual-lumen, percutaneous RV assist device that is inserted via the right internal jugular vein and connects to a centrifugal pump and oxygenator (if required). In contrast to the ProtekDuo, the Dual Lumen Cannula assist device drains blood from the right ventricle and returns blood to the pulmonary artery  $^{\rm 15}$ . The system comes in 31F, 27F and 24F sizes, supporting up to 5 l/min of blood flow. Insertion via the internal jugular

# Box 1

# Maximizing the benefit of temporary MCS

Optimal patient outcome with temporary mechanical circulatory support (MCS) is contingent upon the dynamic balance between the objectives, level of support required, risk of complications, timing and available resources:

- What are the objectives of support (recovery, bridge to transplantation, durable device)?
- What level of support (including univentricular or biventricular) is required to deliver the best haemodynamic benefit?
- · What are the relevant complications for the patient?
- When is the optimal timing of insertion and removal of temporary MCS?
- Are the necessary resources available to support the patient through temporary MCS?



 $vein for both the Protek Duo \ and \ Dual \ Lumen \ Cannula \ devices \ can \ allow \ greater \ patient \ mobility \ than \ with \ a \ device \ inserted \ via \ the \ femoral \ vein.$ 

Percutaneous RV assist device support can also be provided by using two percutaneously placed cannulas, one from a femoral vein for the inflow arm and another from the internal jugular or subclavian vein

into the pulmonary artery for the outflow arm. This circuit can be connected to an extracorporeal centrifugal pump, such as the CentriMag Acute Circulatory Support System (Abbott). The CentriMag consists of a magnetically levitated rotor and can be used to provide support with or without an oxygenator for ECMO  $^{16,17}$ .

**Fig. 1**| **Left ventricular circulatory support devices. a**, The intra-aortic balloon pump uses counterpulsation to provide circulatory support and is commonly inserted via the femoral or axillary artery. **b**, Microaxial flow devices traverse the aortic valve via the femoral or axillary artery and continuously remove blood from the left ventricular (LV) cavity to achieve unloading. **c**, Transseptal percutaneous assist devices are powered by a centrifugal pump and are inserted via the femoral vein, across the intra-atrial septum and into the left atrium, with an outflow cannula in the femoral artery. Devices using centrifugal pumps require a separate control and monitoring module. **d**, Venoarterial

extracorporeal membrane oxygenation uses a centrifugal pump to pull venous blood from the right atrium, through an oxygenator and into the arterial circulation via the outflow cannula in the aorta. Common cannulation sites include the femoral or axillary vessels or via central cannulation by thoracotomy or sternotomy. Extracorporeal membrane oxygenation can be used for left, right or biventricular support. e, Surgical extracorporeal centrifugal devices provide LV support via sternotomy or minimally invasive thoracotomy. Inflow cannulation is from the left ventricle or left atrium, and outflow cannulation is into the aorta.

Contraindications to right-sided device placement include mechanical tricuspid or pulmonary valves, severe tricuspid or pulmonary stenosis or regurgitation, disorders of the pulmonary artery wall that prohibit device placement, and mural thrombus of the right atrium or vena cava<sup>18</sup>.

# Venoarterial extracorporeal membrane oxygenation

Venoarterial (VA) ECMO uses a centrifugal pump to pull venous blood from the right atrium, through a membrane oxygenator and into the arterial circulation via the outflow cannula. Commonly, the venous inflow cannula (18F–28F) is inserted into a femoral vein and advanced to the right atrium, whereas the arterial outflow cannula (15F–19F) is placed in a femoral artery. Other sites of cannulation include the axillary vessels or via central cannulation by thoracotomy or sternotomy.

The haemodynamic effects of VA ECMO are dictated by the cannula size, volume status and pump speed (up to 8 l/min). The objectives of VA ECMO are to improve systemic circulation and reduce myocardial demand by decreasing RV preload, pulmonary blood flow, LVEDP and LV end-diastolic volume. Additionally, by decreasing central venous pressure, blood flow to organs in the portal circulation improves<sup>19</sup>. However, as ECMO flow is increased, LV afterload rises and can result in increased wall stress, LVEDP, pulmonary capillary wedge pressure and myocardial oxygen demand, potentially impeding LV recovery<sup>4,19</sup>. Increased afterload can be attenuated by reductions in systemic vascular resistance and LV decompression or 'venting', usually achieved by early institution of inotropic support, IABP placement, percutaneous LV assist devices, atrial septostomy, percutaneous transseptal venting of the left atrium, percutaneous pulmonary artery venting, or surgical venting of the left atrium or left ventricle<sup>4,20,21</sup>. Although no guideline recommendations exist for how to establish LV decompression, common indications include persistently elevated pulmonary capillary wedge pressure (>15 mmHg) or pulmonary artery diastolic blood pressure (>25 mmHg) when receiving support, aortic valve closure throughout the cardiac cycle, persistent pulmonary oedema, refractory ventricular arrhythmia, or LV distension seen on echocardiography<sup>20,22</sup>. In patients with cardiogenic shock, microaxial flow pump-assisted LV unloading in the setting of ECMO (so-called ECPella), has been shown to decrease 30-day mortality, but its widespread use remains controversial owing to varying rates of complications when compared with ECMO support alone<sup>23,24</sup>.

Increasingly, VA ECMO is being deployed to complement highquality cardiopulmonary resuscitation after cardiac arrest<sup>25</sup>. Compared with conventional cardiopulmonary resuscitation alone, extracorporeal cardiopulmonary resuscitation has been shown to allow increases in coronary perfusion pressure and higher rates of successful defibrillation and return of spontaneous circulation, potentially underlying associations with improved survival rates and neurological outcomes<sup>26,27</sup>.

# Surgical extracorporeal centrifugal devices

Temporary haemodynamic support (univentricular or biventricular) is also provided using surgically implanted cannulas and extracorporeal centrifugal pumps. Implantation is commonly performed via sternotomy or minimally invasive thoracotomy. The CentriMag, which can provide up to 10 l/min of flow, is the most frequently used pump and is approved for prolonged use because of its favourable haemocompatibility profile, with low rates of haemolysis.

# MCS device complications

Temporary MCS devices are associated with several complications that can span the cardiovascular, haematological, immune and neurological systems, or can be intrinsic to the mechanical pump itself. Complications can vary and must be weighed against the potential clinical benefit for individual patients  $^{28}$  (Box 2; Table 1).

# **Cardiovascular complications**

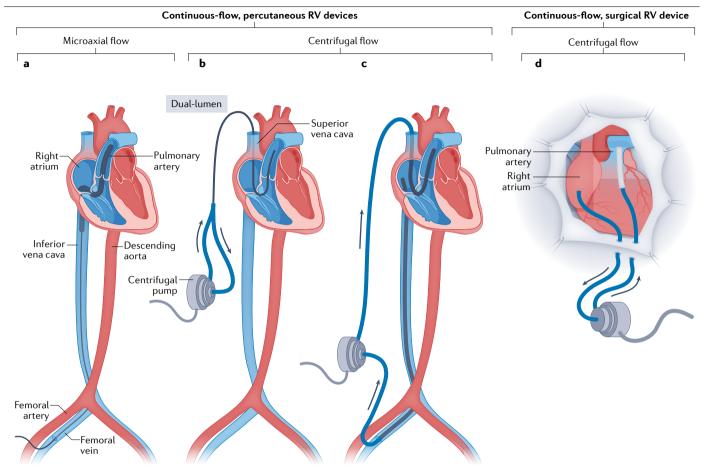
Cardiovascular complications from MCS devices can be related to direct cardiac injury or vascular access. Direct cardiac complications include valvular injury (with aortic valve injury being more common with the use of trans-aortic devices, resulting in early or late development of aortic valve insufficiency) as well as chamber perforation (from cannulas placed in the atrium) potentially resulting in shunting, pericardial effusion and cardiac tamponade. Vascular complications include distal limb ischaemia and dissection of cannulated vessels<sup>28</sup>. The risk of distal limb ischaemia relates to cannula size, patient vessel size, urgency of deployment and concomitant vasopressor use. In extreme cases, limb ischaemia can necessitate amputation. The large femoral arterial cannulas used for ECMO render patients especially vulnerable, necessitating strategies such as distal limb perfusion and near-infrared spectroscopy monitoring to help to reduce the incidence of this devastating complication<sup>29,30</sup>.

### **Haematological complications**

Haematological complications from MCS devices include (but are not limited to) haemorrhage, anaemia, platelet dysfunction, thrombocytopenia and thrombosis. Despite routine anticoagulation, the risk of pump thrombosis persists. With some forms of temporary MCS (in particular ECMO), intracardiac stasis can contribute to this risk and result in pump thrombosis and subsequent thromboembolic events. MCS-related bleeding is multifactorial and secondary to acquired coagulation deficits, haemolysis from high shear forces, thrombocytopenia, access-related issues and requisite anticoagulation.

### **Infectious complications**

Infectious complications are commonly encountered in the setting of MCS, given the multiple sites of external cannulation access combined with critical illness and prolonged hospital stays<sup>28</sup>. Infectious



**Fig. 2** | **Right ventricular circulatory support devices. a**, Microaxial flow devices for right ventricular (RV) support are inserted percutaneously through the femoral vein and into the pulmonary artery. **b**, Dual-lumen percutaneous assist devices draw blood from the right atrium or right ventricle to an external continuous centrifugal pump and out to the pulmonary artery. **c**, Percutaneous

cannulas draw blood from the right atrium to a continuous centrifugal pump and into the pulmonary artery via the femoral, internal jugular or subclavian vein.  $\label{eq:def} \textbf{d}, \text{Surgical extracorporeal centrifugal devices provide RV support via sternotomy or minimally invasive thoracotomy. Inflow cannulation is from the right atrium or right ventricle and outflow cannulation is into the pulmonary artery.}$ 

complications can range from local access-site infections to systemic illness, including bacteraemia and sepsis. Although some institutions use prophylactic antibiotic therapy for patients receiving MCS, no evidence is available to support this generalized approach  $^{28,31}$ .

# **Neurological complications**

Neurological injury can be multifactorial in critically ill patients, but is commonly attributed to the migration of microemboli in an MCS device. Haemodynamically unstable patients requiring MCS often have associated periods of cerebral hypoperfusion, hypoxia or metabolic derangement that contribute to cerebrovascular accidents. The rate of stroke is similar in patients with an IABP, TandemHeart or Impella devices, but is notably higher among those supported with ECMO<sup>28</sup>.

# Practical application by indication

 $Temporary\,MCS\,devices\,are\,relied\,on\,for\,procedures\,in\,the\,catheterization\,laboratory, electrophysiology\,suite, operating\,room\,and\,intensive\,care\,unit.\,Commonly\,used\,devices, corresponding\,indications\,and\,the$ 

rationale for implementation are reviewed below and summarized in Table 2.

# Cardiogenic shock

Despite advances in medical management, mortality in patients with cardiogenic shock, especially in the setting of acute myocardial infarction (AMI-CS), remains remarkably high at  $40-60\%^{32}$ . The objectives of management in cardiogenic shock are to increase cardiac output, maintain systemic blood pressure and preserve end-organ perfusion. Therefore, the most common indication for temporary MCS is cardiogenic shock refractory to medical management. The selection of patients with cardiogenic shock who might derive benefit from temporary MCS is based largely on the Society for Cardiovascular Angiography and Interventions (SCAI) stages, which grade the severity of cardiogenic shock by haemodynamic parameters and markers of end-organ dysfunction 33. Various scoring systems that incorporate major prognostic variables, including haemodynamic, biochemical and other relevant patient factors, have been proposed to identify predictors of adverse outcome and treatment strategies in the setting

# Box 2

# Shared complications of temporary MCS

### Mechanical

- Device migration
- Device malfunction

### Cardiovascular

- Valvular injury
- Chamber perforation
- · Vascular injury
- Limb ischaemia
- · Access-site haemorrhage

# Haematological

- Haemolysis
- Thrombocytopenia

- Thromboembolism
- Haemorrhage

### Neurological

- Cerebrovascular accident
- Peripheral nerve injury

### Infectious

- Sepsis
- Access-site infection

MCS, mechanical circulatory support.

of cardiogenic shock  $^{34}$  (Table 3). Although the potential exists for these scoring systems to guide the use of temporary MCS, varied methodologies and populations of derivation and validation limit their widespread clinical applicability.

All forms of MCS improve cardiac output and blood pressure to varying degrees; however, each interacts with the heart and vasculature uniquely to exert device-specific haemodynamic effects. Unique changes in pressure–volume relationships encountered with the various temporary MCS devices in the setting of cardiogenic shock are depicted in Fig. 3. Consideration of specific temporary MCS device use must be based on the clinical scenario, which can occur de novo, as in the setting of AMI-CS or myocarditis, or as a presentation of worsening disease, as in patients with pre-existing heart failure whose condition deteriorates<sup>35</sup>.

Although use of the IABP has decreased over the past 10 years, it remains the most common temporary MCS device used in the setting of AMI-CS (approximately 70% of patients)<sup>36,37</sup>. However, despite its frequent use, randomized controlled trials have not shown an associated increase in survival. The IABP SHOCK II trial 38-40 randomly assigned 600 patients with AMI-CS undergoing planned revascularization to IABP or no circulatory support and reported no significant difference in mortality at 30 days, 6 months, 1 year and 6 years. Several limitations might account for this lack of demonstrated benefit: a patient population with mild-to-moderate cardiogenic shock, low rates of device insertion before percutaneous coronary intervention (PCI) and a high rate of patient crossover to the IABP group. Importantly, patients with mechanical complications from myocardial infarction (such as ventricular septal defect or severe mitral valve regurgitation) were not included. Nevertheless, the American Heart Association (AHA)/ American College of Cardiology (ACC) guidelines<sup>41</sup> changed the class of recommendation for the use of an IABP in the setting of AMI-CS from

class I to class IIa, with acknowledgement of potential utility among patients with mechanical complications<sup>42</sup>. The European Society of Cardiology (ESC) guidelines<sup>43</sup> take a firmer stance, advocating against the routine use of an IABP in patients with AMI-CS (class III, level of evidence B), but give a class IIa, level of evidence C recommendation for use in patients with AMI-CS and mechanical complications.

Other temporary MCS devices that provide greater levels of haemodynamic support than an IABP have also been investigated in the setting of cardiogenic shock. Of these, percutaneous microaxial flow pumps, such as the Impella device, have gained the most popularity<sup>44</sup>. The ISAR-SHOCK trial<sup>45</sup> randomly assigned 25 patients with AMI-CS to receive an Impella LP 2.5 or an IABP and found that the microaxial flow device produced a greater increase in cardiac index than the IABP at 30 min after device insertion. Similarly, patients with AMI-CS supported with the microaxial flow pump were reported to have lower requirements for inotropes and lower lactate levels than patients supported with an IABP<sup>46</sup>. However, despite these haemodynamic benefits, percutaneous microaxial flow pumps have not been shown to increase survival<sup>45,47</sup>. Specifically, patients with AMI-CS supported with Impella were retrospectively matched to patients included in the IABP-SHOCK trial, and no significant difference in all-cause mortality was reported  $(48.5\% \text{ versus } 46.4\%; P = 0.64)^{48}$ . Additionally, a retrospective, propensity-matched analysis of 3,000 patients undergoing PCI for AMI-CS demonstrated an increase in cost and risk of bleeding and death with a microaxial flow pump compared with an IABP<sup>49</sup>. Given these disparate and limited data, multiple professional cardiovascular societies have emphasized that insufficient evidence is available to support uniform use of percutaneous LV assist devices in the clinical setting of cardiogenic shock (class IIb, level of evidence C)41,50. The results from the ongoing, randomized, prospective DanGer Shock trial<sup>51</sup> might elucidate

Table 2 | Temporary MCS: indications, rationale and commonly used devices

Indication	Rationale	MCS devices
Cardiogenic shock	Haemodynamics refractory to pharmacotherapy Acute myocardial infarction or heart failure related	IABP, pLVAD, VA ECMO
High-risk PCI	Procedural coronary or systemic hypotension Haemodynamic support for complex revascularization	IABP, pLVAD
Cardiac surgery	Haemodynamic compromise before surgery Pre-emptive in high-risk patients undergoing surgery Perioperative circulatory collapse Post-cardiotomy shock	IABP, pLVAD, pRVAD, VA ECMO, extracorporeal centrifugal MCS
Advanced heart failure	Preoperative optimization Bridge to recovery, decision or durable therapy	IABP, pLVAD, pRVAD, VA ECMO, extracorporeal centrifugal MCS
Electrophysiology laboratory	High risk of heart failure or decompensation during procedure High PAINESD score	pLVAD, VA ECMO

IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; pLVAD, percutaneous left ventricular assist device; pRVAD, percutaneous right ventricular assist device: VA ECMO, venoarterial extracorporeal membrane oxygenation.

Table 3 | Comparison of scoring systems to evaluate the indication for MCS

Score	Derivation population	Predictors (points)	Outcomes by score
CardShock <sup>104</sup>	Cardiogenic shock (AMI and non-AMI)	Acute coronary syndrome aetiology (1)  Age >75 years (1)  Previous MI or CABG surgery (1)  Confusion at presentation (1)  LVEF <40% (1)  Blood lactate level (mmol/l): <2 (0), 2-4 (1), >4 (2)  eGFR (ml/min/1.73 m²): >60 (0), 30-60 (1), <30 (2)	Total score: 0–9 In-hospital mortality: Score 1–3 (low risk), 8.7% Score 4–6 (intermediate risk), 36% Score 7–9 (high risk), 77%
SAVE <sup>105</sup>	Cardiogenic shock receiving ECMO	Diagnosis: myocarditis (3), refractory ventricular tachycardia or fibrillation (2), previous heart or lung transplantation (3), congenital heart disease (-3), other (0) Age (years): 18–38 (7), 39–52 (4), 53–62 (3), $\geq$ 63 (0) Body weight (kg): $\leq$ 65 (1), 65–89 (2), $\geq$ 90 (0) Cardiac: pre-ECMO cardiac arrest (-2), pre-ECMO diastolic blood pressure $\geq$ 40 mmHg (3), pre-ECMO pulse pressure $\leq$ 20 mmHg (-2) Respiratory: pre-ECMO duration of intubation (h): $\leq$ 10 (0), 11–29 (-2), $\geq$ 30 (-4); peak inspiratory pressure $\leq$ 20 cmH <sub>2</sub> O (3) Renal failure: acute (-3), chronic (-6), pre-ECMO HCO <sub>3</sub> level $\leq$ 15 mmol/l (-3) Liver failure (-3) Central nervous system dysfunction (-3)	Total score: -35 to 17 In-hospital survival: Score >5 (class I), 75% Score 1-5 (class II), 58% Score -4 to 0 (class III), 42% Score -9 to -5 (class IV), 30% Score ≤-10 (class V), 18%
IABP Shock II <sup>106</sup>	AMI with cardiogenic shock undergoing PCI	Age >73 years (1)  History of cerebrovascular attack (2)  Glucose level >191 mg/dl (1)  Creatinine level >1.5 mg/dl (1)  Lactate level >5 mmol/l (2)  TIMI flow grade <3 after PCI (2)	Total score: 0–9 30-day mortality: Score 0–2 (low risk), 23.8% Score 3–4 (intermediate risk), 49.2% Score 5–9 (high risk), 76.6%

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

whether microaxial flow pumps do confer a survival benefit compared with standard of care in patients with AMI-CS. Furthermore, the National Cardiogenic Shock Initiative<sup>52</sup> is a prospective registry in the USA that will determine whether the use of a prespecified algorithm to identify cardiogenic shock together with early implantation of the Impella CP device leads to improved outcomes in patients with AMI-CS.

In studies from 2005 and 2006 involving patients with AMI-CS, use of the TandemHeart compared with an IABP was associated with improved haemodynamic profiles, but increased rates of complications and no significant difference in 30-day mortality 53,54.

VA ECMO is commonly used in patients with cardiogenic shock  $^{55,56}$ . For patients with profound shock, VA ECMO can serve as a bridge to myocardial recovery, surgery or durable MCS. A retrospective analysis of 105 patients who underwent VA ECMO for cardiogenic shock showed a 1-year survival of 42%, with most survivors receiving heart transplantation or durable MCS $^{57}$ . A similar rate of survival to hospital discharge was demonstrated in a retrospective analysis of 756 patients in the Extracorporeal Life Support Organization registry  $^{58}$ .

Overall, although cardiogenic shock remains the most common indication for temporary MCS in a variety of forms, randomized trials to support the benefit of this approach are lacking. Despite the use of MCS devices in this setting, registry data indicate a persistently high mortality. The Cardiogenic Shock Working Group is establishing a national, multicentre, retrospective registry of real-world experience of patients with cardiogenic shock, including >1,500 patients supported with various forms of temporary MCS, which will hopefully inform best practice and future clinical trials in this field<sup>59</sup>.

### High-risk, assisted PCI

MCS during PCI is most commonly used to support patients with AMI-CS and those undergoing high-risk coronary procedures. Patients who are older, with complex coronary artery disease with or without haemodynamic compromise, low ejection fraction and other relevant comorbidities are considered to be at high risk (Box 3). In these patients, procedures are often longer, with periods of coronary and systemic hypoperfusion, and MCS-assisted PCI can allow time for complete revascularization while providing sufficient cardiac output, LV unloading, and myocardial and end-organ perfusion.

The BCIS-1 trial <sup>60</sup> randomly assigned 301 patients with low ejection fraction undergoing high-risk PCI to elective IABP support or no support. Although no significant difference was reported in major adverse cardiovascular events or mortality at 28 days (the primary end point), the risk of procedural complications, including prolonged procedural hypotension necessitating escalation of support, was lower in the IABP group, but the risk of access-site complications and bleeding was higher <sup>60</sup>. The subsequent observation of a reduction in mortality in the IABP group at 2 years <sup>61</sup> has led to varied interpretations of the overall results.

Numerous retrospective, observational and prospective studies have sought to evaluate the safety and efficacy of using the Impella device in the setting of high-risk PCI<sup>62</sup>. One large observational analysis of 48,000 patients raised concern, because use of the microaxial pump was associated with increased rates of bleeding, stroke and death as well as costs<sup>62</sup>. However, the series of prospective PROTECT studies<sup>63,64</sup> have yielded more promising data. The PROTECT II study<sup>64</sup> found no

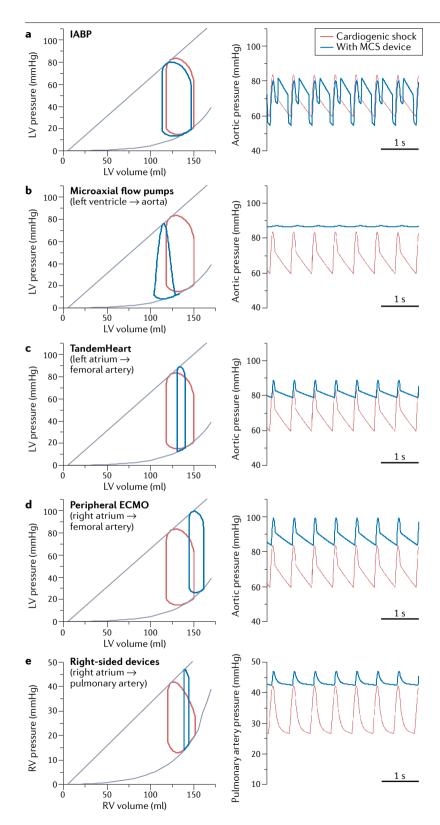


Fig. 3 | Effects of MCS devices on pressure-volume loops and blood pressure. All temporary mechanical circulatory support (MCS) devices improve cardiac output (left) and blood pressure (right) to varying degrees. In this figure, the primary haemodynamic effects of temporary MCS devices are compared to illustrate the fundamental differences in how the devices interact with the heart and vasculature. Red lines indicate tracings under baseline cardiogenic shock conditions; blue lines show tracings after the introduction of the specified MCS device. a, Intra-aortic balloon pump (IABP). The tracings show the effects of counterpulsation, with a small reduction in left ventricular (LV) preload and a small increase in stroke volume. b, Microaxial flow pumps (connecting the left ventricle to the aorta). The tracings show substantial unloading (decreased LV end-diastolic pressure and pulmonary capillary wedge pressure), triangulation of the pressure-volume loop (indicating loss of isovolumic periods), decreased pressure-volume area (correlating with decreased myocardial oxygen consumption) and LV-aortic pressure uncoupling with a closed aortic valve. c, TandemHeart (connecting the left atrium to the femoral artery). The tracings show LV unloading (decreased LV end-diastolic pressure and pulmonary capillary wedge pressure), decreased LV stroke volume, increased aortic pressure (due to overall increased systemic blood flow), decreased pressure-volume area and preserved aortic valve opening (crucial for preventing LV and aortic root stasis and thrombosis).  ${f d}$ , Peripheral extracorporeal membrane oxygenation (ECMO; connecting the right atrium to the femoral artery). The tracings show increasing LV preload (increased LV end-diastolic pressure and pulmonary capillary wedge pressure), decreased LV stroke volume, increased aortic pressure (due to overall increased systemic blood flow), increased pressure-volume area (correlating with increased myocardial oxygen consumption) and preserved aortic valve opening (crucial for preventing LV and aortic root stasis and thrombosis). e, Right-sided microaxial and extracorporeal centrifugal devices (connecting the right atrium to the pulmonary artery). The tracings show right ventricular (RV) unloading (decreased RV end-diastolic pressure and central venous pressure), decreased RV stroke volume, increased pulmonary artery pressure (due to overall increased pulmonary blood flow), decreased RV pressure-volume area and preserved pulmonary valve opening (crucial for preventing RV and pulmonary artery root stasis and thrombosis). All tracings were obtained using the Harvi cardiovascular simulation 108 and are used with permission from PVLoops.

# Box 3

# High-risk PCI criteria

Although no universal definition exists of the criteria for high-risk percutaneous coronary intervention (PCI), the following factors are used to identify patients who might benefit from mechanical circulatory support.

### Clinical

- Acute coronary syndrome
- Severe left ventricular dysfunction (ejection fraction <35%)
- Decompensated heart failure
- Arrhythmias

### **Anatomical**

- Unprotected left main coronary artery disease or equivalent
- Three-vessel disease
- High SYNTAX score
- Multivessel disease
- Last patent conduit
- Complex chronic total occlusion
- · Heavy calcification
- Complex bifurcation
- Large area of myocardium at risk

# Comorbidities

- Advanced age
- Severe valvular disease
- Severe lung disease
- · Chronic kidney disease

significant difference in the composite of major adverse events at discharge or 30 days with the Impella 2.5 device compared with an IABP. The FDA granted premarket approval for use of the Impella 2.5 device in this clinical setting on the basis of secondary and per-protocol analyses, which included improved haemodynamic profiles<sup>64</sup>, ability to accomplish longer rotational atherectomy for plaque modification<sup>65</sup>, reduction in acute kidney injury<sup>66</sup> and fewer adverse events at 90 days. Subsequently, the post-approval, single-group PROTECT III study<sup>67</sup> in 1,143 patients undergoing Impella-supported, non-emergent PCI demonstrated a reduction in the primary composite end point of death, stroke, myocardial infarction and repeat procedures at 90 days when compared with patients supported with the Impella device in the PROTECT II study. In the prospective PROTECT IV trial<sup>68</sup>, high-risk patients with complex coronary artery disease and reduced LV function undergoing revascularization will be randomly assigned to receive Impella circulatory support or no planned haemodynamic support during PCI.

The optimal timing of MCS implementation before revascularization is also a topic of ongoing research. The STEMI Pilot Trial  $^{69}$  randomly assigned 50 patients to PCI or delayed reperfusion after a period of unloading with the Impella device and demonstrated the safety and feasibility of LV unloading using Impella to allow time for cardioprotection and reduced reperfusion injury.

Current AHA/ACC guidelines include a recommendation that elective insertion of an appropriate haemodynamic support device as an adjunct to PCI might be reasonable in carefully selected high-risk patients (class IIb, level of evidence B)<sup>70</sup>. The ESC guidelines recommend that temporary MCS (without device specification) should be considered in non-emergent, high-risk PCI procedures, such as left main coronary artery disease, single remaining patent coronary artery and complex chronic total occlusions, performed by adequately experienced operators at centres that have access to circulatory support and onsite cardiovascular surgery<sup>71</sup>.

# The electrophysiology laboratory

The use of temporary MCS in the electrophysiology laboratory has been implemented to facilitate substrate mapping and ablation of haemodynamically unstable ventricular tachycardia (VT) as well as to mitigate post-procedural heart failure and haemodynamic compromise.

Data on whether temporary MCS leads to better outcomes among patients undergoing VT ablation are mixed. Preliminary studies demonstrated the benefit of safely leaving patients supported with percutaneous LV assist devices in VT for longer periods of time to allow improved mapping and ablation during ongoing VT<sup>72,73</sup>. Safe maintenance in VT led to more VT terminations with radiofrequency ablation (P = 0.03), but did not result in increased freedom from VT during follow-up<sup>72</sup>. In a larger, non-randomized study in which use of the Impella device (n = 109) was compared with no percutaneous LV assist device (n = 85), no significant difference was found in the rate of successful VT termination during ablation or freedom from VT recurrence during follow-up<sup>74</sup>. Although no significant differences were observed, patients who received Impella support were sicker and had lower LV ejection fractions ( $26 \pm 10\%$  versus  $39 \pm 16\%$ ; P < 0.001), with more New York Heart Association (NYHA) class ≥III heart failure (51% versus 25%; P < 0.001) and more frequent electrical storm (49% versus 34%; P = 0.04), leading the researchers to conclude that temporary MCS allowed sicker patients to achieve equivalent outcomes to those in less-sick patients<sup>74</sup>. However, other studies have disproved this theory<sup>75</sup>, rendering the evidence to support the benefit of temporary MCS for the end points of reducing VT recurrence and mortality after catheter ablation uncertain.

Temporary MCS is also used in the electrophysiology laboratory in high-risk patient populations to reduce acute haemodynamic decompensation and worsening heart failure after ablation, which has been reported in up to 11% of patients<sup>76</sup>. Long-term mortality in these patients is driven by heart failure, which was the most common cause of death in the VANISH trial (n = 36/71 deaths)<sup>77</sup>, with registries showing higher mortality in patients with lower ejection fraction and higher NYHA class<sup>78</sup>.

Microaxial flow devices are the most common form of MCS used during VT ablation owing to their relative ease of use; however, the required transaortic position can limit access for endocardial–epicardial mapping and they are also susceptible to electromagnetic interference<sup>79</sup>. ECMO provides a higher degree of circulatory support and oxygenation for sicker, haemodynamically unstable patients. In a report of 64 patients over 5 years, ECMO support for VT ablation was associated with a low procedure-related mortality, and the researchers propose the potential added benefit of being able to bridge decompensated patients to permanent LV assist device implantation or heart transplantation if needed<sup>80</sup>.

High-risk patients presenting for VT ablation can be identified using the PAINESD score, which gives points for the presence of the

following high-risk variables  $^{76,81}$ : pulmonary disease (five points), age >60 years (three points), ischaemic cardiomyopathy (six points), NYHA class III/IV heart failure (six points), LV ejection fraction <25% (three points), VT storm (five points) and diabetes mellitus (three points). A high PAINESD score (typically  $\geq$ 15 points) has been associated with significantly higher rates of acute haemodynamic decompensation and early mortality after VT ablation  $^{76,81}$ . In a study of 75 patients undergoing VT ablation, pre-emptive use of MCS in patients with a high PAINESD score was associated with a reduced rate of death or heart transplantation (33% versus 66%; P < 0.01) compared with when it was not used  $^{82}$ . Therefore, the primary benefit of haemodynamic support during VT ablation is from mitigation of periprocedural acute haemodynamic decompensation and heart failure rather than VT ablation success.

For high-risk patients (with a high PAINESD score) being considered for VT ablation, consultation with heart failure specialists and cardiac surgeons can be prudent, for optimization of symptoms and volume status, for consideration of pre-emptive temporary MCS, and for potential evaluation for advanced therapies (such as heart transplantation or durable MCS) as appropriate.

# **Cardiac surgery**

MCS devices have become an integral component of the repertoire used in most general cardiac surgical programmes. Although most frequently used as a rescue for haemodynamic collapse after surgery, their use as an adjunct in selected patients undergoing complex or high-risk surgery is also increasing. There are three broad applications of temporary MCS in a non-transplantation cardiac surgical practice: management of cardiogenic shock before surgical intervention, pre-emptive implantation for high-risk patients undergoing surgery, and management of perioperative and post-cardiotomy circulatory compromise.

Haemodynamic compromise before surgical intervention. Cardiogenic shock can be a presentation of various valvular, myocardial or coronary pathologies requiring surgical intervention. In addition to the common aetiologies and manifestations discussed above, other pre-surgical conditions that can present with cardiogenic shock include massive pulmonary embolism and iatrogenic complications of percutaneous interventions.

Patients in cardiogenic shock are at high operative risk when undergoing cardiac surgery. For example, coronary artery bypass graft surgery in the setting of cardiogenic shock is associated with an approximately 20% operative mortality, rising to 33% when patients have unknown neurological status at the time of surgery<sup>83</sup> and as high as 50% if there are mechanical complications (ventricular septal or papillary muscle rupture)84. Although some conditions require emergent resolution beyond institution of MCS (such as a ortic valve insufficiency or ischaemia and coronary artery disease), temporary circulatory support can be used as a bridge to optimize organ function and avoid the risk of death associated with a salvage procedure in preparation for a more controlled, urgent surgical operation. For example, in a study of 28 patients with post-infarction ventricular septal rupture, surgery was deferred in those at high surgical risk. These patients were initially managed with VA-ECMO to improve haemodynamic profiles and metabolic status (n = 11). Despite their higher risk profile (assessed by INTERMACS status and the presence of multiorgan failure), the use of temporary MCS in these patients was associated with a perioperative mortality that was similar to that in less-sick patients who underwent surgery without temporary MCS optimization<sup>85</sup>. Temporary MCS in this setting can also allow care teams to weigh the benefits of surgery in moribund patients who would otherwise be at prohibitively high surgical risk.

The effects on preload, afterload and (when applicable) shunt flow must be considered when selecting a bridging device<sup>86</sup>. The adequacy of MCS during resuscitation and patient stability in the ensuing hours and days often determine the timing of surgery.

Pre-emptive application in high-risk patients undergoing surgery. Post-cardiotomy cardiogenic shock and resultant multiorgan dysfunction remain the leading causes of early mortality after cardiac surgery<sup>87</sup>. Therefore, efforts are focused on its prevention, ensuring preoperative optimization and modern myocardial protection, as needed. Risk factors for post-cardiotomy cardiogenic shock include pre-existing ventricular dysfunction, long ischaemic periods and low baseline cardiac output. In patients with these high-risk characteristics who are undergoing surgery, pre-emptive, temporary MCS can help to avoid high doses of pharmacological support and promote cardiac recovery in the early postoperative period. Pre-emptive MCS, placed before weaning from cardiopulmonary bypass or if weaning fails, carries a relatively low incremental risk compared with when deployed for cardiogenic shock88. Given that the requirement for biventricular support is less common, percutaneous LV assist devices (as opposed to ECMO) are ideal. The microaxial flow pump Impella 5.5 device is becoming increasingly popular for this application owing to its relative ease of implantation via the axillary artery or aorta, offering the potential for full LV support as well as the option of removal without

Post-cardiotomy shock and perioperative circulatory collapse.

In addition to pre-existing cardiac dysfunction or injury, inadequate myocardial protection, ischaemia—reperfusion injury and/or surgical complications all contribute to the risk of post-cardiotomy cardiogenic shock. Post-cardiotomy shock can manifest after unsuccessful weaning from cardiopulmonary bypass as a progressive haemodynamic decline after cardiopulmonary bypass separation or in the postoperative intensive care unit setting, and is associated with up to 60% mortality during or shortly after the index hospitalization  $^{90,91}$ . In these scenarios of extreme haemodynamic compromise, ECMO is the most commonly used form of temporary MCS. However, if cardiac recovery or repair is unlikely, temporary MCS (ECMO) is not generally recommended unless durable support or heart transplantation are options. Further, advanced therapeutic options should be considered if a patient cannot be weaned after 3–4 days of MCS, because the likelihood of cardiac recovery after  $\geq 7$  days of post-cardiotomy MCS are low  $^{91}$ .

Although circulatory collapse after cardiac surgery is infrequent, it is associated with a 30-day postoperative mortality of >50%  $^{92}$ . When conventional resuscitation efforts fail in the setting of postoperative cardiac arrest, extracorporeal cardiopulmonary resuscitation (ECMO or cardiopulmonary bypass) can be performed centrally or peripherally. Although the likelihood of patient survival is based on several factors, such as the underlying cause of cardiac arrest, comorbidities, effectiveness and duration of initial resuscitation, and the promptness of the institution of ECMO, survival rates in the range of 30–40% have been reported  $^{93}$ .

### Advanced heart failure

re-sternotomy89.

Although AMI-CS has traditionally been the focus of clinical and research inquiry for the use of temporary MCS, heart failure-related cardiogenic shock is currently more prevalent<sup>35</sup>. Patients with heart

Table 4 | Comparison of old and new systems for adult heart allocation in the USA

Old system for adult heart allocation	New system for adult heart allocation	Criteria
Status 1A	Status 1	Venoarterial extracorporeal membrane oxygenation
		Non-dischargeable surgical biventricular assist device
		Mechanical circulatory support with life-threatening ventricular tachycardia
	Status 2	Non-dischargeable, surgically implanted, non-endovascular left ventricular assist device
		Intra-aortic balloon pump
		Ventricular tachycardia or ventricular fibrillation, mechanical support not required
		Mechanical circulatory support device with device malfunction or mechanical failure
		Total artificial heart, biventricular assist device, right ventricular assist device, or ventricular assist device for patients with single ventricle
		Percutaneous endovascular mechanical circulatory support device
	Status 3	Dischargeable left ventricular assist device for discretionary 30 days
		Multiple inotropes or single high-dose inotrope with continuous haemodynamic monitoring
		Venoarterial extracorporeal membrane oxygenation after 7 days; percutaneous endovascular circulatory support device or intra-aortic balloon pump after 14 days
		Non-dischargeable, surgically implanted, non-endovascular left ventricular assist device after 14 days
		Mechanical circulatory support device with one of the following: device infection, haemolysis, pump thrombosis, right-sided heart failure, mucosal bleeding or aortic valve insufficiency
Status 1B, status 2	Status 4	Dischargeable left ventricular assist device without discretionary 30 days
		Inotropes without haemodynamic monitoring
		Re-transplantation
		Diagnosis of one of the following: congenital heart disease, ischaemic heart disease with intractable angina, hypertrophic cardiomyopathy, restrictive cardiomyopathy or amyloidosis
-	Status 5	On the waiting list for at least one other organ at the same hospital
-	Status 6	All others

The updated United Network for Organ Sharing (UNOS) allocation system prioritizes patients in urgent need of transplantation. Those patients receiving temporary mechanical circulatory support are designated as UNOS status 1 and 2, with the shortest waiting list times. Table modified with permission from ref. [10], Elsevier.

failure often also constitute the 'high-risk' populations undergoing the various interventions (including PCI, cardiac ablation procedures and cardiac surgery), in whom the use of temporary MCS has already been discussed. The following section uniquely focuses on the role of temporary MCS in patients with advanced heart failure under consideration for durable MCS and heart transplantation.

The use of temporary MCS can be considered before durable MCS surgery in selected patients at high surgical risk with pre-existing heart failure for the purposes of achieving clinical stability and maintaining end-organ perfusion. Similar considerations to those discussed in the previous section on pre-emptive MCS in cardiac surgery are relevant.

In patients with advanced heart failure who are on the waiting list for heart transplantation in the USA<sup>94</sup>, the use of temporary MCS has particularly increased over the past 4 years, tied to important implications for transplantation prioritization. In 2018, the United Network for Organ Sharing (UNOS) allocation system was modified in an effort to ensure appropriate prioritization of patients in most urgent need of transplantation (Table 4). Patients receiving temporary MCS are accordingly designated status 1–3, with shorter waiting list times than patients designated status 4–6. Patients receiving ECMO or biventricular support devices are designated status 1, followed by patients supported with an IABP or a percutaneous ventricular assist device, who are designated status 2–3. Patients are maintained on these forms of temporary MCS for longer periods of time than originally intended, via alternative access (often axillary rather than femoral artery) to allow mobility. Although shown to be safe and effective in

some studies<sup>94</sup>, the increased use of temporary MCS in this setting has sparked debate about appropriateness of use as well as effects on longer-term outcomes after heart transplantation<sup>95</sup>.

If allograft function is suboptimal (primary graft dysfunction) at the time of heart transplantation, ECMO, IABP or another form of temporary MCS can be used to rest the allograft and allow adequate end-organ perfusion. Although its causes remain elusive, primary graft dysfunction is encountered in approximately 10–30% of all heart transplantations and is a challenging clinical scenario 6. Observational reports in which the prompt use of VA ECMO allowed myocardial recovery and even a possibility of decreased mortality have been encouraging, but further studies are needed 7. Advances to increase access to heart transplantation are progressing at a rapid pace, demanding dedicated studies to improve our understanding of the role and effects of temporary MCS in the management of patients with advanced heart failure.

# **Future development**

Despite the major advances and varied technologies for providing MCS, important opportunities exist for additional innovation, including improvements to pump flow capacity, pump size, haemocompatibility and vascular access.

Expandable pumps and sheaths allow device insertion and withdrawal at smaller French sizes, while facilitating increases in the flow rate that is typically possible given the constraints of native vessel size. One novel expandable microaxial flow pump can be advanced through

a 9F sheath and expanded to 18F to achieve peak flows of approximately 3.5 l/min, a rate similar to that of flow pumps requiring substantially larger access<sup>98</sup>.

Temporary MCS in the ambulatory setting is an area of investigation intended to facilitate physical rehabilitation and allow outpatient support while the patient awaits cardiac recovery or more definitive therapy. The Intravascular Ventricular Assist System (iVAS; NuPulse)<sup>99</sup> is an extended use, minimally invasive, ambulatory IABP intended to be used as a bridge to transplantation. The initial feasibility trial demonstrated early positive experiences with the device<sup>100</sup>, and larger investigations are underway. For patients with decompensated heart failure, the current UNOS allocation system limits opportunities for assessment of recovery, given the shorter waiting list times for urgent transplantation candidates receiving temporary MCS. Higher flow devices (>5 l/min) providing nearly full support and greater levels of LV unloading for longer durations (>14 days) might allow cardiac recovery without proceeding directly to durable LV assist device or transplantation and are currently being studied for this purpose<sup>101</sup>. Furthermore, support systems are being developed for longer-term outpatient applications (up to 1 year) in which the purge line will be eliminated but, much like durable ventricular assist devices, there will be a percutaneous drive line and an external controller and battery. These devices will be implantable without a thoracotomy or large-bore outflow graft requiring surgical anastomosis to the proximal aorta.

Novel cannulas and cannulation strategies for MCS systems are being investigated and developed. Transcaval implantation of microaxial flow devices is a novel approach introduced for patients with small, tortuous or diseased femoral or iliac arteries. An electrified needle with guidewire crosses the inferior vena cava into the aorta, and the microaxial device can then be advanced to its final transvalvular position<sup>102</sup>. Another strategy known as left atrial venoarterial (LAVA) ECMO<sup>103</sup> uses a fenestrated cannula (24F VFEMO24; Edwards Lifesciences) inserted via the femoral vein and advanced through the interatrial septum. Blood is simultaneously withdrawn from the right and left atria, which offers the potential advantage of LV unloading without additional access for venting.

Finally, a major area of innovation is the development of smart pumps that monitor haemodynamics and can predict instability for preemptive intervention. Additionally, artificial intelligence-based software algorithms are being used to aid in choosing which support strategy (drug-based and/or device-based) is optimal for an individual patient.

# **Conclusions**

Although historically reserved for rescue therapy, temporary MCS devices are now being routinely used in a variety of clinical scenarios. Expanded indications and applications demand multidisciplinary team education and collaborative efforts to establish best practices. Continued innovation in bioengineering coupled with clinical trial assessment is required to elucidate the specific scenarios, patient populations and timings in which temporary MCS confers clinical benefit that outweighs potential complications.

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### **Author contributions**

B.S.S., C.R.G., S.R.D., G.W.S., N.M., A.C.A., D.B. and A.L. researched data for the article. B.S.S., C.R.G., A.C.A., D.B. and A.L. discussed the content. All the authors wrote the manuscript. B.S.S, C.R.G., M.M.W., A.C.A., D.B. and A.L. reviewed and/or edited the article before submission.

### **Competing interests**

S.R.D. declares receiving research grant support from Biosense Webster and owning equity in Farapulse (acquired by Boston Scientific) and Manual Surgical Sciences. D.B. declares receiving an unrestricted educational grant from Abiomed, acting as a consultant to PVLoops and receiving consulting fees from CardioDyme. A.L. declares receiving speaker honoraria from Zoll, being on a data safety and monitoring board for Sequana, being on the advisory board of Bioventrix and being a speaker for Novartis. The other authors declare no competing interests.

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