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GUIDELINE

The International Society for Heart and Lung Transplantation/Heart Failure Society of America Guideline on Acute Mechanical Circulatory Support

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See page 49 for disclosure information.

List of abbreviations: ACT, activated clotting time; aPTT, activated partial thromboplastin time; ACHD, adult congenital heart disease; ADHF, acute decompensated heart failure; AHA, American Heart Association; AI, aortic insufficiency; AMI, acute myocardial infarction; ARDS, acute respiratory distress syndrome; BiV, biventricular; BMI, body mass index; *C. difficile*, *Clostridium difficile* infection; CrCl, creatinine clearance; CS, cardiogenic shock; CO, cardiac output; CPB, cardiopulmonary bypass; CXR, chest radiograph; CT, computerized tomography; CVP, central venous pressure; DCCV, DC cardioversion; ESC, European Society of Cardiology; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; eCPR, extracorporeal cardiopulmonary resuscitation; ECLS, extracorporeal life support; ELSO, Extracorporeal Life Support Organization; EN, enteral nutrition; FAC, fractional area change; GP, glycoprotein; HF, heart failure; IABP, intra-aortic balloon pump; ICH, intracranial hemorrhage; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; INR, international normalized ratio; IV, intravenous; LMWH, low-molecular weight heparin; LAP, left atrial pressure; LV, left ventricular; LVAD, left ventricular assist device; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; MCS, mechanical circulatory support; MS, mitral stenosis; MR, mitral regurgitation; MV, mitral valve; NIS, Nationwide Inpatient Sample; NSTEMI, non-ST elevation myocardial infarction; PAC, pulmonary artery catheter; PAPi, pulmonary artery pulsatility index; PA, pulmonary artery; PCI, percutaneous coronary intervention; PCWP, pulmonary capillary wedge pressure; RHC, right heart catheterization; RCTs, randomized clinical trials; ROSC, return of spontaneous circulation; RV, right ventricular; RVSWI, right ventricular stroke work index; RVAD, right ventricular assist device; SC, subcutaneous; SCAI, Society for Cardiovascular Angiography and Interventions; STEMI, ST elevation myocardial infarction; SVR, systemic vascular resistance; TAPSE, tricuspid annular plane systolic excursion; TDI, tissue doppler imaging; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram; TEG, thromboelastography; UFH, unfractionated heparin; UTI, urinary tract infection; VAD, ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation; VKA, vitamin K antagonist; VTE, venous thromboembolism; VV-ECMO, venovenous extracorporeal membrane oxygenation; VWF, von Willebrand factor

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Despite medical advances, cardiogenic and pulmonary shock are associated with high mortality and morbidity.[1–4] The availability and use of acute or temporary mechanical support devices has grown over the years, with the goal of improving patient outcomes by temporarily providing support to allow time for organ recovery or for longer term decisions including transition to durable therapies.[5–7] A collaborative effort commissioned by the International Society of Heart and Lung Transplantation and the Heart Failure Society of America has developed this critically needed guideline for the management of patients requiring acute mechanical circulatory support (MCS). This document covers definitions of cardiogenic and pulmonary shock, medical treatment and surgical interventions, management of patients supported with temporary devices, complications, special populations, and social and ethical dilemmas. The writing groups include multidisciplinary members from both societies with a focus on diversity in gender, geography, area of expertise and level of seniority. The target audience includes cardiologists, especially interventional and advanced heart failure specialists, pulmonary and critical care specialists, intensivists, and cardiothoracic surgeons, as well as referring providers.

Table Definitions of Class of Recommendation and Level of Evidence*

Class (Strength) of Recommendation	
Class I	Strong recommendation
Class II	Moderate recommendation (benefit likely > risk)
Class III	Harm or no benefit
Level (Quality) of Evidence	
Level A	High-quality evidence from 1 or more RCTs or meta-analyses of RCTs
Level B	Moderate quality evidence from 1 or more RCTs or meta-analyses of RCTs or well-designed observational studies
Level C	Randomized or non-randomized observational or registry studies with limitations of design or execution, or consensus of expert opinion

RCTs, randomized clinical trials.

*Adapted from the American College of Cardiology/American Heart Association Clinical Practice Guideline Recommendation Classification system.[8]

After a review and evaluation of available literature and incorporation of the collective experience of the group, specific recommendations were assigned a class of recommendation and level of evidence. The definitions of the class of recommendation and level of evidence are listed in the Table and they are simplified into fewer categories given the paucity of high quality of evidence from randomized clinical trials of acute MCS.

Task Force Overview

Task Force 1: Timing, Patient and Device Selection of Acute MCS, and Periprocedural and Postprocedural Care for Cardiogenic and Pulmonary Shock

This section provides contemporary definitions and outlines pathophysiology and epidemiology of cardiogenic and pulmonary shock. The severity and classification of shock is further defined along with underlying causes and hemodynamic profiles. The timing and requirements for acute MCS are detailed, including the role of shock teams, intensivists, nursing, and supportive care. Finally, specific indications, contraindications, techniques, and risks of available devices for left ventricular (LV), right ventricular (RV) and biventricular (BiV) support are reviewed.

Task Force 2: Adjunctive Pharmacological Management

This section focuses on the management of bleeding, thrombosis, and infection. Risk factors for hemocompatibility-related adverse events are reviewed and the importance of periprocedural planning is highlighted, including formulation of anticoagulation targets and discontinuation of background therapy. Device-specific recommendations regarding periprocedural and postprocedural antithrombotic therapy are provided along with pharmacokinetic information. The management of early and late bleeding, thromboembolism, and heparin-induced thrombocytopenia (HIT) are discussed. Definitions, types, and rates of infection during acute MCS support are outlined, and prophylactic, empiric, and targeted treatment approaches recommended.

Task Force 3: Specific Patient Populations

The population of patients presenting with CS is heterogenous. A range of patient characteristics, comorbidities, and specific shock etiologies may alter the risks and benefits of acute MCS. This section provides guidance in the management of women, racial and ethnic minorities, patients with adult congenital heart disease (ACHD), the elderly or frail, and those with obesity or cachexia who require acute MCS. In addition, specific recommendations are provided for patients with acute fulminant and those with post cardiotomy or post–cardiopulmonary resuscitation (CPR)-related shock. Owing to marked differences in body size, clinical

presentation, and available devices, pediatric patients are not covered in this guideline.

Task Force 4: Goals of Care and Role of Palliative Care, Social Work, and Ethics

Decision-making for acute MCS is typically rapid and complex, and involves a variety of invasive options, a high degree of uncertainty in outcomes, and the potential for significant patient and family suffering. This section highlights the importance of shared decision-making and informed consent while engaging necessary stakeholders. Tools to frame conversations, including use of decision aids, are discussed. The important roles of palliative care specialists, social work, ethics consultation, and local religious leaders are detailed. Finally, the concept of medical futility is defined and a decommission check-list is provided.

Task Force 1: Timing, Patient and Device Selection of Acute MCS, and Periprocedural and Postprocedural Care for Cardiogenic and Pulmonary Shock

Cardiogenic Shock Definition

Cardiogenic shock (CS) results from a multitude of cardiovascular (CV) disorders and remains a highly fatal (30%−60%) and morbid syndrome despite different therapeutic approaches. CS is defined as a state of tissue hypoperfusion and end organ dysfunction owing to a primary cardiac disorder with low cardiac output (CO) that can present in different stages (Society for Cardiovascular Angiography and Interventions [SCAI]/Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS]).[9,10] Notably, invasive hemodynamics are not always required for the diagnosis of CS.[3,5]

Pathophysiology

A primary cardiac insult (eg, acute myocardial infarction [AMI], acute-on-chronic heart failure (HF), fulminant myocarditis, massive pulmonary embolism) triggers CS. This initial insult results in an abrupt onset of acute or acute-on-chronic ventricular dysfunction (either systolic or diastolic) and stimulates a cascade of pathologic and compensatory reactions including systemic vasoconstriction, systemic inflammatory response syndrome, fluid retention, and impaired tissue microcirculation among others.[5] These mechanisms in turn result in progressive tissue hypoperfusion, coronary/myocardial hypoperfusion, and increased afterload with resultant further decrement in CO, thus propagating the death spiral of CS.[5]

Epidemiology

AMI is the predominant etiology of CS with ST-elevation AMI (STEMI) more culpable compared with non−ST-elevation MI.[3,11] In the United States, analyses using the Nationwide Inpatient Sample (NIS) and the CATH-PCI registry, show a rising incidence of CS complicating STEMI from 6.5% in 2003 to 10.1% in 2010.[12,13] European registry data show trends based on region and type of AMI (non-ST elevation MI vs STEMI) with incidence ranging from 5% to 10% for STEMI.[11,14]

Data surrounding CS incidence for non−AMI-related etiologies are more limited. Recent data from the NIS demonstrate a rising rate of non−AMI-related CS of 8.7 of 1000 hospitalizations compared with the previous era, with high mortality and 30-day readmission rates.[15] Concomitantly, there is an increase in health care costs.[12,15,16]

Racial, gender, and age disparities exist regarding risk of developing CS. Women, Asian/Pacific Islanders, and patients over the age of 75 demonstrate a higher incidence of AMI CS.[3,12] Furthermore, significant regional and hospital heterogeneity in CS management persists. Paralleling data seen with other conditions, higher volume centers are associated with improved outcomes, and as a result regionalization of CS care using a hub-and-spoke model has been proposed.[5,17]

Shock Classifications by Severity: INTERMACS and SCAI Classifications

The INTERMACS profiles were developed to classify clinical severity of patients with advanced HF undergoing durable ventricular assist device (VAD) implantation.[10] Patients with acute CS by definition belong to INTERMACS 1 ("the crashing and burning" patient profile), potentially too sick for durable VAD therapy, with more chronic shock states being INTERMACS 2 to 4.

To provide further granularity, the SCAI classification system was created and jointly supported by the American College of Cardiology, the American Heart Association, the Society of Critical Care Medicine, and the Society of Thoracic Surgeons in 2019.[9] The SCAI classification is an easily performed, bedside assessment that stratifies patients with CS into 5 categories: stage A, the at-risk patient; stage B, the patient with beginning CS; stage C, the patient with classic CS; stage D, the deteriorating/doom patient; and stage E, the extremis patient.[9] By design, the SCAI classification has several advantages over the INTERMACS system: the SCAI classification system accounts for changes in clinical trajectory, allows for more granularity in patient description, is specifically designed for this patient population, and can be used to optimize patient selection for future CS trial enrollment. This classification may further elucidate appropriate timing of acute MCS.[18]

Hemodynamic Profiles

The hemodynamic profile of patients in CS can also be classified along similar metrics as patients presenting with acute decompensated HF (ADHF), namely, that of (1) volume status: wet vs dry and (2) systemic perfusion: warm vs cold. Patients with CS typically present as cold and wet, characterized by decreased CO with elevated filling pressures and

systemic vascular resistance.[5] Cold and dry patients or euvolemic CS may be due to either true CS or due to volume depletion. The warm and wet CS subset refers to patients with mixed shock either owing to the well-established inflammatory response seen after an AMI or owing to concomitant infection and sepsis.

Post hoc analyses from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial found that among patients with AMI-related cardiogenic shock (AMI-CS) with predominant LV shock, 64% of patients were cold and wet, 28% cold and dry, and 5% were warm and wet.[19] Analysis of blood pressure data from the same trial also revealed that despite inclusion criteria of hypotension, 5% of enrolled patients had normotensive shock, defined as a systolic blood pressure of greater than 90 mm Hg despite evidence of end-organ hypoperfusion, with hemodynamic data demonstrating higher systemic vascular resistance than the remainder of the trial cohort.[19,20] Interestingly, normotensive patients with CS demonstrated elevated in-hospital mortality rates compared with hypotensive patients (66% vs 43%; $P = .001$).[19]

RV and BiV Shock

RV dysfunction can either be a primary insult triggering CS, that is, RV-predominant CS or the result of LV dysfunction precipitating BiV CS.[20] RV failure (Table 1.1) is associated with poor outcomes.[21] In patients with AMI without CS, RV involvement is associated with increased mortality.[22,23] Secondary RV involvement in AMI-CS is noted in more than one-third of patients,[21,24] whereas primary RV-predominant CS is rare, representing 3%−5% of the study population in the SHOCK trial and registry.[25,26] Compared with patients with LV-predominant CS, patients with RV-predominant CS demonstrate a shorter time to diagnosis of shock, less prevalence of multivessel disease or prior MI, and a higher incidence of inferior or posterior MI.[26] RV involvement in non AMI-CS can often be seen with a variety of etiologies, most commonly with acute-on-chronic LV failure. RV-predominant shock is also seen in decompensated pulmonary hypertension, pulmonary embolism, right sided valvular disorders, RV predominant cardiomyopathies, and right HF after heart transplantation or after left ventricular assist device (LVAD) implantation.

Table 1.1 Hemodynamic and Echocardiographic Data that may be Supportive of RV Failure[21,27]

Cardiac index <2.2 L/min/m^2 despite continuous high dose inotropes or >1 inotrope or vasopressor medication + any of the following criteria:	
	CVP >10 mm Hg
	CVP/PCWP ratio >0.63
	PAPi <2
	RVSWI <450 mm Hg*mL/m^2
	RV dysfunction and/or dilation on echocardiography:
	TAPSE <17 mm
	RV systolic TDI S′ velocity <10 cm/sec
	RVFAC <35%
	RV free wall longitudinal strain <−20%
	RV basilar diameter >42 mm
	RV short axis (or mid cavity) diameter >35 mm
Severe RV dysfunction	CVP >15 mm Hg
	CVP/PCWP ratio >0.8
	PAPi <1.5
	RVSWI <300 mm Hg*mL/m^2
Clinical	Ascites
	Edema
	Bilirubin elevation
	Creatinine elevation

CVP, central venous pressure; FAC, fractional area change; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RV, right ventricular; RVFAC, right ventricular fractional area change; RVSWI, right ventricular stroke work index; TAPSE, tricuspid annular plane systolic excursion; TDI, tissue Doppler imaging.

Etiologies of Shock

AMI-Related CS

CS complicating AMI remains the predominant etiology accounting for up to 80% of cases.[28] CS complicates 5%−10% of AMI and remains a deadly complication with a mortality rate of 30%−50% in contemporary registries and trials.[12,28−31] In patients presenting with AMI-CS, early revascularization remains the cornerstone of therapy.[28,32−34] Ejection fraction, moderate or greater mitral regurgitation, presence of CS on admission or CS developing early rather than later in the course, successful percutaneous coronary intervention (PCI), and the culprit vessel are independent predictors of survival in AMI-CS.[35−38]

ADHF

CS owing to non-AMI causes span a range of etiologies and constitutes about 20% of CS cases. The majority (58% of non AMI-CS and 11% of total CS population) present with acute decompensation of chronic HF, 32% with valvular or mechanical causes (6% of total CS), 10% with stress cardiomyopathy (2% of total CS), and 10% with myocarditis (2% of total CS).[28] Compared with AMI-CS, non-AMI patients with CS are younger, more likely to be women, with larger ventricles, a higher degree of mitral regurgitation, and higher N-terminal pro-B-type natriuretic peptide levels.[28] Approximately 8% of chronic cardiomyopathies present with CS as their initial manifestation.[39] Takotsubo or stress cardiomyopathy, typically considered benign, carries a 9.5% incidence of CS with in-hospital mortality ranging from 15% to 23.5% as compared with 2.3% ($P < .001$) in patients with stress cardiomyopathy who do not develop CS.[40]

Postcardiotomy Shock

Postcardiotomy shock, defined as CS after cardiac surgery, affects 1%−6% of cardiac surgical cases depending on the

definition and criteria used.[41] The pathophysiology is characterized by a multifactorial etiology in which vasodilatation and hemorrhage owing to cardiopulmonary bypass impact the final outcome. The spectrum of clinical settings varies from the situation in which the heart does not recover sufficient myocardial function to be weaned from cardiopulmonary bypass to abrupt cardiac arrest in the intensive care unit (ICU) during the postoperative period.

Obstructive Shock

The treatment of specific causes of cardiogenic or obstructive shock such as acute pulmonary embolism and cardiac tamponade require timely diagnosis and directed management such as drainage, anticoagulation, systemic or directed thrombolytics, manual thrombectomy, or surgery. Pharmacological support with vasopressors and/or acute MCS with temporary devices may be needed for patient stabilization.

Indications for Acute MCS

The indications for acute MCS in patients in CS vary owing to the heterogeneity in both etiology and severity of presentation. In addition to the baseline characteristics of patients with CS, the indication may also vary by the expected end points of the support (recovery, bridge to decision, mid- to long-term support). It is important to consider exit strategies from acute MCS to minimize medically futile cases. A multidisciplinary team-based approach is warranted to ensure the appropriate referral and timely treatment that are keys to survival benefit. An overview of selected acute MCS devices is displayed in Fig. 1.1.

Recently, data from the Detroit Cardiogenic Shock initiative showed for the first time a higher survival to discharge of 72%. Indeed, such results were achieved through an aggressive use of right heart catheterization, performed in 92% and acute MCS implanted in 74% of patients before PCI.[1] This study is one of the first demonstrating improved outcomes from CS through an organizational effort for early referral to a shock center, escalation of monitoring and eventually implantation of acute MCS. The study suggests that implementation of a coordinated shock team can improve outcomes through a multidisciplinary effort (Table 1.2).[42]

Parameters of Evaluation to Select Device and Timing

When hypoperfusion persists despite preload and afterload optimization, the need for more CO should be considered. A higher inotropic dose and multiple inotropes have been demonstrated as significant risk factors and should drive referral to centers or an ICU, where acute MCS is feasible. The etiology of CS has a paramount role in the decision of the need for support and its timing. A reversible cause of CS (ie, successful reperfusion of ischemic lesions, myocarditis, postcardiotomy failure and post-transplant graft failure) should be a factor favoring timely implantation of a short-term device.

Timing of Acute MCS

Given the numerous etiologies of CS, diverse patient presentations, and differences in individual treatment practices, the optimal timing for acute MCS remains ill-defined. Historically and currently, inotropes and vasopressors are first-line therapies for hemodynamic instability and CS. These agents lack data showing benefit and have potential harm with coronary and peripheral vasoconstriction. Early initiation of acute MCS can mitigate the consequences of systemic hypoperfusion, worsening ischemia, and declining cardiac function by relieving ischemic burden, augmenting CO and minimizing medications with high cardiac oxygen demands.[43] Although data for this strategy exist in AMI-CS, more data are needed in non-AMI CS.[44]

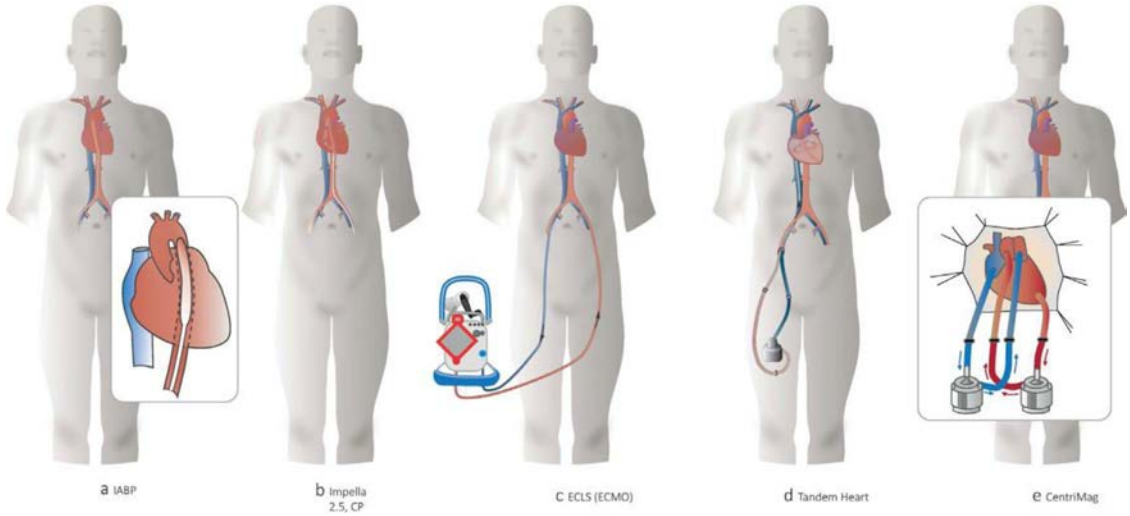

Fig. 1.1 Overview of devices for acute mechanical circulatory support. ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

Table 1.2 Recommendations for Parameters for Identification of CS and Need for Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
Classification of degree of shock, and laboratory tests including complete blood count, electrolytes, renal function, liver function, coagulation profile, arterial blood gas and lactate, and serial cardiac troponin levels should be routinely assessed.	I	C
Multidisciplinary evaluation by a shock team with use of an algorithmic approach is recommended.	I	B
Goals of care should be clearly defined when considering acute MCS.	I	C
Admission to an intensive care unit is recommended as soon as possible.	I	C
Aortic regurgitation should be systematically evaluated before MCS implantation.	I	C
Developing systems of care integrating MCS-capable hospitals (hubs) and spoke centers with defined protocols for early recognition, treatment, and transfer has the potential to improve outcomes of patients with CS.	II	C
Acute MCS hospitals should be available to provide support at all times.	I	B

CS, cardiogenic shock; MCS, mechanical circulatory support.

Early acute MCS can be considered in those who fail to stabilize after initial intervention in an attempt to avoid multiorgan or BiV failure.[45–47] In patients with refractory CS with uncertain neurological prognosis (eg, after cardiorespiratory arrest), acute MCS can be used before durable therapies to allow for declaration of long-term candidacy.[45–50] Temporary rather than durable MCS as a first-line device should be considered when immediate stabilization is needed to enable recovery of the heart and other organ systems, when surgical risk is prohibitive but may be attenuated by such stabilization, when support is required to facilitate a definitive procedure or intervention (such as revascularization or arrhythmia ablation), or when time is required to allow transplantation or durable MCS evaluation.[5] In situations such as AMI, stress cardiomyopathy and myocarditis, acute MCS may be used as a bridge to recovery or a bridge to therapy.[43,51–53]

Extracorporeal membrane oxygenation (ECMO)–CPR (eCPR) is increasingly being considered based on observational data. eCPR involves the placement of VA-ECMO emergently during chest compression to restore circulation when the heart is in cardiac arrest. Although overall post-eCPR survival to hospital discharge has been approximately 30%, at present there is insufficient evidence to recommend a widespread adoption of this approach.[54] Importantly, eCPR might be feasible in tertiary care centers with an established VA-ECMO program with rapid deployment teams, usually restricted to patients with a witnessed cardiac arrest, short no-flow time, a primary rhythm that may be cardioverted, and/or a reversible etiology (Table 1.3).

Recommendations for Timing in Acute Coronary Syndromes

Despite prompt revascularization, patients with anterior STEMI and a significant amount of myocardium at risk suffer from high mortality and HF at mid-term follow-up. There is no survival benefit from routine intra-aortic balloon pump (IABP) regarding mortality, reinfarction, HF or infarct size reduction.[55] Although standard therapy for STEMI is rapid myocardial reperfusion, up to one-third of STEMI patients do not experience effective reperfusion as assessed by resolution of ST segment elevation. Moreover, reperfusion itself may cause myocardial damage (reperfusion injury) and life-threatening ventricular arrhythmias. Large registries have reported a potential benefit of acute MCS in CS, particularly if implanted before revascularization.[2,43,44,51,52,56–74]

Growing translational evidence associates pre-PCI LV mechanical unloading with myocardial protection and augmented myocardial recovery.[51,63,68] LV mechanical

Table 1.3 Recommendations for Timing of Acute MCS in CS

Recommendation	Class of Recommendation	Level of Evidence
Acute MCS should be initiated as soon as possible in patients with CS who fail to stabilize or continue to deteriorate despite initial interventions.	I	B
The use of acute MCS should be considered in patients with multiorgan failure to allow successful optimization of clinical status and neurologic assessment before placement of durable MCS or organ transplantation.	II	C
In patients with cardiac arrest receiving cardiopulmonary resuscitation, VA-ECMO can be considered.	II	C
When considering VA-ECMO, the need for left ventricular venting/unloading (pharmacologic or mechanical) should be considered.	II	B

MCS, mechanical circulatory support; VA ECMO, venoarterial extracorporeal membrane oxygenation.

unloading before culprit vessel reopening may reduce reperfusion injury and prime (biologically and mechanically) the myocardium for reperfusion, thus limiting infarct size and preventing subsequent adverse remodeling.[75] Observational data suggest that pre-PCI LV mechanical unloading may be associated with improved survival.[59,65,72] Implantation can usually be achieved within 5−10 minutes and should not exceedingly delay standard care.

Experience with the Impella device (Abiomed, Danvers, MA, USA) in stable patients with STEMI is limited, but preclinical studies have shown that the beneficial effect of acute LV unloading could be seen only when it is initiated 30 minutes before reperfusion but not within 15 minutes or after reperfusion.[52,56] Early initiation of hemodynamic support before PCI with Impella is associated with more complete revascularization and significantly improved survival in the setting of refractory CS complicating AMI,[59,72] whereas patients supported after PCI seem to have poor survival at 30 days. The Door to Unloading Trial (NCT03947619) will assess the impact of primary unloading before reperfusion vs standard care in AMI. The results of this ongoing trial will provide more definitive data on the role of acute MCS in combination with emergency PCI in patients with AMI.[60]

If patients are in preshock, reperfusion might rapidly lead to hemodynamic deterioration. Acute MCS placement before revascularization is feasible,[60] may improve myocardial salvage,[51,68] confer myocardial protection, and prevent deterioration to overt CS.[52] Acute left anterior descending coronary artery occlusion or left main lesions are often accompanied by acute HF (reduced LVEF, increased LV end-diastolic pressure) and CS with mortality exceeding 50%,[13] despite guideline-recommended early revascularization and vasopressors and inotropes to maintain organ perfusion.[47,64] In progressive organ dysfunction owing to low CO, it seems intuitive to restore CO as quickly as possible without stressing the myocardium with catecholamines. Some acute MCS modalities can simultaneously unload the LV and augment CO.[59,65,72] For CS, a similar quality metric that reflects the time between the onset of CS and the initiation of acute MCS should be developed as the "door to support" time. Several recent reports support the concept of a door to support time, and have observed improved survival with early initiation of short-term MCS before PCI or before the initiation of inotropes and vasopressors in the setting of AMI-CS.[64,72] In AMI-CS, revascularization is immediately required along with early LV unloading. Even cases of preshock may be considered for short-term MCS facilitating a time to support concept.[44]

In nonischemic CS treated with inotropes and vasopressors, acute MCS should be provided if first line therapy fails or either recovery or future cardiac replacement therapy (transplantation or LVAD) is being considered.[43]

Recommendations for Timing According to Hemodynamic and Laboratory Parameters

Patients with CS should undergo a structured evaluation using right heart catheterization and echocardiography. Hemodynamic and echocardiographic evaluation may help to address the phenotype of the failing heart (eg, RV vs LV vs BiV failure).[76] RV dysfunction is common in patients with AMI-CS, as defined in Table 1.1.[77]

Cardiac power output in watts, calculated as (CO × mean arterial pressure)/451, is the strongest independent hemodynamic correlate of in-hospital mortality in patients with CS. In the SHOCK trial, cardiac power output of 0.53 W or less was associated with a 58% in-hospital mortality rate. Advancing age and female sex are independently associated with lower cardiac power output.[78]

Biomarkers are important for the diagnosis, monitoring, and management of patient with CS. Standard parameters such as serum lactate or serum creatinine are most useful. At rest, most cardiac energy results from beta-oxidation of fatty acids and pyruvate,[79] whereas during exercise or other stress situations lactate appears to be an important source of energy.[80] High lactate levels may reflect a stress response of the body with activation of the sympathetic nervous system, increased glycolysis, and a modified bioenergetic supply in patients with CS.[81] Elevated arterial lactate levels are nonspecifically indicative of tissue hypoxia, and are associated with mortality in CS.[82,83] A peripheral oxygen demand −delivery mismatch will result in low central venous oxygen measurements. Serial measurements of arterial lactate and mixed venous oxygen saturation levels may be helpful to temporally monitor responses to therapeutic interventions. Arterial blood gas measurements also permit the assessment of arterial oxygenation and ventilation, as well as metabolic and respiratory acid−base status.[68]

Biomarkers of cardiac myonecrosis are useful to gauge the severity of acute underlying myocardial injury in conditions such as fulminant myocarditis. In AMI, cardiac troponin is noted to be elevated and has a rise-and-fall pattern consistent with acute ischemic injury.[84]

N-terminal pro-B-type natriuretic peptide—a routinely used prognostic marker in HF—was not associated with short-term mortality in multivariable analysis in CS.[85] The development of multiorgan dysfunction has a major impact on prognosis in CS.[86] Therefore, early recognition of loss of function of single organs may be useful to assess prognosis and possibly for treatment decisions regarding timing of intervention with MCS. Acute kidney injury, which is reflected by a rise in serum creatinine and a potential reduction in urinary output in the setting of CS may indicate renal hypoperfusion and is associated with poor outcomes.[85,87,88] Acute ischemic or congestive liver injury can occur in the setting of CS and manifests as a marked elevation in serum aspartate aminotransferase, alanine aminotransferase, bilirubin, and lactate dehydrogenase levels, often accompanied by an increase in prothrombin time. These patients have a 2.5-fold higher 30-day mortality than patients without acute liver injury.[89−91]

A paradigm change has expanded the pathophysiology in CS from a simple low output syndrome to a more complex syndrome involving inflammation and nitric oxide production.[92] Currently, the well-accepted pathophysiological concept in CS includes activation of a systemic inflammatory response.[68] Classical inflammatory markers such as

interleukins have been associated with mortality in these patients.[93,94]

Recommendations for Timing According to Scoring Systems

Multiple scoring systems to predict clinical outcomes in CS have been proposed (Table 1.4). Several models were derived in the general ICU population and include the Acute Physiology and Chronic Health Evaluation (APACHE)-II score and Simplified Acute Physiology Score (SAPS)-II scoring systems.[77,95,96] APACHE-II includes 13 physiological variables and was designed to be measured during the first 24 hours after ICU admission for patients more than 16 years of age. The APACHE-III scoring system adds variables such as pathogenesis of shock, sex, race, and comorbidities to the APACHE-II system and was validated in more than 17,000 ICU patients in the United States. The SAPS-II includes 12 physiological and 3 disease-related variables, was validated in 12,997 patients from 12 countries, and is used to predict in-hospital mortality. A small study comparing the APACHE-II, APACHE-III, SAPS-II, and the Sequential Organ Failure Assessment scoring systems in CS reported that APACHE-III and SAPS-II had the best mortality discrimination.[97] The CardShock study was a series of 219 patients with all-cause CS, and identified 7 variables associated with in-hospital mortality (c index 0.85). However, it lacked external validation.[28] Among patients with an acute coronary syndrome (ACS) complicated by CS, the Global Registry of Acute Coronary Events score has good discrimination and calibration for in-hospital and long-term mortality among all patients presenting with ACS, but it is not applicable to non-ACS presentations.[98] Limitations of available models include the lack of a CS-specific derivation population, external validation, dynamic application (ie, single point in time only), applicability to all CS types, and capture of all potentially prognostic clinical, laboratory, hemodynamic, imaging, and biomarker data.[68]

Identifying the preshock state is appealing as it may reduce mortality by preventing progression to overt CS through initiation of adequate management strategies. The best validated score in this setting is the recently introduced Observatoire Regional Breton sur l'Infarctus (ORBI) score to predict the development of CS.[99] Based on 11 routinely collected variables available in the catheterization laboratory, the ORBI score allowed independent prediction of the development of in-hospital CS after primary PCI (low risk, 0−7 points; low to intermediate risk, 8−10 points; intermediate to high risk, 11−12 points; high risk, >13 points). The score may be useful in the selection of high-risk patients in the setting of future randomized trials designed to provide a tailored aggressive management to preshock or patients with CS (Table 1.4).

Currently, the only CS score with both internal and external validation is derived from the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial.[102] Based on 6 variables—including the biomarkers lactate, creatinine and glucose—with a maximum of 9 points, the IABP-SHOCK II score divides patients into 3 risk groups. Patients in the low (0−2 points), intermediate (3 or 4 points), and high-risk categories (5−9 points) have 30-day mortality risk of 20%−30%, 40%−60%, and 70%−90%, respectively. This score may also be a suitable tool to tailor more aggressive treatment strategies such as acute MCS. However, this requires further validation in randomized trials.

Several risk scores have been proposed for assessing the likelihood of survival to hospital discharge in patients with ECMO, such as Predicting Death for Severe ARDS on VV-ECMO (PRESERVE),[107] Survival After Veno-Arterial ECMO (SAVE),[103] ENCOURAGE,[104] PREDICT VA-ECMO,[105] and the Simple Cardiac ECMO scores.[106] Risk assessment based on established risk models in patients with ECMO remains difficult.[28,102] Only the SAPS II and the SAVE score were found to be suitable specifically for short- and long-term outcome prediction in this vulnerable patient population.[106] Biomarkers have been incorporated in both scores. These multiparametric scores can assist the HF team in arriving at comprehensive risk assessments to inform decisions. However, there are several important considerations and limitations that are often overlooked when applying these tools in clinical settings and in clinical trial design, including the fact that these risk scores have modest discrimination at best.

In light of the high in-hospital mortality, costs, and ethical issues, appropriate patient selection for MCS requires careful consideration of the aforementioned factors.

Requirements for the Use of MCS in Acute CS

Many hospitals have developed multidisciplinary care teams for patients with AMI-CS. Cardiac surgeons, interventional cardiologists, advanced HF cardiologists and critical care specialists have collaborated to institute shock teams. These teams are based on several requirements: (1) the multidisciplinary approach must be maintained on every patient, (2) consistent treatment options must be available 24 hours a day and 7 days a week, (3) team members should ideally commit to rounds with representation from each member specialty, and (4) information must flow to all team members in a timely manner.[108−111]

Shock Team Coordination, Notification, and Communication

The most important aspect of team-based care of the CS patient is the relational coordination of the multidisciplinary team, not the management of materials or resources. The shock team evaluation of patients with CS begins with multidisciplinary team notification, and assessment and information must continue to flow to team members with changes in status and care in a timely manner. Initial presentation may be accomplished through a central referral center with some or all team members receiving the initial information and determining suitability for treatment/

Table 1.4 Selected Scoring Systems to Predict Mortality in Patients with Cardiogenic Shock

Score	Population	General	Neurologic	Metabolic	Hepatic	Renal	Cardiac	Hematologic	Respiratory
APACHE III[77]	ICU	Age, temperature, chronic health score/organ failure		Lactate, pH	Bilirubin	BUN, creatinine, sodium, potassium, urine output	Cardiac arrest, heart rate, mean arterial pressure	Hematocrit, WBC	Respiratory rate, PaO_2, FiO_2
APACHE IV[100]	ICU	Age, temperature, chronic health variables, ICU diagnosis, emergency surgery, hospitalization variables	Glasgow Coma Score	pH, glucose	Bilirubin, albumin	BUN, creatinine, sodium, urine output	Heart rate, mean arterial pressure	Hematocrit, WBC	Respiratory rate, PaO_2, FiO_2, pCO_2, mechanical ventilation
Sequential Organ Failure Assessment[101] to predict morbidity related to sepsis	Sepsis		Glasgow Coma Score, neurological evaluation		Bilirubin	Creatinine, urine output	Mean arterial pressure or vasopressor/inotropes	Platelets	PaO_2, FiO_2
SAPS II[96]	ICU	Age, temperature, chronic health variables, type of admission	Glasgow Coma Score		Bilirubin	BUN, sodium, potassium, bicarbonate, urine output	Heart rate, systolic blood pressure	WBC	PaO_2 if mechanical ventilation
CardShock[28]	Cardiogenic shock	Age	Confusion	Lactate		eGFR	Ejection fraction < 40%, CAD variables		
Global Registry of Acute Coronary Events[98]	Acute coronary syndrome	Age		Bicarbonate		Creatinine	Heart rate, systolic blood pressure, cardiac arrest, Killip class, ST segment changes, timing of cardiac enzyme elevation		
ORBI[99] to estimate risk of development of in-hospital CS	STEMI treated with PCI without CS at admission	Age	Prior stroke	Hyperglycemia			Cardiac arrest, heart rate, systolic BP, Killip class, anterior MI, post-PCI TIMI flow <3, LM culprit lesion, delayed PCI		
IABP-SHOCK II[102]	AMI-CS	Age	Prior stroke	Lactate, hyperglycemia		Creatinine	TIMI flow <3		
SAVE[103]	VA-ECMO	Age, weight, underlying diagnoses, cause of CS					Cardiac arrest, diastolic blood pressure, pulse pressure		Duration of intubation/ventilation, peak inspiratory pressure
ENCOURAGE[104]	VA-ECMO for AMI	Age, sex, BMI	Glasgow Coma Score	Lactate		Creatinine		Prothrombin activity	
PREDICT VA-ECMO[105]	VA-ECMO			Lactate, pH		Bicarbonate			
SIMPLE CARDIAC ECMO[106]	VA-ECMO	Postcardiotomy		Lactate		RIFLE kidney injury score			

AMI, acute myocardial infarction; APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; BUN, blood urea nitrogen; CS, cardiogenic shock; ENCOURAGE, Prediction of cardiogenic shock outcome for acute myocardial infarction patients salvaged by VA-ECMO; GRACE, Global Registry of Acute Coronary Events; IABP-SHOCK, intra-aortic balloon pump in cardiogenic shock; ICU, intensive care unit; ORBI, Observatoire Regional Breton sur l'Infarctus; RIFLE, risk, injury, failure, loss, end stage kidney disease; SAPS, Simplified Acute Physiology Score; SAVE, survival after venoarterial ECMO; STEMI, ST-elevation myocardial infarction; VA-ECMO, venoarterial extracorporeal membrane oxygenation; WBC, white blood cell count.

transfer. This assessment may suggest an initial treatment strategy and determine the receiving location (ICU, catheterization laboratory, or operating room). Once the decision is made to accept and treat, the multidisciplinary team evaluates the patient and formulates further treatment strategy.[5,16] Despite initial treatment efforts, frequent multidisciplinary reassessment is a requirement for collaborative team care. The use of encrypted apps and dedicated communication tools for diagnostic imaging and patient data has aided in real-time updates and information flow so that members of the shock team can remain informed and collaborate. Robust communication protocols and electronically available diagnostic data allow collaboration without the need for physical presence in many systems. Last, to improve local care and outcomes, regular review of process benchmarks and patient outcomes with stakeholders allows for continuous performance improvement.[2,10,108,109]

Location, Materials, Equipment, and Networks

The successful implementation of multidisciplinary shock teams/treatment programs requires the coordination of a complex operation and appropriate application of technical skill involving personnel, facilities, or supplies in the background of other competing clinical entities with a similar time urgency. Further, successful deployment depends on estimating and providing the multilevel resources to meet the needs of patients with CS where and when they present for treatment. To support shock teams, resources must be allocated and defined, monitoring established to assess adequacy of treatment and to prevent complications, and communication protocols established to allow multidisciplinary evaluation, treatment and escalation of care when appropriate.[108−111]

Team members define the support techniques and tools for the spectrum of clinical scenarios and deploy personnel and resources to best meet these needs in their system. Few programs possess every treatment tool available for CS but rather focus on excellence in the use of the tools and skills already present. Programmatic assessment of capacity and use can be determined by historical treatment patterns projecting additional resources for potentially longer durations of care and increased survival rates with team-based treatment. Reconciliation between projections and actual utilization is important to avoid oversupply or under-capacity. Teams must establish program benchmarks and expectations for deployment and capacity as well as response time, process, and performance. Metrics such as time to deployment and survival should be monitored for a program to improve over time.[109,110]

Lessons and structure adopted from ACS and trauma systems of care have allowed shock teams to form and evolve rapidly. The effectiveness of therapy in CS is limited if not deployed rapidly. Like the Trauma Center paradigm, organization of the process of trauma care delivery is crucial to optimize outcomes.[109,111,112] The initial goal in both systems is the same: rapid reversal of low output state to maintain end-organ perfusion. Initial management goals of "triage," "recognize," and "transfer" in CS can be accomplished in most hospitals. Hospitals with additional acute MCS capabilities can further stabilize and treat these patients. When care in these facilities exceeds local resources, transfer to the closest, appropriate facility offering long-term MCS/heart transplant capabilities is needed for definitive care. Similar to the trauma system, patient care is optimized when networks comprised of centers with differing capabilities develop to triage, stabilize, and treat this patient population.[112]

Monitoring

Once the multidisciplinary evaluation and initial treatment has begun, invasive and noninvasive monitoring allows the assessment of initial treatment efforts and remaining physiologic challenges. Hemodynamic instability and vasopressor use in CS warrant invasive arterial blood pressure monitoring to guide drug titration and escalation of care. Central venous catheter insertion should be considered to monitor central venous pressure and central venous oxygen saturation. Repeated assessments of plasma lactate have been shown to offer prognostic information as well.[113]

The selective use of pulmonary artery catheters (PACs) should be used in diagnostic or CS management uncertainty or in patients with moderate to severe CS who are unresponsive to initial therapy.[113] Hemodynamic data provided by a PAC can confirm the severity of CS, assess RV involvement as well as determine pulmonary artery pressures and the vascular resistance of the pulmonary and systemic arterial beds.[111−113] Finally, PACs enable clinicians to monitor responses to therapeutic interventions and assess recovery. Alternatives to invasive monitoring include noninvasive CO devices, tied to arterial blood pressure, or collateral pressure monitoring available on percutaneous LVADs, and some ECMO systems.[109,111,113] However, the data on use of noninvasive devices in management of CS and acute MCS are limited.

Once initial efforts have stabilized the patient, ongoing hemodynamic monitoring focuses on the detection and treatment of LV distention, pulmonary edema and RV dysfunction. These parameters should be serially assessed to guide therapies such as direct or indirect LV venting to prevent complications of MCS such as acute lung injury.[114] Last, invasive and noninvasive monitoring of intrinsic cardiac function offer a window into the detection of myocardial recovery and allow timing and weaning of cardiac and systemic support or transition to LVAD or heart transplantation (Table 1.5).[113−115]

Pulmonary Shock

Definitions of Acute Pulmonary Failure

The contemporary definition of acute pulmonary failure is the short-term (hours to days) inability of the respiratory system to maintain either an arterial partial pressure of oxygen (PaO_2) of at least 60 mm Hg or an arterial partial pressure of carbon dioxide between 35 and 45 mm Hg,

Table 1.5 Recommendations for Monitoring of CS and Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
Selective use of invasive monitoring such as PACs should be considered in diagnostic or CS management uncertainty or in patients with moderate to severe CS who are unresponsive to initial therapy.	II	B
Monitoring of left ventricular distention, pulmonary edema, and right ventricular filling should be available for serial assessment and to guide therapy and prevent complications of MCS.	II	C
Monitoring of intrinsic cardiac and systemic blood flow/output with the ability to assess cardiac recovery with weaning should be available.	II	C

CS, cardiogenic shock; MCS, mechanical circulatory support; PACs, pulmonary artery catheters

according to demands of cellular metabolism at sea level. However, these values are a general guide that must be considered in the context of other test results, past medical history, and physical examination. A thorough evaluation is often necessary to differentiate between primary pulmonary and extrapulmonary dysfunction, especially in later stages of disease progression.[116] Acute hypoxemic failure is defined as severe arterial hypoxemia refractory to supplemental oxygen. It is caused by intrapulmonary shunting of blood as a consequence of airspace filling or collapse and may be pulmonary or extrapulmonary in origin.

Airspace filling may result from elevated alveolar capillary hydrostatic pressure (as occurs in LV failure or hypervolemia), pulmonary hemorrhage that originates from the pulmonary microcirculation (including the alveolar capillaries, arterioles, and venules as occurs in diffuse alveolar hemorrhage), inflammatory exudates (as in pneumonia or lung cancer), or from pulmonary and systemic insults to the alveolar-capillary membrane, resulting in increased alveolar capillary permeability and development of interstitial and alveolar edema (as in any of the conditions predisposing to acute respiratory distress syndrome [ARDS]). ARDS is a heterogeneous syndrome with sub-phenotypes that are associated with differences in responses to therapy (and thus, outcomes), which remain difficult to predict. Despite the prognostic challenges, several models have been developed in pursuit of this endeavor. An important early ARDS classification scheme with prognostication was developed by Murray and colleagues,[117] and Murray scores (for which there are easy-to-access online calculators) are commonly used today in assessing the need for ECMO support, typically indicated by scores of 3 or more prompting consideration of venovenous (VV)-ECMO use. The Berlin Definition of ARDS categorized severity based upon physiologic, radiographic, and gas exchange parameters, and was shown to be useful in assessing risk of death.[118] Two other scoring systems that can be used in prognosticating ARDS (and for consideration of ECMO use) include the age-adjusted oxygenation index and the age, PaO_2/FiO_2, and plateau pressure score.[119]

Acute hypercapnic respiratory failure, in which inadequate gas exchange results in a PCO_2 value of more than 50 mm Hg owing to carbon dioxide retention, is pathophysiologically explained by reduced alveolar ventilation, resulting in respiratory acidosis. Retention of carbon dioxide may be an acute or chronic process, with the former less well clinically tolerated owing to less time for metabolic compensation. Hypercapnia may be precipitated by fever, sepsis, seizures, increased dead space (eg, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis), hypoventilation with depressed central respiratory drive (such as occurs with opioid overdose), neuromuscular transmission malfunction, mechanical defect of the ribcage (eg, trauma or kyphoscoliosis), or fatigue of the respiratory muscles. Some degree of hypercapnia can also be an anticipated and acceptable consequence of a lung-protective ventilation strategy used as part of ARDS treatment, where reduced ventilation volumes (used to avoid barotrauma and volutrauma) also prevent adequate pulmonary CO_2 removal. In selected patients who are not responsive to usual management strategies and have inadequate gas exchange despite such supportive measures and ventilation strategies, ECMO can be a useful modality.

ECMO and Acute Pulmonary Failure

There have been 3 major prospective trials in the last 40 years using ECMO for treatment of ARDS or "severe acute pulmonary failure" (used before the term "ARDS" was coined). The first one by Zapol et al. in 1979, using VA-ECMO, showed no improvement in patient survival, although lung protective mechanical ventilation strategies were not used and the patients had been ventilated for longer times before initiation of ECMO compared with later trials.[117,118] Furthermore, technological advances in hardware and circuitry have occurred in conjunction with improvements in medical management, with the adoption of evidence-based algorithms and personnel dedicated to the initiation and maintenance of ECMO. A second trial was done by Morris et al. in 1994 and compared pressure-control inverse ratio ventilation with extracorporeal carbon dioxide (CO_2) removal through an ECMO circuit.[120,121] Once again, no significant difference in survival was found between the 2 groups. Subsequently, a consensus was developed that ECMO should not be used in the treatment of acute pulmonary failure. In a more contemporary trial examining the use of ECMO for acute pulmonary failure, the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial randomized 180 adult patients with severe reversible pulmonary failure to conventional management

vs referral to an ECMO center for this advanced therapy.[122] The ECMO group had a 16% absolute decrease in the primary end point of death or severe disability, although the study was criticized for its lack of a standardized ventilator management protocol in the control group.[7] Nonetheless, the favorable results ushered in a renewed optimism about use of ECMO for pulmonary failure and convinced many centers to offer it as salvage treatment.

An unexpected challenge to the critical care community occurred in 2009 with the outbreak of pandemic influenza A (H1N1), where many healthy young people developed respiratory failure and ARDS as the result of infection. A network of ICUs in Australia and New Zealand reported 75% survival to discharge in suspected H1N1-associated ARDS when supported by ECMO.[6] In the UK, the hospital survival rate was 76% for ECMO-referred patients with influenza ARDS,[121] and 78% in the Italian ECMO network in patients with H1N1 influenza ARDS in whom ECMO was initiated within 1 week from the onset of invasive mechanical ventilation.[123] These experiences increased confidence in the use of ECMO and accelerated its adoption in centers around the globe. Most recently, ECMO has been deployed successfully in the management of critically ill patients with coronavirus disease 2019.[124–126]

The Extracorporeal Life Support Organization (ELSO) registry benchmark for survival to discharge is 61% for acute respiratory failure in adults supported on ECMO.[127] A retrospective analysis of adult trauma patients with acute hypoxemic respiratory failure reported similar results.[128] Current literature supports the use of ECMO for acute respiratory failure when severe and not amenable to other forms of support, and only when the condition is deemed to be reversible (ie, bridge to recovery) or when used as a bridge to lung transplantation in suitable candidates.[129–132]

Indications and Contraindications

The primary indications for VV-ECMO in acute pulmonary failure include:

- Hypoxemic respiratory failure
- Hypercapnic respiratory failure
- Respiratory failure while awaiting lung transplantation
- Pulmonary air leaks and complex airway management

Indications in Hypoxemic Respiratory Failure

Different criteria have been described to support initiation of VV-ECMO in hypoxemic respiratory failure. According to ELSO, VV-ECMO in hypoxemic respiratory failure owing to any cause (primary or secondary) should be considered when the risk of mortality is 50% or greater (PaO_2/FiO_2 < 150 on FiO_2 > 90% and/or Murray score 2–3, age-adjusted oxygenation index score of 60), and is indicated when the risk of mortality is 80% or greater (PaO_2/FiO_2 < 100 on FiO_2 > 90% and/or Murray score 3–4, age-adjusted oxygenation index >80, age, PaO_2/FiO_2 and plateau pressure score 8) despite optimal care for 6 hours or less. Early institution after onset of respiratory failure (1–2 days) is associated with better outcomes. PaO_2/FiO_2 ratios of less than 80 with high positive end-expiratory pressure of 15–20 cm H_2O were proposed by Brodie and Bachetta.[133] According to the Extracorporeal Support Study Group of San Pablo, Brazil, ECMO support is indicated based on major and complementary criteria as shown elsewhere in this article.[134]

Major Criteria (Both Required)

1. Acute pulmonary disease AND
2. Possibility of recovery from disease

Complementary Criteria (At Least One Required)

1. PaO_2/FiO_2 ratio < 50 with an FiO_2 of 1 for at least 1 hour, with or without rescue maneuvers
2. PaO_2/FiO_2 ratio < 50 with an FiO_2 of more than 0.8 for at least 3 hours, despite rescue maneuvers
3. Murray score > 3.0 in the presence of clinical deterioration

The French Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA) trial included patients that had been receiving invasive mechanical ventilation for less than 7 days, with a PaO_2/FiO_2 ratio of less than 50 for more than 3 hours or PaO_2/FiO_2 ratio of less than 80 for 6 hours; or an arterial blood pH of less than 7.25 with a $PaCO_2$ 60 mm Hg or greater for more than 6 hours.[6]

Indications in Hypercapnic Respiratory Failure

According to ELSO criteria, ECMO indication for hypercapnic respiratory failure is CO_2 retention on mechanical ventilation despite high plateau pressures (plateau pressure of >30 cm H_2O). Brodie and Bachetta recommend initiating extracorporeal support whenever uncompensated hypercapnia with acidemia (pH < 7.15) or excessively high end-inspiratory plateau pressure (>35–45 cm H_2O) persists despite the provision of optimal care with invasive mechanical ventilation.[133] The Brazilian group suggests initiation of ECMO for a pH of 7.20 or less despite a respiratory rate of 35 breaths/min or more (whenever possible), a tidal volume of 4–6 mL/kg, and a plateau pressure 30 cm H_2O or less.[134]

Contraindications in Hypoxemic or Hypercapnic Respiratory Failure

The ELSO guidelines do not delineate any absolute contraindications, but there are certain conditions that are related to poor outcomes, and thus are considered relative contraindications[127]:

1. Mechanical ventilation at high settings (FiO_2 > 0.9, plateau pressure > 30) for 7 or more days. Many centers do not consider time on a ventilator to be a contraindication.
2. Major pharmacologic immunosuppression (absolute neutrophil count < 400/mm^3)

3. Central nervous system hemorrhage that is recent or expanding
4. Nonrecoverable comorbidity such as major central nervous system damage or terminal malignancy
5. Age: no specific age contraindication, but consider increasing risk with advancing age

Other Considerations. Use of anticoagulant therapy is considered a strong relative contraindication to use of ECMO in any condition that carries a high risk of bleeding, although its use has been described in refractory hypoxemic respiratory failure owing to diffuse alveolar hemorrhage, a condition for which anticoagulation is typically contraindicated.[135] Although several centers consider obesity a relative contraindication, Kon et al. found that class III obesity was not associated with poorer outcomes, and suggested that ECMO support not be withheld from this patient population.[136]

Septic shock was previously considered a contraindication to initiation of VV-ECMO. It remains in the almost exclusive purview of the VA-ECMO modality, and is associated with poor survival.[137,138] In a bid to identify which patients would benefit from ECMO support, several predictive survival scoring systems have been devised, including the Resp Score, ECMONet Score, and PRESERVE score. These scoring systems may have the added benefit of allowing for optimal use of resources required for ECMO.[107,139,140] The validation of these scoring systems and their application are forthcoming.

Indications for ECMO Before and After Lung Transplantation

Lung transplantation is a treatment for end-stage lung disease. However, there is a paucity of donors, and when a listed candidate's disease progresses or when there is an acute decompensation, invasive support may be required to support the failing lungs. If maintained on a mechanical ventilator, complications may arise that preclude transplantation, such as the development of multiorgan failure, extreme frailty and/or neuropathy, or septic shock. Should these conditions become irreversible, the patient will be removed from the transplant waiting list, with an almost certain fatal outcome. However, early deployment of preoperative ECMO as a bridge to transplantation has recently improved these outcomes. This has been largely attributed to improvements in ECMO pump circuitry and medical management.[131] This early use of ECMO, particularly with the use of an ambulatory cannula, allows for aggressive physical therapy and pulmonary rehabilitation to maintain musculoskeletal strength and endurance before transplant surgery. Additionally, in select candidates, extubation may allow for spontaneous respiratory excursion which assists in clearance of secretions and optimization of nutritional status before surgery. Furthermore, there is growing evidence of ECMO outcomes outpacing those of mechanical ventilation as a bridge to transplantation.[26,28] These measures will also assist in a more rapid recovery post-transplant, minimizing complications and decreasing hospital length of stay.[129,141–144]

Some patients may develop primary graft dysfunction and require ECMO following lung transplantation. In such patients, shorter duration of pretransplant ECMO is associated with better outcomes. Intraoperative ECMO may be used in patients with severe pulmonary hypertension or those with intolerance to intraoperative single lung ventilation (severe hypoxia or inadequate ventilation). In some centers, conventional cardiopulmonary bypass is being replaced by use of intraoperative ECMO, requiring lower levels of anticoagulation and with a subsequent lower risk of bleeding. ECMO may also be associated with a lower inflammatory response and fewer postoperative complications.[145,146] Postoperative primary graft dysfunction that requires ECMO is best treated with VV-ECMO, a strategy that improves oxygenation and ventilation while maintaining allograft perfusion. In cases of severe RV hypertrophy and pulmonary hypertension, it may be necessary to use VAV-ECMO. Isolated VA-ECMO can result in pulmonary hypoperfusion and should be avoided.[147]

The circumstances most commonly associated with the need for post-lung transplant ECMO include:

1. Transplant for pulmonary hypertension or Eisenmenger syndrome
2. Elevated pretransplant pulmonary artery pressure
3. Pretransplant mechanical ventilation or ECMO
4. Cardiopulmonary bypass during transplant
5. Advanced allograft donor age[145]

Although the use of postoperative ECMO in support of patients with severe primary graft dysfunction has had encouraging results (especially when used early), such patients still have significantly lower long-term survival than patients without severe primary graft dysfunction.[148–150]

Indications in Respiratory Failure for Other Causes

The ELSO guidelines consider severe air leak syndromes as a formal indication for the use of VV-ECMO, allowing for the use of protective ventilation, which facilitates fistula healing (Table 1.6). ECMO can also be useful in management of severe diffuse alveolar hemorrhage and status asthmaticus.[151] An overview on VV ECMO cannulation options is given in Fig. 1.2.

General Management of Patients with Acute MCS

Refer to Table 1.7 and Table 1.8.

VA-ECMO

ECMO is increasingly used as the first-line acute circulatory support in patients with cardiac and respiratory failure. Whether the device is providing gas exchange alone or both gas exchange and hemodynamic support, is determined by

Table 1.6 Recommendations for VV-ECMO/Respiratory Failure

Recommendation	Class of Recommendation	Level of Evidence
When placing percutaneous VV-ECMO, suitable central vein(s) should be identified (typically the femoral and internal jugular veins) with large venous access lines placed using point of care ultrasound.[52,55,57,58,61,68,70,152,153]	I	C
An inability to achieve anticipated blood flow with VV-ECMO should trigger an evaluation of cannula position (eg, by chest radiograph) or for cannula kinking, assessment of the patient's volume status, adjustment of the speed of the pump as needed, and hemodynamic optimization.	I	C
Extubating while on ECMO can be considered.	II	C
In patients expected to be on ventilatory support for more than 1 week, early tracheostomy can be considered.	II	C
In patients expected to be on VV ECMO support for more than 1 week, an early mobilization strategy should be considered when able.	II	C
In patients expected to be on ECMO support for more than 2 weeks, early transfer to or communication with a lung transplant capable center should be considered.	II	C

ECMO, extracorporeal membrane oxygenation; VV-ECMO, venovenous extracorporeal membrane oxygenation.

the configuration of the device. VA-ECMO is a configuration used to provide CO for end organ function and simultaneous gas exchange for acute cardiorespiratory failure.[183,246] Fig. 1.3 provides an overview of VA-ECMO configurations.

Peripheral Cannulation. Femoral vessels have become the most common site to establish VA-ECMO. Cannulas can be placed percutaneously or by a surgical cut-down.[247,171] Percutaneous insertion is performed using a modified Seldinger technique. Ultrasound guidance facilitates identification of vessels, assessment of vessel quality and diameters, and needle and wire insertion. Arterial cannula sizes range from 15F to 25F and venous sizes from 19F to 25F. The arterial cannula is typically placed from the common femoral artery into the common iliac artery. The risks of vascular complications such as bleeding and limb ischemia are likely greater with larger size cannulas.[171] In contrast, smaller cannulas are associated with less complications but compromise ECMO flow. Optimal size of cannula and ECMO flow need to be determined on a case-by-case basis.

To prevent limb ischemia, a distal perfusion cannula can be placed through the superficial femoral artery (5F−8F) or through the posterior tibial artery in a retrograde fashion. Venous cannulas often have end and side holes to permit better drainage and are positioned at the junction of the intrahepatic portion of the inferior vena cava and right atrium. Venous cannula malposition causes frequent suction and suboptimal drainage. Open cannula placement is often chosen when the patient is already in the operating room (eg, postcardiotomy shock). By cut-down, femoral vessels are exposed and a guidewire and cannula are placed under direct vision. Cannulas are usually secured with purse string sutures and tourniquets. To allow closure of the femoral

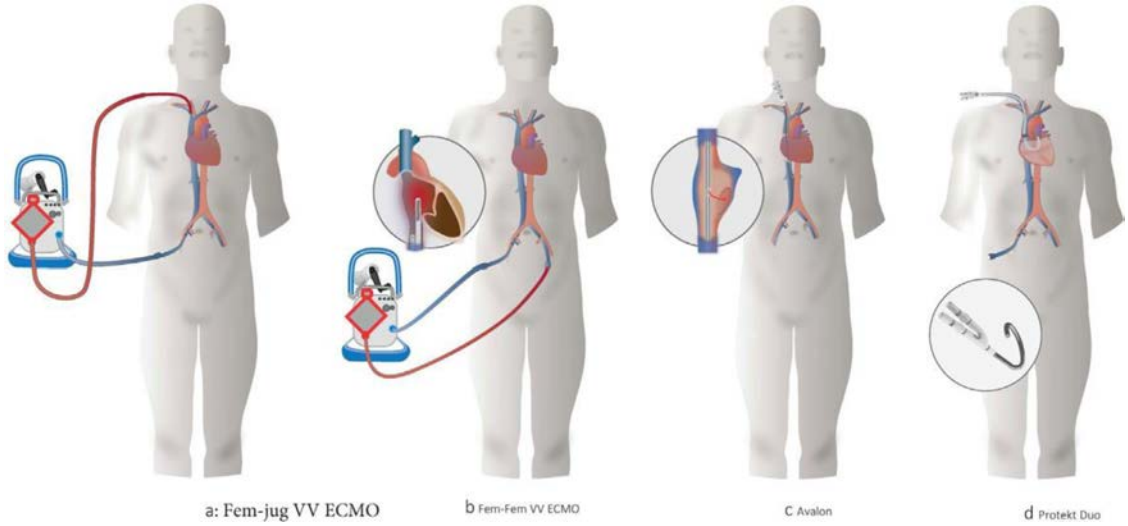

Fig. 1.2 Different cannulations for VV ECMO. Fem-Fem, femoral-femoral; Fem-jug, femoral−jugular; ECMO, extracorporeal membrane oxygenation; VV, venovenous.

Table 1.7 General Recommendations for Acute MCS Devices[154–187]

Recommendation	Class of Recommendation	Level of Evidence
Device selection should be based on ability to achieve an expected level of hemodynamic support with a target resuscitative CI of >2.2 L/min/m^2, PCWP of <18 mm Hg, CVP of <10 mm Hg, SBP of ≥90 mm Hg, or MAP of 60–80 mm Hg.	II	C
Standard cardiovascular monitoring including arterial line and pulmonary artery catheter for hemodynamic guidance of supportive vasoactive and inotrope infusion dosing is recommended peri-implant.	II	C
Point of care ultrasound imaging should be used for obtaining percutaneous vascular access when available. If unsuccessful, surgical cut-down may be considered.	I	C
When large bore arterial access is used, consider a priori distal bypass strategies.	II	C
Placement of preclosure devices can be considered.	II	C
Pump position monitoring with imaging is recommended.	I	C
For patients in whom prolonged support with acute MCS is anticipated, a cannulation strategy to facilitate mobilization should be considered.[164,188–196]	II	C
Vasopressors and inotropes should be minimized to achieve targeted hemodynamics with acute MCS while promoting lactate clearance and improved end-organ function.[197–199]	II	C
Diuretics can be used to optimize hemodynamics and relieve congestion.[197,200]	II	C
Once hemodynamically optimized, cautious mobilization can be considered and, when possible, is encouraged.[201–203] a. For patients selected for mobilization, a multidisciplinary approach to this undertaking should be used and include physical therapists, occupational therapists, respiratory therapists, ECMO specialists, nurses, intensivists, and surgeons where appropriate.[189,204,205](For patients already supported by more than 1 femorally inserted hemodynamic support device, mobilization should not be pursued.[206])	II	B
In extremities in which acute MCS is implanted, limb surveillance for ischemia, bleeding and neurologic function is recommended.[207–217]	I	C
Patients with acute MCS should be monitored and treated for hemolysis (see text for device specifics)[50,59,160,161,218–227] a. Hemolysis surveillance - monitor markers of hemolysis (LDH, plasma free Hgb, haptoglobin, bilirubin, urine color change, hematocrit decrease). b. LDH is nonspecific but plasma-free hemoglobin not always rapidly resulted, especially if send-out test. c. If indications of hemolysis, attempt to lower rotational speed as tolerated (lower risk of hemolysis at lower speeds), check device position, and reposition as clinically indicated d. Consider thrombosis of pump. e. If hemolysis cannot be controlled, device removal should be considered.	I	C
Patients with acute MCS should be monitored for infection.	I	B
For patients with acute MCS, renal replacement therapy can be considered to optimize hemodynamics, relieve congestion, and correct metabolic abnormalities.[228-234]	II	B
In patients on acute MCS, early weaning of the ventilator with the goal of extubation may be considered.[235]	II	C
Early tracheostomy should be considered if weaning of the ventilator to extubation is not possible.[235]	II	B
Movement of patients should be minimized and performed by staff specifically trained in the management of acute MCS devices to avoid device dislodgement.	I	C
For patients with biventricular failure, biventricular support should be considered with: - VA-ECMO - Bilateral centrifugal pumps - Bilateral axial flow pumps	II	C
In centers where a patient has acute cardiac and/or pulmonary failure who meets criteria for acute MCS but is in a non-MCS capable hospital, early transfer and/or mobile MCS (primary ECMO) should be considered	I	C
Experienced MCS centers should develop mobile capabilities to expand access to acute MCS in non-MCS centers when able	II	C

CI, cardiac index; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; LDH, lactate dehydrogenase; MAP, mean arterial pressure; MCS, mechanical circulatory support; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

See Task Force 2 for management of anticoagulation and antiplatelet therapy during acute MCS.

Table 1.8 Recommendations for Weaning of Acute MCS Support

Recommendation	Class of Recommendation	Level of Evidence
Patients supported with acute MCS for CS should be monitored for signs of improved end organ function and early weaning/discontinuation of MCS.[154–163,220,236–241]	II	B
Potential signs of LV recovery include: - Maintenance of improved hemodynamics on minimal mechanical support/serial weaning trials. - Readiness to wean from IABP can be assessed using PAC-derived data during serial reductions in degree of support provided by the device. - Increased pulsatility. - Echocardiographic criteria: - Aortic time-velocity integral of ≥12 cm. - LVEF of >25%. - Lateral mitral annulus peak systolic velocity ≥ 6 cm/s.	I	C
If weaning is not tolerated, resume pump speed at prior level and reassess in 24–48 hours.	I	C
For those patients supported in centers without a durable MCS and/or transplant program(s), early transfer to a center with these programs should be considered.	I	C
The decision for RVAD weaning should be based on hemodynamic and echocardiographic parameters - Pump support should be minimized to evaluate for recovery/explant candidacy. - A device flow of <2 L/min for >20 minutes should be avoided without anticoagulation. - In patients with a concurrent LVAD, LVAD parameters should be assessed during the weaning process.[225,242–245]	II	C
In patients supported by acute MCS for CS (RVAD/LVAD or ECMO) that are unable to wean, early consideration of exit strategy such as heart transplant (with or without additional organ transplant), durable MCS or transition to end-of-life care should be considered.	I	C
In patients supported by acute MCS for respiratory failure (ECMO) that are unable to wean, early consideration of exit strategy such as lung transplant (with or without additional organ transplant) or transition to end-of-life care should be considered.	I	C

CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; LV, left ventricular; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; PAC, pulmonary artery catheter; RVAD, right ventricular assist device.

incision, the cannulas can be tunneled to a more distal thigh incision. This approach may reduce the risk of site infection. Some centers sew the graft onto the femoral artery to preserve distal perfusion.

Access sites for VA-ECMO are typically femoral and axillary artery and jugular or subclavian veins.[188,248,249] The location of peripheral VA-ECMO cannulation will have a significant impact on the upper body oxygenation

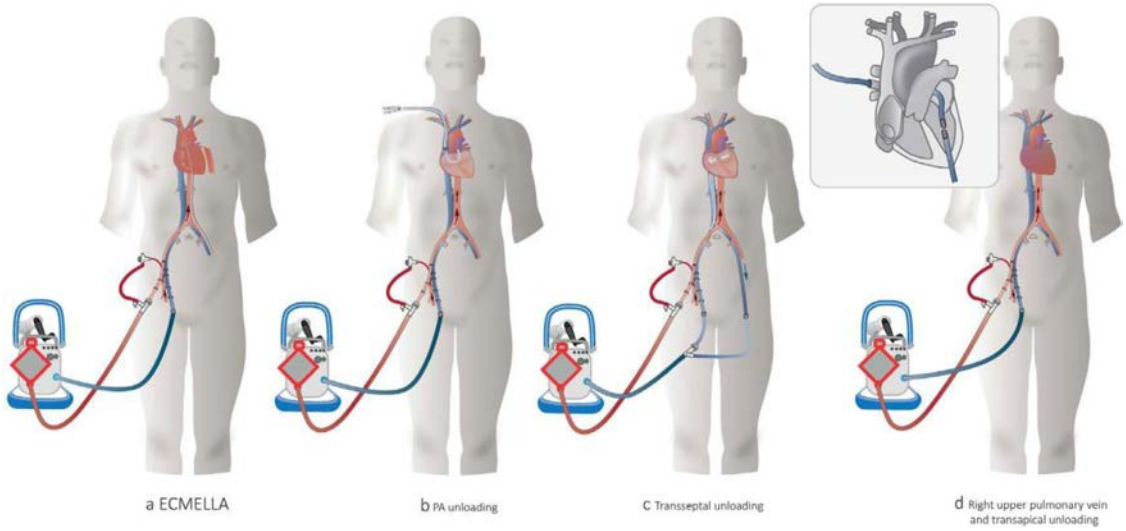

Fig. 1.3 Different cannulations for VA-ECMO: (A) Femoral VA-ECMO: (B) Axillary VA-ECMO. (C) Thoracic, central VA-ECMO. (D) VAV ECMO. VA, venoarterial; VAV, venoarterial-venous; ECMO, extracorporeal membrane oxygenation.

and the ability to perform early mobilization. Femoral cannulation may be associated with "the Harlequin syndrome" (upper body desaturation) if pulmonary function is impaired, and often restricts patient mobility.[248] Upper body configuration to prevent these disadvantages of femoral cannulation include venous drainage via the jugular vein and reinfusion into the axillary artery. Axillary artery cannulation requires surgical cut-down, and an 8- or 10-mm graft is sewn.[188] However, ECMO flow may be limited depending on the artery size and quality, and axillary cannulation is accompanied by the risk of specific complications such as axillary nerve injury and ipsilateral upper extremity hyperperfusion.

The main advantage of peripheral VA-ECMO is easy and rapid establishment of cardiopulmonary support that can be performed in multiple locations (bedside, operating room, catheterization laboratory, ICU, or even in the field). Disadvantages may include difficult cannulation owing to small vessels, flow restriction, and specific upper or lower limb complications.

Central Cannulation. As opposed to peripheral cannulation, surgical placement is mandatory for central cannulation. Unless axillary cannulation is used, central cannulation generally requires an open sternum, therefore occurs in the operating room or surgical ICU, most typically for patients with postcardiotomy shock.[184,250,251] Alternatively, central VA-ECMO can be used as an upgrade from peripheral VA-ECMO when it does not provide enough end-organ function or to overcome problems inherent to peripheral VA-ECMO. Ascending aorta (outflow) and right atrium (inflow) are the preferred cannulation sites. The size of the cannulas can be determined by patient body size and calculated total CO. Usually, a 18F−24F cannula is used for the aorta, and a 28F−36F cannula is used for the right atrium. Cannulas manufactured for cardiopulmonary bypass can be used for central VA-ECMO. To prevent bleeding from cannulation sites or migration of cannulas, it is important to secure the cannula in position with multiple purse string sutures, tourniquets, and anchor sutures to the skin. The chest is usually left open with occlusive dressing but can be closed by tunneling the cannulas through soft tissue to the subxiphoid portion or upper sternal incision. Closing the chest may facilitate extubation on VA-ECMO and mobilization, and decrease the risk of infection.[250] Minimally invasive approaches for VA-ECMO without full sternotomy have also been used to establish central VA-ECMO for non−postcardiotomy shock patients.[252] The innominate artery or ascending aorta can be cannulated via upper hemisternotomy and central VA support can be established in combination with peripheral vein access. The surgeon also can cannulate the aorta and right atrium through a mini thoracotomy approach.[164,248]

The advantages of central VA-ECMO include no flow limitation, antegrade flow, no limb complications, and capability to place LV vent if necessary. Main disadvantages include surgical invasiveness, bleeding, increased risk of infection associated with open chest, potential aortic dissection, and ischemic embolic events (Table 1.9).[184,250,251]

LV Distention and Venting. During peripheral VA-ECMO, the arterial outflow cannula generates retrograde flow towards the aortic valve, resulting in higher afterload on the heart than a normal physiologic state.[288] This marked increase in afterload may lead to LV distension and increases in LV wall stress and myocardial oxygen demands.[288,289] The high LV end-diastolic pressure results in ongoing subendocardial ischemia. These further impair LV function, making LV recovery even more difficult, particularly in patients with CS complicating AMI. Patients with acute CS have a noncompliant LV and may have a competent mitral valve, and are at the greatest risk for LV distension. This is in comparison to patients with acute decompensated chronic HF with ventricles that are dilated at baseline and mitral valves that may be incompetent owing to annular dilatation. Mitral regurgitation may serve as a "pop-off" for the LV, but leads to pulmonary edema. Thus, the incidence of LV distension may vary among patient populations.[290]

If the aortic valve is unable to open and eject blood owing to increasing afterload, blood stasis and thrombus formation may/will occur inside the LV as well as in the aortic root. This could happen regardless of ECMO cannulation site (central or peripheral). Thrombus formation can lead to catastrophic embolization to the coronary arteries, cerebral vessels or body. The distended LV and elevated LV end-diastolic pressure will subsequently result in elevated left atrial and pulmonary venous pressures, leading to pulmonary edema, possible pulmonary hemorrhage, and subsequent systemic, cerebral and myocardial hypoxia.

In addition to clinical signs (eg, differential hypoxia, ventricular arrhythmia), LV distension can be detected at the bedside by hemodynamic monitoring and echocardiography.[47,291,292] On echocardiography, LV distention is evidenced by a dilated and hypocontractile LV, with or without severe mitral regurgitation, stagnation of blood within the LV, and a nonopening aortic valve. Lack of arterial pulsatility is an obvious sign of a closed aortic valve. As measured with a PAC, an elevated pulmonary artery diastolic pressure greater than PCWP suggests that the LV is not properly decompressed.

There are several different strategies for LV unloading, each with its own advantages and limitations (Fig. 1.4).

Reducing ECMO Flow. Reduction of ECMO flow could reduce LV loading and increase the chance of aortic valve opening. However, this approach decreases the degree of cardiopulmonary support. The choice of ECMO flow will need to achieve a balance between the competing goals of providing sufficient CO while allowing the LV to maintain some ejection so as to avoid LV and aortic root thrombosis and pulmonary edema.

Medical Management. Inotropic support can enhance aortic valve opening by increasing myocardial contractility. However, inotropes increase myocardial oxygen consumption and total LV work. This may not be an optimal approach particularly in the setting of myocardial ischemia. The use of vasodilators also can decrease afterload and may allow increasing aortic valve opening. However,

Table 1.9 Recommendations for Venoarterial Extracorporeal Membrane Oxygenation—Left, Right or Biventricular Cardiac Support

Recommendation	Class of Recommendation	Level of Evidence
When placing percutaneous VA-ECMO, a suitable central artery and vein should be identified (typically femoral artery and vein) with large bore arterial and venous access lines placed using point of care ultrasound.[165–173]	I	C
Distal limb protection should be considered a priori for large bore arterial access.[175,188,212,247,248,253–264]	II	B
Consider surgically placed VA-ECMO for a Postcardiotomy failure. b When percutaneous approach is anatomically challenging.[175,188,248,253–260]	II	C
Limited sternotomy/thoracotomy for central ECMO cannulation may be considered.[180]	II	C
For both peripheral and central VA-ECMO: a Anticoagulation should be provided and monitored according to institutional protocols (see Task Force 2). b Distal and cerebral perfusion should be routinely assessed.	II	C
ECMO flow should be optimized to allow cardiac ejection and a priori venting/unloading strategies should be considered.[265–275] a Unloading strategies include: inotropes, intra-aortic balloon pump. b Venting strategies include: Impella, LV vent, atrial septostomy.	II	C
Surgical LV apical cannulation via a mini-thoracotomy and femoral venous cannulation as inflows and right axillary artery/aortic cannulation as an outflow can be considered when[164,253,276,277]: - Transitioning from ECMO to a temporary LVAD. - Assessing both RV function and lung oxygenation capacity. - Allowing for early mobilization.	II	C
Sedative agents with greater lipophilicity and potential for sequestration within the ECMO circuit may require higher doses.[278–282]	II	C
Troubleshooting mechanical problems during VA-ECMO include[208,210,214,215,269,270,283–287]: a Echocardiography before implant to identify contraindications to device insertion (eg, severe aortic insufficiency) or other structural lesions that may affect the strategy for cannulation (eg, severe mitral regurgitation or ventricular septal rupture). b Routine use of echocardiography while on VA-ECMO support should focus on prevention of complications such as intracardiac and aortic root thrombus (ie, to ensure adequate ventricular ejection and aortic valve opening) and signs of inadequate LV unloading (worsening LV dilation). c Serial assessment of the oxygenator including evaluation of gas-exchange (can monitor pressure gradients to assess the risk of emergent oxygenator failure). d An inability to achieve anticipated blood flow with VA-ECMO should trigger an evaluation of cannula position (eg, by chest radiograph) or for cannula kinking, assessment of the patient's volume status, adjustment of the speed of the pump as needed, and hemodynamic optimization targeting excess afterload.	II	C
For patients with VA-ECMO using femoral cannulation, oxygenation should be assessed by measurement of blood gases drawn from the right upper extremity when able to identify differential hypoxemia (also known as North—South syndrome or Harlequin syndrome).	II	C

ECMO, extracorporeal membrane oxygenation; LV, left ventricular; LVAD, left ventricular assist device; RV, right ventricular; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

vasodilator use is often limited owing to low systemic blood pressure in the setting of CS.

IABP. The IABP has a well-known 2-fold benefit: augmentation of coronary blood flow during diastole and decreasing afterload. Some centers routinely place an IABP for all patients on VA-ECMO, convinced of its significant reduction of PCWP. One European study demonstrated an important reduction in radiographic signs of pulmonary edema and more days off mechanical ventilation in patients with combined IABP-ECMO vs those on VA-ECMO alone.[268] In patients with CS requiring VA-ECMO, the concomitant use of IABP has been associated with significantly lower mortality,[268,293] although direct unloading by the concomitant use of a (more expensive) Impella device might be even more effective.[271,294] However, a recent large pooled analysis of more than 1500 patients showed no survival benefit by adding IABP to VA-ECMO.[295]

Septostomy. Small case series have documented the feasibility of nonsurgical LV venting in ECMO patients using septostomy.[296–298] These include trans-septal puncture and

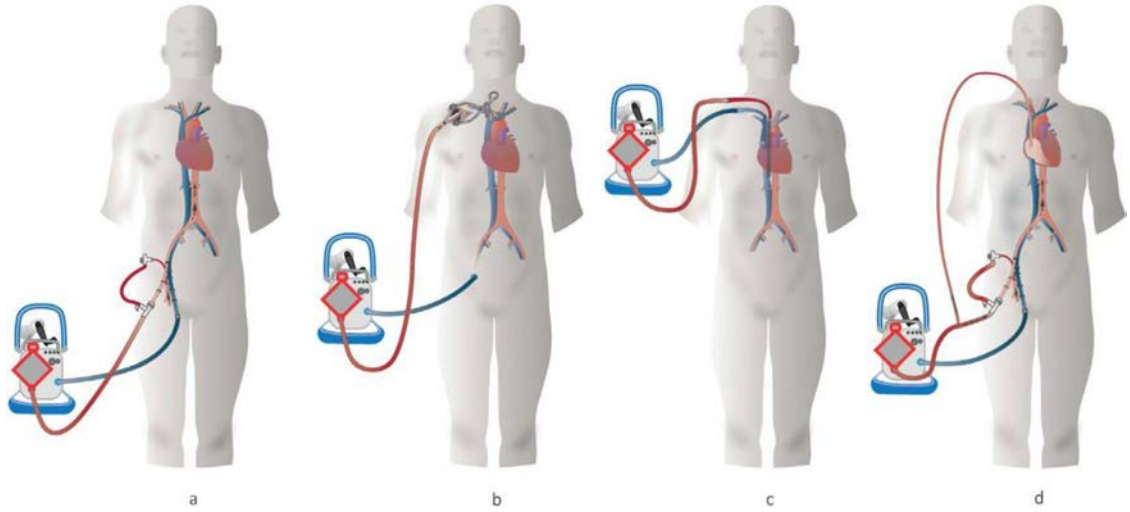

Fig. 1.4 Overview of unloading strategies on VA-ECMO. (A) ECMELLA. Femoral VA-ECMO with an additional femorally implanted Impella device. (B) An additional PA cannula is connected to the venous VA-ECMO line. (C) An additional transseptal interatrial cannula is connected to the venous cannula. (D) An additional intracardial catheter is connected to the venous cannula. These cannula are either implanted using the apex of the left ventricle or using the right upper pulmonary vein and going through the left atrium and the mitral valve into the left ventricle. VA-ECMO, venoarterial extracorporeal membrane oxygenation; ICU, intensive care unit; PA, pulmonary artery.

insertion of left atrial drain; trans-septal balloon and blade septostomy, and percutaneous insertion of a pulmonary artery or retrograde transaortic catheter functioning as a vent. Trans-septal balloon and blade septostomy remains a common practice in the pediatric population but is less commonly performed in adults.

Percutaneous Insertion of a Left Atrial Venting Cannula. The left atrium is accessed via a transseptal puncture, after femoral venous access has been established. Oxygenated blood is aspirated from the left atrium and can be connected into the venous limb of the ECMO circuit.[299] This results in reduction of preload to the LV, but does not directly drain the LV, thereby protecting the lung from pulmonary edema but acting only marginally on the likelihood of LV recovery.[300] Moreover, a transseptal puncture can lead to a left-to-right shunt after decannulation. Atrial suction events can occur more frequently than in a device with ventricular placement.

Impella. More recently, the Impella device has frequently been used for LV venting during VA-ECMO.[271,294,301,302] Impella can decompress the LV and decrease pulmonary congestion, but also can provide additional antegrade flow in the ascending aorta. Because the LV is directly unloaded, stasis of blood within the LV is not a concern. Furthermore, the Impella generates antegrade flow into the aortic root, and prevents aortic root stasis and thrombus formation. Several retrospective series have demonstrated that the combined use of VA-ECMO and Impella facilitated myocardial recovery and improved outcomes compared with VA-ECMO alone.[271,274,294] There are, however, several drawbacks to this dual therapy including frequent complications such as hemolysis and vascular injury and considerable cost.[43,303]

Surgical Venting. Direct LV unloading can be achieved by placing an additional cannula into the left atrium or LV apex though the sternotomy or mini thoracotomy. This cannula is then connected to the ECMO venous line as an additional inflow. Strong and reliable LV unloading is possible but because of its invasiveness, this approach is often limited to postcardiotomy shock patients.

There is no universally accepted definition of LV distension during VA-ECMO. Moreover, there is no consensus about the optimal timing and approach for LV venting. However, LV distension is an increasingly appreciated nuance of VA-ECMO support. The consequences of failing to anticipate, recognize, and treat LV distension are grave, making myocardial recovery of the vulnerable LV more difficult.[152] After the recent demonstration of a survival benefit with LV unloading during VA-ECMO support,[294] consensus criteria for LV distention are required and further efforts are mandatory to elucidate and measure the effect of each venting strategy for the patient requiring VA-ECMO.

CentriMag

The CentriMag system (Abbott, Abbot Park, IL) is an acute circulatory support system that can be used as a cardiopulmonary circuit for up to 6 hours of support time, or extracorporeal bypass circuit for periods up to 30 days to support left, right or both ventricles. The system includes the console, motor, drive, flow probe, and pump. The CentriMag pump includes a free-floating magnetically levitated rotor, which enables the device to rotate without friction or wear and eliminates heat production. This serves to minimize blood trauma and avoids mechanical failure. Because the rotor surface is uniformly washed, blood stagnation and turbulence in the pump are minimized. Hemolysis is reduced because the mechanical gaps in the pump are wider than 0.6 mm, decreasing shear forces. The device can produce flows of up to 10 L/min at a low rotational speed of 5500 rpm with a priming volume of 31 mL. Another useful

feature of the device is the ease of adjustment of the device speed and resulting flow. Based on the patient's clinical scenario (ie, to increase flow during periods of acute shock and decrease flow when attempting to wean from the device), the speed of the device can be increased or decreased simply by pushing a button.

The CentriMag can be surgically implanted in patients with various etiologies of acute CS including AMI, ADHF, postcardiotomy shock, myocarditis, primary graft dysfunction after heart transplant, and RV failure after LVAD insertion.[304−307] Implantation techniques of a CentriMag are very similar to those used for routine cannulation in cardiopulmonary bypass. Various types of cannulas can be connected to the CentriMag system, facilitating an easy insertion procedure and flexible configuration.

Although surgical insertion of CentriMag is more invasive than other percutaneous circulatory support devices, this disadvantage may be offset by its versatility and longer support time. This system can be used as an isolated LVAD, RVAD or as a full-support BiV assist device (BiVAD).[304−307] An oxygenator can be spliced into the circuit as an ECMO for concomitant profound hypoxia.[308] Classically, cannulation is performed through sternotomy. For the LVAD, the inflow cannula is inserted into the left atrium or LV apex, and the outflow cannula is inserted in the ascending aorta. For the RVAD, the inflow cannula is inserted in the right atrium or RV, and the outflow cannula is inserted in the main pulmonary artery using direct cannulation or more typically a graft anastomosis. With the combination of LVAD and RVAD, BiVAD can be configured. Because it is central cannulation, there is no cannula size restriction compared with peripheral cannulation. Therefore, BiVAD allows full decompression of both ventricles and provides complete end-organ perfusion. Several minimally invasive approaches without sternotomy can also be used to establish CentriMag support. Surgeons can approach the aorta, right or left atrium and ventricle through mini-thoracotomy approaches. Peripheral vessels including the axillary artery, jugular or femoral vein are alternative CentriMag cannulation sites.[309,310]

With regard to device management, anticoagulation strategy, weaning protocol, or bridge strategy to durable VAD or heart transplantation, there is considerable variability among centers.[304−310] Published studies are also limited to nonrandomized and small cohorts and outcomes vary depending on etiology of shock as seen with other acute circulatory support devices. An initial multicenter study using the CentriMag system included 38 patients.[305] The mean duration of support was 13 days (interquartile range, 1−60 days) and 30-day survival was 49%. A larger cohort study including 143 patients showed 30-day and 1-year survival of 69% and 49%, respectively with median support duration of 14 days (interquartile range, 8−26 days).[307] In this study, the device was used for BiVAD in 67%, RVAD in 26%, and LVAD in 8%. Destination was bridge to recovery in 30%, durable VAD in 15%, and heart transplant in 18%. Another study of 80 isolated RVAD patients demonstrated 36% early mortality with median RVAD support of 6 days. Similarly, a postcardiotomy shock cohort had poor outcomes.[304]

Complications during CentriMag support are relatively common. Major early complications include bleeding, central nervous system events, infection, and respiratory failure. In 1 study, the cumulative incidence of infection and bleeding events was directly related to support duration while the incidence of pump failure or hemolysis seemed rare even with use beyond 30 days (Table 1.10).[311]

Impella (2.5, CP, LD, 5.0, and 5.5)

The Impella device is a continuous flow micro-axial VAD used in the management of low CO states and as a periprocedural support strategy in cardiac procedures at risk for hemodynamic instability. Currently available versions of the Impella are differentiated based on size and magnitude of flow that the device can generate. The Impella 5.0 provides up to 5.0 L/min of circulatory flow.[312] With a 21F caliber, Impella 5.0 requires a surgical cut-down to the femoral artery, or if intended for longer term use, to the axillary artery. Recently, the Impella 5.5 has been developed, receiving a CE mark (Europe) for 30 days.[48,313,314] The 12F Impella 2.5 and 14F Impella CP are typically deployed percutaneously via the femoral artery and generate flows up to 2.5 L/min and 3.8 L/min, respectively.

The Impella is advanced into the LV using conventional catheterization techniques. The distal tip of the Impella is a

Table 1.10 Recommendations for Surgically Placed LVAD or RVAD

Recommendation	Class of Recommendation	Level of Evidence
A tunneled subxiphoid or intercostal exit of an outflow graft can be considered to significantly decrease the invasiveness of the VAD removal intervention.	II	C
Prolonged retention of prosthetic material in-situ (in case of a prosthetic graft anastomosed to the pulmonary artery and tunneled intercostally or subxiphoid) could increase the risk of infection.	II	C
The use of an oxygenator can be considered in line on the outflow limb with a surgically placed RVAD or LVAD and may help with recovery.	II	B

LVAD, left ventricular assist device; RVAD, right ventricular assist device; VAD, ventricular assist device.

pig-tail loop (except for 5.5) that helps buttress the device against the ventricular wall and stabilizes its position against further ventricularization with device activation. Using the design principle of the Archimedes screw, the Impella generates circulatory flow by drawing blood from the LV and ejecting it into the ascending aorta. Accordingly, appropriate Impella positioning is critical for device functioning and can be facilitated by either fluoroscopy or echocardiographic guidance. Optimal device placement ensures the inlet aperture on the pump shaft is both within the ventricle and within 3.5−4.0 cm distal to the aortic valve. This further ensures that the outlet aperture is both within the aorta and sufficiently distal to the aortic valve. Unlike the IABP, the Impella is not dependent on intrinsic LV function or cardiac rhythm. As an LV assist device, however, it will have some dependence on RV systolic function to ensure adequate LV preload.

The indications for Impella use focus on temporary hemodynamic support in high-risk PCI, high-risk ventricular tachycardia ablation and CS. For high-risk PCI, the Impella devices may be used for ≤ 6 hours of temporary support in either elective or urgent cases to prevent hemodynamic instability in patients who are hemodynamically stable but are at risk owing to the severity of their coronary artery disease and ventricular function. The Impella 2.5 and CP devices are approved for 4 or fewer days, and the Impella 5.0 for 10 days in cases of CS arising within 48 hours of an AMI, postcardiotomy or owing to an acute left HF syndrome, including peripartum cardiomyopathy, myocarditis, or progression of underlying chronic cardiomyopathy refractory to optimal vasoactive therapies.

Contraindications for Impella use include LV thrombus, a mechanical aortic valve, severe aortic stenosis, at least moderate aortic insufficiency, severe peripheral arterial disease, severe right HF, presence of an atrial or ventricular septal defect for which the Impella could worsen right to left shunting, LV rupture and cardiac tamponade. Additional considerations include coagulopathy, blood stream infections, and medical futility.

Published clinical studies involving the Impella devices have consistently demonstrated an expected improvement in hemodynamics albeit in the absence of improved survival. These studies have typically been non-randomized and derived from small patient samples. The ISAR-SHOCK trial (Impella 2.5 versus IABP in Cardiogenic Shock) demonstrated an improvement in cardiac index at 30 minutes following Impella deployment as compared with an IABP in 26 patients with an AMI.[70] Mortality was not different in the 2 groups and the overall hemodynamic benefit observed in the initial 30-minute time point was lost within 4 hours. In a more clinically challenged patient cohort in which 92% of patients with AMI and CS had a recent history of cardiac arrest, Impella CP support did not confer a survival advantage at 30 days or 6 months compared with IABP.[67]

The Impella 5.0 and 5.5 may reduce complications from VA-ECMO and can be used as a viable bridge-to-bridge and bridge-to-decision option (Table 1.11).[48,50,315,316]

Impella RP

The Impella RP is a continuous flow axial pump that can deliver up to 4 L/min of flow, is placed percutaneously and is approved by the US Food and Drug Administration for use in right HF (see Table 1.1).[327] The RECOVER RIGHT study found the device to be safe and easy to deploy, and showed a hemodynamic benefit when deployed in 2 cohorts of patients: those with right HF after LVAD placement and those with right HF after cardiotomy or AMI for less than 48 hours.[328] The prospective pooled cohort study combining premarket and postmarket approval cohorts showed a 73% survival at 30 days or discharge after device explant, or to induction of anesthesia for a long-term therapy. Overall survival at 180 days was 62%.[225] There are also case reports of using bilateral Impellas as mid-term support for patients with BiV failure.[329,330] One note of caution: when the Impella RP was used outside the RECOVER Right study protocol, outcomes revealed an increase in mortality. This led to a warning letter to health care providers in May 2019.[331]

TandemHeart

TandemHeart (LivaNova, Houston, TX) has a left sided device that is percutaneously placed with a transseptal puncture as well as a right sided support device, the ProtekDuo. The TandemHeart percutaneous LVAD has been shown in both AMI CS and mixed AMI and decompensated HF CS to improve hemodynamics above that of an IABP; however, a mortality benefit has not yet been proven.[58,198] Data also suggests that even though hemodynamics are improved in the setting of CS, placement of the TandemHeart LVAD is more complicated owing to the transseptal approach (Table 1.12).[332]

The ProtekDuo is a percutaneous right sided ventricular support device that has been successfully placed via femoral or internal jugular approach for RHF. Most commonly, it has rescued patients with medically refractory RHF after durable LVAD placement.[336] This device does not require cardiopulmonary bypass for placement or removal once the right ventricle has recovered from the early surgical insult (Table 1.13).

IABP

The IABP was first introduced into clinical practice in 1968 as an intra-aortic cardiac assistance system for patients in CS following myocardial infarction.[341] Current device design has remained largely unchanged from its initial descriptions. The IABP is a catheter mounted balloon that is advanced over a guidewire into the descending aorta and positioned within the aortic lumen with its distal tip inferior to the left subclavian artery and its proximal tip superior to the renal arteries. Confirmation of IABP position occurs either by fluoroscopy or a chest radiograph using the carina as the classic landmark for distal IABP tip alignment.

Table 1.11 Recommendations for Axial Flow Pumps (Impella)

Recommendation	Class of Recommendation	Level of Evidence
Peri-implant recommendations[155–157,159–162] Impella CP, 5 or 5.5 can be considered for adult patients with CS	II	B
- Size can be guided by a calculated deliverable cardiac index of >2.2 L/min/m^2.		
Placement should be performed with the use of imaging/monitoring (fluoroscopy and/or TEE) to confirm no interaction with mitral valve apparatus or endocardial suction	I	B
Contraindications to Impella implantation	II	B
- Moderate to severe aortic insufficiency		
- Severe aortic stenosis		
- Mechanical aortic valve		
- Aortic dissection		
- Myxomatous MV		
- LV thrombus		
- LVOT narrowing/obstruction		
Relative contraindications		
- Access vessel diameter of <6 mm		
- Presence of heavy calcifications		
- Obstruction or dissection		
- Preexistent extremity ischemia related to implant site		
- Prior open cannulations or surgical access/scar of unknown procedure		
- Active insertion site infection		
Recommendations on complications[65,154–156,158,160,161,218–221,317–321]	I	B
a Reported complications of Impella placement include vessel perforation, extensive bleeding at insertion site, rapid progression of cardiac failure or acute RV failure. These should be addressed as clinically appropriate.		
b Rarely device complications such as ingestion of material into motor during insertion, device fracture, cardiac perforation, valvular damage or stroke have been documented and require unique and urgent interventions.		
c Sudden deterioration should prompt rapid evaluation for device malfunction or malposition (eg, pulled out of LV, interfering with MV apparatus or perforating LV).		
Postimplant recommendations[59,154,155,159–161,218,222,236,319,321–325]	II	B
1 Hemodynamic monitoring on Impella support		
a Diuretic therapy should be used to achieve PCWP of <15 mm Hg and central venous pressure of <12 mm Hg.		
b Elevated arterial pressure can result in reduction of effective pump flows and should be reduced appropriately.		
c Arterial line for accurate blood pressure monitoring, PAC for hemodynamic measurements, and urinary catheter for close urine output monitoring are recommended.		
d Very low pulse pressure (<20 mm Hg) will result in "Impella position unknown" alarm.		
2 Echocardiographic		
a Use transthoracic echo to confirm location of inflow and outflow cages at initial insertion, any attempted changes, any patient movements, or any alarms of the pump system.		
b Device change/exchange — TEE can be used to visualize pump during exchange in operating room setting if fluoroscopy not available.		
3 Medical issues		
a Start with purge solution of D_5W with heparin.		
b See Task Force 2 for anticoagulation recommendations.		
4 Mechanical issues		
a Flattened motor current can imply device out of position (both inflow and outflow seeing same pressure) or profound LV hypocontractility.		
b Elevations in purge pressures can suggest kinking or thrombus development.		
c Sudden changes in flows, motor current or purge pressures can imply serious malposition or mechanical complication of device and warrant imaging via echo, chest radiograph, or chest CT scan.		
Recommendation on mechanical cardiac injuries[155–157,160,161,324,325]	II	B
Sudden changes in hemodynamics should warrant echo imaging to assess presence of AI, position of inflow and outflow cages, functional MS or MR owing to injury or obstruction, and even ventricular puncture.		
Recommendation on pump stoppage[155,156,160,161,222,324,326]	II	B
This is usually owing to kinking or obstruction from thrombus or other ingested material. If no kink is seen on chest radiograph or fluoroscopy, removal of the device and possible replacement may be needed. Usually this requires another vascular access to be obtained although there have been anecdotal reports creating methods with large bore sheaths to exchange at the same site.		
Loss of sensor signal can occur, especially with traumatic insertion, or prolonged support. Monitoring motor current and patient parameters for change in clinical status can continue without pump replacement.		
The decision to perform chest compressions should be based on standard criteria.	II	B
- If compressions are indicated, consider dropping to P2 speed during manual compressions.		
If ROSC occurs, resume prior speed and confirm location in LV via echo. If DCCV needed, avoid touching Impella system at time of shock.		

AI, aortic insufficiency; CS, cardiogenic shock; CT, computed tomography; DCCV, DC cardioversion; LV, left ventricular; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; PAC, pulmonary artery catheter; PCWP, pulmonary capillary wedge pressure; ROSC, return of spontaneous circulation; TEE, transesophageal echocardiogram.

Table 1.12 Recommendations for Centrifugal Pumps (TandemHeart)

Recommendation	Class of Recommendation	Level of Evidence
Before the implant procedure, the patient should be assessed for candidacy for transseptal puncture.[74,197,333–335]	II	C
Placement should be performed with the use of imaging (fluoroscopy and/or TEE) to confirm septal puncture and appropriate positioning	I	B
The TandemHeart device should not be inserted in the presence of known left atrial thrombus.	III	C
The TandemHeart device should not be inserted without the appropriate equipment for and expertise in transseptal puncture.	III	C
Daily transthoracic echocardiogram should be performed to evaluate device position	II	B

TEE, transesophageal echocardiogram.

Table 1.13 Recommendations for Right-sided Devices

Recommendation	Class	Level
ProtekDuo or Impella RP can be considered for acute RV failure.	II	B
Use of imaging to ensure precise positioning and to prevent outflow graft kinking, twisting and obstruction is recommended.	I	C
Careful hemostasis of the PA cannulation/graft anastomosis site is essential.	I	C
Described vascular complications are femoral vein dissection, inferior vena cava tear and iliac vein perforation. Monitor for intrabdominal bleeding if drop in hemoglobin/hematocrit.[319,328]	I	C
For Impella RP monitor for - Suction events: if noted, the speed should be adapted to avoid cavitation/suction events. - Placement signal, motor current waveform, purge pressure (300–1100 mm Hg) and infusion rate.[226,242,328,337–339] - Device migration with daily imaging (CXR or TTE). - Waveforms and flows of the pump to identify migration of the pump. Echocardiography should be performed if movement of the device is suspected. - Fracture, kink or damage of different components of the Impella RP should be evaluated routinely.[340]	II	C
An Impella device reposition can be attempted under echocardiographic guidance.[226,227]	II	C
With all RVAD devices in the absence of an LVAD, monitor the patient for pulmonary edema resulting from LV failure (RVAD flow should not exceed LV flow).	I	C
Additional recommendations - Monitoring with a PAC is recommended. - The tip of the PAC should be placed opposite to the pump outflow. - Echocardiography can be used to optimize RVAD flow by simultaneously assessing biventricular function, compliance or diastolic function.[242,328] - Monitoring for an increase of tricuspid valve regurgitation of more than 1 grade on echocardiography should be performed.[106]	II	C
Pulmonary vasodilators (inhaled or IV) are indicated in patients with a PVR of >250 dynes/sec/cm^{-5} or transpulmonary gradient of >12 mm Hg to lower pulmonary vascular resistance.	II	C

CXR, chest radiograph; LVAD, left ventricular assist device; LV, left ventricular; PA, pulmonary artery; PAC, pulmonary artery catheter; RV, right ventricular; RVAD, right ventricular assist device; TTE, transthoracic echocardiogram.

IABP inflation and deflation are timed to the electrocardiographic onset of diastole and systole, respectively. Helium is used to inflate the balloon as its low viscosity permits rapid balloon inflation and deflation and is benign in the event of balloon rupture. By principle, diastolic balloon inflation augments diastolic blood pressure leading to improved coronary perfusion. Rapid balloon deflation decreases LV afterload and thereby decreases myocardial oxygen requirements and overall myocardial work. This counterpulsation results in volume displacement at both proximal and distal ends of the balloon resulting in the Windkessel effect whereby the intrinsic elastic recoil of the aorta is converted into kinetic energy leading to improved systemic circulatory flow.

The IABP depends on intrinsic ventricular function and may augment the overall CO by 0.5–1.0 L/min. The effectiveness of IABP counterpulsation is dependent on multiple factors. Aortic compliance inversely impacts diastolic augmentation which may explain the observation of reduced IABP effectiveness in the young and in patients with distributive shock resulting in low systemic vascular resistance. As the IABP is gated to the ECG, tachycardia reduces the opportunity for diastolic augmentation. Moreover, the IABP is rendered ineffective with a pulseless rhythm such as ventricular fibrillation. The magnitude of volume displacement is theoretically proportional to the size of the IABP balloon. In adults, IABP sizes are typically matched to body height and are typically 34 mL (152 cm to 163 cm) and 40 mL (> 164 cm). Since 2011, a 50-mL IABP has become commercially available.

Early IABP use necessitated a surgical cut-down to gain access to the femoral artery.[341] Femoral arterial access has evolved to a predominantly percutaneous strategy mainly owing to the established approach to cardiac catheterization. The IABP sheath size ranges from 8.5F to 9.5F. More recently, the axillary artery has emerged as an alternative vascular route owing to challenging femoral arterial access owing to obesity and severe peripheral arterial disease as well as the need for mobilization for patients in whom longer duration IABP support is warranted.[342]

Although the first IABP study in 30 patients with CS demonstrated both hemodynamic and survival benefits, subsequent small, non-randomized studies including meta-analyses questioned the clinical effectiveness of IABP

therapy in AMI CS. The IABP SHOCK II (Intra-Aortic Balloon Pump in Cardiogenic Shock II) Trial randomized 600 patients who underwent early revascularization with optimal medical therapy to adjuvant IABP support or no support. The 30-day mortality was no different between the 2 groups and secondary end points were similar.[31] Subsequent analysis of long-term outcomes confirmed the absence of a survival benefit with IABP therapy in this patient population after 6.2 years of follow-up. The negative findings of the IABP-SHOCK II Trial prompted downgrading of IABP use in AMI CS in both European and US guidelines.

In contrast, randomized control trials of IABP use in non-AMI CS (eg, severe ADHF) are lacking. Single center studies have demonstrated adverse outcomes with IAPB therapy in non-AMI patients with CS requiring inotropes or vasopressors and with low cardiac power indices.[343–345]

Complications of IABP therapy include vascular injury and cholesterol and atheroembolic events, including stroke. Ischemia owing to balloon and catheter occlusion may compromise perfusion to the visceral organs and the ipsilateral limb to the site of vascular access. Worsening renal failure may be a consequence of impaired renal perfusion owing to IABP malposition. Thrombocytopenia may result from consumption and/or use of heparin products.

Management. Optimal IABP management includes serial chest radiography to ensure appropriate device position, anticoagulation, and monitoring for device complications (Table 1.14).

Nursing Care

Center-based acute MCS device training and device-specific competency assessment is recommended for all nursing and support staff caring for patients with acute MCS devices. This will best ensure staff achieve and maintain an acceptable degree of understanding of the device and its interactions with the patient. Immediately following MCS placement, consideration should be given to increased bedside nursing presence beyond the typical 1:1 care if patient acuity warrants. This can be lessened depending on clinical status of the patient. In addition, increased personnel are often needed for significant interventions such as transfers, patient maneuvers, dressing changes and physiotherapy in patients with large bore cannulas. All relevant medical staff should be informed of significant interventions as this will aid support if necessary.

Patient monitoring and care include:

- Regular observation and documentation of MCS parameters
- Strict monitoring for signs of infection
- Regular monitoring for signs of limb ischemia via observation, pulse palpation, and/or Doppler examination
- Compartment syndrome surveillance with immediate surgical consultation if suspected compromise of the limb
- Ensuring adequate oxygenation by both physical examination and arterial blood gases because pulse oximetry may be challenging owing to lack of arterial pulsatility
- Scheduled and frequent monitoring of line positions and cannula sites; where possible dressings on cannulas should be transparent to aid in monitoring for bleeding, hematoma, cannula position, and infection
- Avoiding the use of MCS lines for routine blood draws, where possible; limited access to the MCS circuit to minimize risk of infection, bleeding, and mechanical complications
- Pressure injury prevention should be commenced as soon as possible; skin should be monitored frequently with care to avoid development of pressure ulcers
- When possible, the head of the bed should be elevated at 15°–30° to minimize the risk of aspiration
- Nutrition should be implemented as soon as possible; careful attention to feeding quality is important with monitoring of intake, output, and caloric intake when needed
- As per American Heart Association and European Society of Cardiology guidelines, targeted temperature management may be indicated early after resuscitation of cardiac arrest in patients who remain unresponsive; however, in a recent large randomized trial of patients with coma after out-of-hospital cardiac arrest, targeted hypothermia did not lead to a lower incidence of death by 6 months compared with targeted normothermia[352]

Table 1.14 Recommendations for the Intra-aortic Balloon Pump

Recommendation	Class	Level
Routine IABP use in CS complicating AMI is not recommended.	III	A
IABP can be placed via a femoral or axillary artery using standard techniques for CS. a When placed via the femoral artery, the IABP distal marker should be advanced to the level of the descending aorta below arch vessels. b When placed via the axillary artery, the IABP proximal marker should be advanced to descending aorta below arch vessels.[346–351]	II	C
Conversion of existing femoral arterial access to IABP access may be performed though the risk of incomplete sterility should be weighed against the benefit of atraumatic femoral arterial access.	II	C

AMI, acute myocardial infarction; CS, cardiogenic shock; IABP, intra-aortic balloon pump.

Task Force 2: Adjunctive Pharmacological Management

Antithrombotic Therapy

Acute MCS devices vary in size, deployment strategy, and expected duration of use leading to variation in

Table 2.1 Risk Factors for Bleeding

General	Acute
Older age	Worsening renal function
Female sex	Impaired hepatic synthetic function
Hypertension	Reduced vitamin K production owing to reduced oral intake and antimicrobial agents
Diabetes	
Chronic kidney disease	
Chronic liver disease	Altered platelet count and function owing to marrow suppression, splenic sequestration, abnormal blood flow and shear stress, and medication toxicity
History of bleeding	
	Right heart failure leading to hepatic congestion
	Acquired von Willebrand's disease
	Anticoagulation and antiplatelet therapy
	Size of acute MCS device

MCS, mechanical circulatory support.

antithrombotic therapy requirements. The most common adverse events for all acute MCS devices are thrombosis, bleeding and infection. Thrombus can form within a device or cannula, but also within the heart chambers and around valves. Bleeding results from a variety of factors including requirements for concomitant anticoagulation and antiplatelet therapies as warranted by device- or patient-specific features. General risks for bleeding (eg, older age, renal and hepatic dysfunction) can be exacerbated by these devices. Ischemic or thromboembolic stroke and intracranial hemorrhage are the most devastating events and are associated with high mortality. Duration of MCS support also factors into these risks (Table 2.1).

Risk Factors for Bleeding and Thrombosis

Baseline risk factors for bleeding are exacerbated by the critical status of the patient and need for antithrombotic therapy (Table 2.1). Shock physiology results in ischemic tissues and associated declines in renal and hepatic function that may be further exacerbated by multiple medications. Reduced oral intake and treatment with antimicrobial agents reduce vitamin K production needed for coagulation factor synthesis. Marrow suppression, splenic sequestration owing to passive hepatic congestion, and medication toxicity can affect platelet count and function. In addition, abnormal flow and shear stress from the MCS device results in platelet activation, increased platelet clearance, and in some cases decreased platelet function despite a normal platelet count.

Age is a stand-alone risk factor for bleeding, while chronic kidney disease, diabetes, and hypertension cause stiffer, more fragile vessels that increase the risk for bleeding. The risk of spontaneous intracranial hemorrhage is of particular concern in patients over age 75, especially in the setting of anticoagulants. Certain cardiac physiologies (eg, aortic stenosis) and other conditions are associated with development of gastrointestinal angiodysplasia. The use of anticoagulant and antiplatelet agents exacerbates these intracranial hemorrhage and gastrointestinal tract bleeding risks. As described with durable LVADs, acquired von Willebrand's disease can occur with temporary ECMO support.[353] Shear stress results in unfolding of the larger von Willebrand factor multimers allowing ADAMTS13 to cleave high molecular weight multimers into smaller multimers. Some degree of acquired von Willebrand's disease can exist pre-LVAD implant, which may reflect severity of HF.[354]

Although bleeding events are more frequent, thrombotic events can have more severe consequences, especially thromboembolic stroke. Thrombotic events can be device- or patient-related or a combination. In addition to typical atherosclerotic risk factors, other patient factors (eg, obesity, inflammation, thrombophilia) and medications can increase thrombotic risk. The devices themselves are the strongest culprits, as contact activation of coagulation factors drives thrombin generation. Additional device components such as cannulas and external circuits further augment thrombosis owing to contact surfaces and stasis. In particular, patients cannulated for ECMO without LV venting are at high risk for systemic thromboembolism.[355] The risk of thrombosis is also compounded by the need to hold or decrease anticoagulation intensity in patients with bleeding. With weaning of ECMO flow rates, risk of bleeding may be enhanced.[356]

Preprocedural Management

Most acute MCS devices require anticoagulation unless contraindicated (eg, ongoing bleeding, profound coagulopathies, bleeding diatheses such as disseminated intravascular coagulation). Vascular complications (eg, hematoma, pseudoaneurysm, arteriovenous fistula, retroperitoneal hemorrhage) can occur with any device, and anticoagulation may further complicate these circumstances or result in complications of its own (eg, heparin-induced thrombocytopenia (HIT)).

Several factors need consideration in formulating anticoagulation targets including preimplant requirements (eg, mechanical prosthetic value, recent PCI) and end-organ function.[357] Before device insertion, current use of any antiplatelet and anticoagulant therapies should be addressed. Factors used to determine timing of discontinuation include mechanism of action and duration of pharmacologic effect. To minimize bleeding risk, duration of withholding therapy is determined by balancing urgency for acute support with indication for, and risk of withholding such therapy. In addition, device-specific requirements (eg, approach to insertion, coadministration of purge solution) will also determine early antithrombotic management. Although this guideline is focused on urgent or emergent acute MCS in the setting of cardiogenic or pulmonary shock, elective acute MCS (as noted in the Tables in this section) refers to planned procedures such as high-risk PCI, ablation of ventricular tachycardias, or transcatheter valve procedures.

Table 2.2A Recommendations for Antiplatelet Agents for Preoperative Management of Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
Clopidogrel and ticagrelor should be discontinued for ≥24 hours before ***urgent*** MCS, unless there is a compelling indication for continued use (see Table 2.2B).	I	C
Clopidogrel and ticagrelor should be discontinued for ≥5 days and prasugrel for ≥7 days before ***elective*** MCS, unless there is a compelling indication for continued use.	I	C
Cangrelor should be discontinued for ≥6 hours before ***urgent*** MCS, unless there is a compelling reason for continued use.	II	C
Short-acting intravenous GP IIb/IIIa inhibitors (eptifibatide or tirofiban) should be discontinued for ≥2 to 4 hours, and abciximab for ≥12 hours, before acute MCS, unless there is a compelling indication for continued use.	I	C
In patients requiring surgery within 6 weeks of bare metal stent placement or within 6 months of drug-eluting stent placement, we suggest continuing dual antiplatelet therapy perioperatively instead of stopping therapy 7 to 10 days before surgery.	II	C

GP, glycoprotein; MCS, mechanical circulatory support

Antiplatelet Therapy

To limit bleeding and the need for blood product transfusions, oral thienopyridine antiplatelet agents and intravenous glycoprotein IIb/IIIa inhibitors should be discontinued before surgical procedures (Tables 2.2A and 2.2B), with extrapolations made from data in the coronary artery bypass grafting[358–360] and durable MCS[361] population. Time since placement of bare metal vs drug-eluting stents should also be considered. Data on bridging to acute MCS with intravenous cangrelor, a potent inhibitor of the platelet P2Y12 receptor with a short half-life, is lacking.[362]

Anticoagulant Therapy

Similar to antiplatelet therapy, perioperative management of anticoagulant therapy is based on risk of thrombosis vs bleeding. Discontinuation of IV and oral anticoagulants depends on pharmacokinetics and, for select agents, renal and hepatic function (Tables 2.3A and 2.3B). In patients with an indication for anticoagulation (eg, mechanical heart valve), bridging should be based upon risk of thromboembolism. While reversal of vitamin K antagonist or IV anticoagulant may be warranted in select patients, administration of a direct oral anticoagulant reversal agent for FXa inhibitors is not recommended if there is a need for intraoperative anticoagulation with unfractionated heparin (UFH), such as with cardiopulmonary bypass or ECMO, because the reversal agent also reverses the UFH such that significantly higher doses of UFH are required to achieve the target activated clotting time (ACT).

Table 2.2B Discontinuation of Thienopyridine Antiplatelet Agents

Medication	Minimum Discontinuation before Operation	Urgent/Emergent Procedures
Cangrelor	6–24 hours	1 hour
Clopidogrel	5 days	24 hours
Prasugrel	7 days	24 hours
Ticagrelor	5 days	24 hours

Periprocedural and Postprocedural Management

The primary complexity surrounding periprocedural and postprocedural management is the variability of anticoagulant requirements among the approved devices (Tables 2.4A and 2.4B), including (1) anticoagulation goals with device insertion and for duration of use, (2) need for heparinized purge solution, and (3) device-specific adverse effects. With select devices, the manufacturer recommends a goal ACT with no recommendation for activated partial thromboplastin time (aPTT). Yet, many institutions use the aPTT for the management of acute MCS devices.

When selecting anticoagulation therapy, patient safety must be prioritized. Standardization is key, including the development of different indication-specific heparin order sets and use of standardized anticoagulant concentrations. When indicated, the administration of heparin from 2 different sources (ie, peripheral intravenous and Impella purge solution) requires clear measures to distinguish the heparin solutions and prevent adverse outcomes. Institution-specific protocols should establish anticoagulation goals and titration parameters. Staff and clinician education are imperative.[363]

IABP

No specific anticoagulation protocol is recommended by IABP manufacturers. Although IV UFH is considered standard of care, data supporting this indication is scarce. The incidence of limb ischemia with IABP use ranges from 1%

Table 2.3A Recommendations for Anticoagulant Agents for Preoperative Management of Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
VKAs should be discontinued approximately 5 days before ***elective*** MCS, unless there is a compelling indication for continued use.	I	B
Vitamin K administration may be warranted for VKA reversal before ***urgent*** MCS, with oral administration preferred but intravenous administration warranted for more acute onset.	I	C
In patients with a mechanical heart valve, atrial fibrillation or VTE at ***high risk*** for thromboembolism, bridging anticoagulation is recommended during interruption of VKA therapy.	II	C
In patients with a mechanical heart valve, atrial fibrillation or VTE at **low risk** for thromboembolism, bridging anticoagulation is not recommended during interruption of VKA therapy.	II	C
For patients receiving VKA, a preoperative goal INR of ≤1.4 is recommended before acute MCS. Hence, vitamin K or other reversal agents should be considered if the INR is >1.5.	I	C
In patients who are receiving bridging anticoagulation with therapeutic dose IV UFH or SC LMWH, protamine administration may be warranted for heparin reversal before ***urgent*** MCS.	I	C
In patients who are receiving bridging anticoagulation with therapeutic dose IV UFH, UFH should be discontinued 4–6 hours before ***elective*** MCS.	II	C
In patients who are receiving bridging anticoagulation with therapeutic-dose SC LMWH, the last preoperative dose of LMWH is recommended about 24 hours, instead of 12 hours, before ***elective*** MCS. This duration should be extended to greater than 24 hours in the presence of renal dysfunction.	II	C
In patients who require temporary interruption of a VKA before surgery, anticoagulation should be resumed approximately 12–24 hours after surgery (evening of or next morning) and when there is adequate hemostasis.	II	C
In patients who are receiving bridging anticoagulation with therapeutic dose SC LMWH and are undergoing high bleeding risk surgery, anticoagulation should be resumed 48–72 hours after surgery.	II	C
The timing of discontinuation of anticoagulant agents before acute MCS should be individualized based on pharmacokinetics of the drug and end-organ function of the patient (see Table 2.3B)	I	C

INR, international normalized ratio; IV, intravenous; LMWH, low-molecular-weight heparin; MCS, mechanical circulatory support; SC, subcutaneous; UFH, unfractionated heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.

to 8%, whereas the risk of bleeding varies from 4% to 39%. Proposed bleeding mechanisms include a reduction in platelet count and plasminogen activator inhibitor-1 and an increase in D-dimer and fibrin degradation products.[364,365] Studies conducted with contemporary IABPs support the omission of heparin with no significant difference in limb ischemia and significant increase in bleeding in heparin-treated patients. Studies evaluating a universal strategy (all patients treated with UFH) vs a selective strategy (only patients with additional indications for UFH) also suggest a higher incidence of bleeding with a universal strategy.[364,366]

Table 2.3B Discontinuation of Anticoagulant Agents

Medication	Minimum Discontinuation Before Operation	Additional Considerations
Oral agents		
Apixaban	48 hours	
Dabigatran	CrCl > 50 mL/min: 48 hours CrCl 30–50 mL/min: 5 days	Extend for renal dysfunction
Edoxaban	48 hours	
Rivaroxaban	48 hours	Extend for renal dysfunction and hepatic dysfunction
Warfarin	5 days	Preoperative goal INR of ≤1.4 Consider reversal if INR of >1.5
Parenteral agents		
SC LMWH	24 hours	Extend for renal dysfunction
IV UFH	4–6 hours	

CrCl, creatinine clearance; INR, international normalized ratio; IV, intravenous; LMWH, low-molecular-weight heparin; SC, subcutaneous; UFH, unfractionated heparin.

Table 2.4A Recommendations for Anticoagulant Agents for Perioperative and Postoperative Management of Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
IABP		
Systemic anticoagulation ***may be considered*** when 1:1 balloon support is provided. Selective anticoagulation may be beneficial in decreasing bleeding complications (implantation site, gastrointestinal and cerebral hemorrhage).	II	C
Systemic anticoagulation ***is recommended*** when balloon support is provided every other (1:2) or every third (1:3) cardiac cycle.	I	C
In the absence of bleeding, systemic anticoagulation ***is recommended*** regardless of balloon support if another indication exists (eg, atrial fibrillation).	I	C
After PCI, if using a GP IIb/IIIa antagonist, additional intravenous UFH is not indicated. Intravenous UFH is recommended after cessation of GP IIb/IIIa therapy to target a goal aPTT of 50—70 seconds.	II	B
Impella Device		
During device insertion, intravenous UFH is recommended to target a goal ACT of ≥250 seconds (≥200 seconds if patients are also receiving a GP IIb/IIIa inhibitor).	II	C
For the duration of support a heparinized purge solution (base fluid dextrose) is recommended to target an ACT of 160—180 seconds or an aPTT of 55—80 seconds or anti-Xa of 0.3—0.7 U/mL. Additional systemic intravenous UFH may be needed or the concentration of heparin in the purge and/or systemic solutions may need to be decreased.	II	C
TandemHeart		
Before device implantation, intravenous UFH is recommended to target a goal ACT of 250—300 seconds.	I	C
For the duration of support a heparinized purge solution (base fluid saline) is recommended to target a goal aPTT of 65—80 seconds, ACT of 180—220 seconds, or anti-Xa of 0.3—0.7 U/mL.	I	C
The standard concentration of heparin in the purge solution may require supplemental intravenous UFH to maintain therapeutic anticoagulation.	I	C
CentriMag		
After device insertion using cardiopulmonary bypass, anticoagulation is not recommended for 6—12 hours until clotting profile is normalized. ***After device insertion not utilizing cardiopulmonary bypass,*** a target ACT goal of 200—250 seconds is recommended.	II	C
Once chest tube drainage is low per institutional protocol for 2—3 hours, anticoagulation with intravenous UFH is recommended to target goal aPTT of 60—80 seconds and/or ACT 160—180 seconds. By approximately postoperative day 4, the target aPTT is 70—90 seconds and/or ACT 190—210 seconds.	II	C
Antiplatelet therapy with 81—325 mg of aspirin per day should be initiated when indicated by improved platelet function. TEG may be used once per day to evaluate antiplatelet needs.	II	C
VA-ECMO		
Anticoagulation is recommended for patients on VA-ECMO.	I	B
If using intravenous UFH, target a goal aPTT of 50—70 seconds and/or ACT of 180—220 seconds, obtained 2 hours after initial dose and then every 6 hours.	I	C
If using an antithrombin agent, the recommended loading dose is between 80% and 120% of the normal level found in human plasma (45 IU/kg) followed by maintenance doses at 60% of the loading dose. Obtain antithrombin level at 20 minutes and every 12 hours thereafter or may use aPTT with a goal of 50—70 seconds.	I	C

ACT, activated clotting time; aPTT, activated partial thromboplastin time; GP, glycoprotein; IV, intravenous; PCI, percutaneous coronary intervention; TEG, thromboelastography; UFH, unfractionated heparin; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Anticoagulant use for 1:1 support remains controversial while systemic anticoagulation is more consistently administered when IABP support is provided every other (1:2) or every third (1:3) cardiac cycle.[367] Regardless, each center should consistently follow a protocol that includes monitoring for thrombocytopenia, infection and bleeding as well as for thrombotic and vascular complications.

Left Ventricle to Aorta Assist Device

For the Impella device, anticoagulation is achieved by UFH contained in a purge solution released from the motor housing. The solution is released in the opposite direction of blood flow, creating a pressure barrier to prevent blood entry. A built-in sensor automatically adjusts the purge flow (typically between 2 and 30 mL/h) to maintain a pressure between 300 and 1100 mm Hg that is required to prevent thrombosis. In addition, intravenous UFH may also be indicated to achieve goal ACT or aPTT. A heparin concentration of 50 U/mL in 5% dextrose is recommended as the initial purge solution.

Given the device determines the purge flow rate, frequent adjustment of systemic UFH may be required necessitating anticoagulant monitoring every 4—6 hours. In addition, the UFH concentration in the systemic and/or

Table 2.4B Summary of Anticoagulant Goals for Perioperative and Postoperative Management of Acute MCS

Device	ACT Goal	aPTT Goal	Anti-Xa Goal
IABP		Device insertion: 50−70 seconds	0.2−0.5 U/mL
Impella	Device insertion: 250 seconds or longer Duration: 160−180 seconds	Duration: 55−80 seconds	0.15−0.30 U/mL 0.3−0.7 U/mL
TandemHeart	Device insertion: 250−300 seconds Duration: 180−220 seconds	Duration: 65−80 seconds	0.2−0.5 U/mL 0.3−0.7 U/mL
CentriMag	Device insertion: 200−250 seconds Duration: 160−180 seconds	Duration: 60−80 seconds	
VA-ECMO	180−220 seconds	Heparin: 1.5−2.5 times baseline Argatroban: 1.5−3 times baseline	0.3-0.7 U/mL

ACT, activated clotting time; aPTT, activated partial thromboplastin time; IABP, intra-aortic balloon pump; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

purge solution may need to be reduced, especially in low weight patients.[367] Finally, patients with axillary cannulation have demonstrated a higher median heparin requirement compared with femoral cannulation.[368] If the heparin purge solution is insufficient to achieve anticoagulation goals, the addition of titratable, supplemental non-purge UFH is required. In cases of HIT, a direct thrombin inhibitor (DTI) (bivalirudin or argatroban) outside the purge solution is recommended. In patients with baseline elevated aPTT (eg, antiphospholipid syndrome), a customized anticoagulation plan can include monitoring heparin anti-Xa levels, modification of the goal aPTT range, or using an aPTT reagent insensitive to lupus anticoagulant.[363]

Clinical trials of the Impella device vary widely in anticoagulation administration and goals. In the ISAR-SHOCK study, the purge solution contained no heparin and only intravenous UFH (goal aPTT 60−80 seconds) was administered.[70] In PROTECT II, intravenous UFH or bivalirudin was used with a goal ACT of more than 250 seconds; the purge solution was not described.[369] The IMPRESS in Severe Shock trial with the Impella CP did not report anticoagulation management.[67] Recently, 2 reports of anticoagulation practices with Impella devices were published. One review of 6 studies found that purge solutions of 5% and 20% dextrose were used as well as UFH 12, 25 or 50 U/mL to reach target aPTTs between 55 and 85 seconds and target ACTs of 160−200 seconds.[363] Similar therapeutic aPTTs, thrombotic events and bleeding events were observed; pump thrombosis was not reported. In another survey of 65 centers, clinical practices varied considerably and often diverged from manufacturer recommendations.[370] Less than 20% of centers had an alternative strategy for patients with contraindications to heparin, although approximately 60% reported using argatroban or bivalirudin.

Left Atrial to Aorta Assist Device

With the left atrial to aorta assist device (TandemHeart), anticoagulation is necessary to prevent thromboembolism or in situ thrombosis. The external controller directs flow rate of a purge solution to prevent thrombus formation in the centrifugal pump housing. The manufacturer recommends different anticoagulation goals at device insertion vs the duration of device support. For the purge solution, a default UFH concentration of 90 U/mL is used and a saline-based fluid is mandatory as dextrose-containing products may damage the device motor.

In a single center trial, an ACT of 180−200 seconds was targeted in patients randomized to TandemHeart verses IABP, the former received UFH via the purge solution and the latter received intravenous UFH.[200] The TandemHeart group experienced significantly greater blood product requirement and limb ischemia. In another study, patients in the TandemHeart group were anticoagulated to a target ACT of 400 seconds or longer with device insertion and ACT of 180−200 seconds during device support. Although the complication rates were similar between groups, 1 patient in the TandemHeart group experienced device failure and another required device explantation owing to cannula thrombosis.[198]

CentriMag

Although the CentriMag was designed to minimize blood trauma, special consideration with anticoagulation is still warranted. Owing to postoperative bleeding, recommendations for time to re-initiation of anticoagulation vary by implantation method. In addition, pump thrombosis may be minimized by maintaining pump flow of greater than 4 L/min. Anticoagulation goals are increased as organ function and hemostasis improve.

No randomized clinical trials for anticoagulation with CentriMag are available. In 3 small retrospective studies, anticoagulation with UFH was initiated once the chest drainage was less than 50 mL/h. The target ACT was 160−180 seconds or aPTT of 60−80 seconds or, alternatively, an aPTT of 50−60 seconds.[306,371] An UFH dosage of 5 U/kg/h to achieve target values was cited in only 1 study. Antiplatelet therapy in 2 studies consisted of aspirin 75 mg and 100 mg/d from the first postoperative day. Bleeding complications with re-exploration rates varied from 29% to 37%.

VA-ECMO

Similar to cardiopulmonary bypass circuits used in cardiac surgery, VA-ECMO involves both a venous and arterial cannula. The nonendothelial surface of ECMO leads to an inflammatory and prothrombotic response associated with a consumptive coagulopathy. While surface coatings (heparin, albumin, or phosphorylcholine) aim to reduce activation, anticoagulation is standard practice. Both hemorrhagic and thrombotic complications can develop from excessive or inadequate anticoagulation resulting in embolic or hemorrhagic stroke, or cannulation complications (eg, venous thrombosis or distal arterial ischemia). Unfortunately, the ideal level of anticoagulation or monitoring targets are not defined.[357]

The most widely used anticoagulant for patients on ECMO support is UFH. At the time of cannulation, an initial bolus of 50−100 U/kg is recommended, but this may be unwarranted if the patient has previously been anticoagulated. Although the ACT and aPTT are most commonly used to monitor UFH for ECMO, it is unclear which method has greater reliability. The ELSO 2017 guidelines recommend an ACT range of 180−220 seconds.[372] In conjunction with ACT, target aPTT 1.5−2.5 times baseline and anti-Xa levels of 0.3−0.7 IU/mL may be used.[357,373] Lower goals may be considered with high bleeding risk. Thrombotic events were reported with anti-Xa levels of 0.09 (0.06 −0.25) U/mL compared with patients with no thrombotic complications at levels of 0.36 (0.26−0.44) U/mL despite no difference in median aPTT between groups.[374]

The sensitivity of aPTT to UFH is reduced in the setting of an inflammatory response, which induces high fibrinogen levels.[181] Monitoring with thromboelastography or rotational thromboelastography has been explored. In the setting of ECMO, rotational thromboelastography, and aPTT do not provide equivalent information to guide heparin administration and may lead to excessive anticoagulation.[375] ACT measurement reproducibility is limited by the activator used and the measurement technique. Measured aPTT in platelet-poor plasma is not influenced by the platelet count or hematocrit, which explains why aPTT may better correlate to heparin concentration during ECMO support compared with ACT.[375] Recent ECMO guidelines include reference to thromboelastography monitoring, fibrinogen replacement, cryoprecipitate supplementation as well as AT III monitoring and supplementation. For patients with HIT, bivalirudin or argatroban should be considered—heparin must be avoided. With hemodynamic instability contributing to reduced hepatic or renal clearance, conservative initial doses and judicious monitoring are warranted.

In a systematic review and meta-analysis of VA-ECMO studies, major bleeding and thromboembolic events were compared as follows: no anticoagulation (0%−91% and 0% −45%), a target ACT of less than 180 seconds (0%−35% and 0%−35%), a target ACT of more than 180 seconds (0%−69% and 0%−47%), an aPTT at target value (32% −38% and 0%−16%), and mixed methods of anticoagulation (7%−40% and 0%−15%). Major bleeding events were highest in the postcardiotomy (0%−91%) and eCPR (10% −38%) groups.[376] In patients with postcardiotomy shock treated with VA-ECMO, central cannulation is associated with increased risks of bleeding and in-hospital mortality compared with peripheral cannulation.[377]

eCPR

The existing literature around anticoagulation during eCPR is limited to descriptive practices of procedures in emergency departments. Overall bleeding risk is high, with disseminated intravascular coagulation observed in 50% of cases. Patients with overt disseminated intravascular coagulation less frequently received anticoagulants, and if started later received a larger quantity of blood products.[378] Before cannulation, intravenous UFH bolus dosage varies between 3000 and 5000 IU.[379] The initial aPTT target is 40−60 seconds; after stabilization, the aPTT target may be increased to 70−90 seconds. Bleeding events have been reported regardless of aPTT values, including fatal bleeding from chest trauma (Table 2.5).

Management of Bleeding

Early vs Late Bleeding

Bleeding complications in acute MCS are common and frequently necessitate withdrawal of anticoagulation (Table 2.5). Early bleeding is often associated with vascular damage during device implantation at larger bore access sites. Procedure-related bleeding rates vary between 17% and 30% with a lower incidence in high volume centers.[67,74,380−383] If bleeding occurs in the femoral vessels following acute MCS insertion, a femoral compression device should be used to control bleeding, and acute surgical revision performed to avoid blood loss and leg ischemia. In cases of early bleeding with the subclavian/axillary artery approach, compression and acute surgical revision is also required.[157,318] If the source of bleeding is unclear, computed tomography angiography is suggested to rule out vessel injury.

After device insertion, parameters for monitoring anticoagulation with each device (eg, ACT, aPTT) are provided above (Tables 2.4A and 2.4B). Daily monitoring of additional parameters (eg, international normalized ratio, prothrombin time, factor X and V, fibrinogen, and platelet count) may also be warranted for safety. In the absence of bleeding, minor deviations from normal clotting parameters may occur but corrections should be avoided owing to the risk of thrombosis and stroke.[383] If bleeding occurs, potential etiologies for coagulopathy should be addressed, followed by the use of fresh frozen plasma or other appropriate factor concentrates. Because acquired von Willebrand disease is also commonly reported with acute MCS, substitution of von Willebrand factor is recommended.[384,385]

If bleeding is persistent, anticoagulation targets may be lowered. Complete discontinuation of anticoagulation is warranted in the setting of severe, life-threatening bleeding.

Table 2.5 Recommendations for Management of Early and Late Bleeding

Recommendation	Class of Recommendation	Level of Evidence
In early bleeding owing to insertion of acute MCS in the femoral or subclavian vessels, local compression and acute surgical evaluation is recommended.	I	C
If unclear etiology of bleeding, CT angiography is recommended to rule out vessel injuries.	I	C
Acute or late non-surgical bleeding may be managed with platelet administration (target 100,000), coagulation factors and discontinuation of other contributing therapies (eg, antiplatelet agents) unless compelling indications exist for continued use.	I	C
For acute or late bleeding which cannot be stopped by correction of platelet count or coagulation factors, UFH may be lowered to achieve an ACT of 140—160 seconds and/or an aPTT of 40—50 seconds.	I	C
In the setting of bleeding, substitution of vWF is recommended; substitution of other coagulation factors should be considered cautiously.	I	C
In the setting of life-threatening bleeding, full discontinuation of all anticoagulation may be necessary.	I	C
To prevent and manage bleeding, careful monitoring of anticoagulant therapy (eg, ACT, aPTT) and platelet count is warranted.	I	C
In the case of stroke, specialists in neurology and neurosurgery should guide anticoagulation. Depending on stroke type, discontinuation of anticoagulation as well as acute MCS therapy may be necessary.	I	C

ACT, activated clotting time; aPTT, activated partial thromboplastin time; CT, computed tomography; MCS, mechanical circulatory support; UFH, unfractionated heparin; vWF, von Willebrand factor.

Acute and late nonsurgical severe bleeding may be managed with platelet administration (target platelet count 100,000), coagulation factor support and discontinuation of other contributing therapies (eg, antiplatelet agents) until bleeding ceases. Compelling indications for continued use (eg, antiplatelet therapy with recent PCI) should be considered.

Management of Other Bleeding Events

Bleeding events such as gastrointestinal or uterine bleeding are common during long-term acute MCS (eg, days-weeks) owing to required anticoagulant administration and damage to blood components owing to device-related sheer stress. Reported rates of non-device related bleeding vary between 13% and 30%.[67,381] When bleeding occurs, direct correction by transfusion or modification of anticoagulation may be necessary. In severe cases, discontinuation of anticoagulation and administration of coagulation factors may be required. In the case of stroke owing to intracranial hemorrhage, the prevention of neurological damage is of greatest importance and anticoagulation should be guided by the treating neurologist and neurosurgeon.

Implications of Blood Transfusions

Many patients requiring acute MCS are likely to become candidates for heart transplantation. As such, transfusion of blood products should be administered cautiously and only if strictly necessary given the risk for allosensitization.[386] Nevertheless, as many as 30% to 40% of acute MCS patients require blood transfusions especially females.[381,387] An acute decline in hemoglobin or hematocrit, increasing vasopressor requirement, continuous suction events associated with the device, and declining central venous pressure or mixed venous oxygen saturation may warrant blood transfusion. Some centers have policies in place that mandate the use of irradiated, leukoreduced blood products to reduce the risk of allosensitization.

Management of Thrombosis and Thromboembolic Events

Thrombosis during acute MCS is a severe complication that may necessitate discontinuation of device support.[388] Standard of care in the setting of hemodynamically significant thrombosis is urgent replacement of the original device with a new temporary device. In cases of severe hemodynamic instability, urgent replacement with durable MCS should be considered. Medical treatment is advised for hemodynamically stable patients with suspected device thrombosis or peripheral thromboembolic events. Possible therapeutic options include heparin, GP IIb/IIIa inhibitors and DTIs. Given that most devices require anticoagulation, the use of thrombolytic agents that further increase the risk of bleeding and hemorrhagic stroke is not recommended. Currently no randomized, prospective data exist on the treatment of thrombosis with temporary MCS devices and experience comes only from retrospective case series.

UFH and Low-molecular-weight Heparin

Although the use of purge solution without heparin in acute MCS devices is described, suspected device thrombosis warrants strict compliance with ACT levels of more than 160 seconds.[389] Further intensification of UFH to achieve

an ACT of 180−200 seconds may also be considered. The addition of titratable, supplemental nonpurge heparin may be required for optimal anticoagulation.[363,368,390−393] Because the risk of bleeding complications remains high, UFH is preferred over low-molecular-weight heparin given short half-life and ease of titration.

GP IIb/IIIa Inhibitors

There is currently no evidence to support the use of GP IIb/IIIa inhibitors for the treatment of device thrombosis or thromboembolic events in patients with acute MCS.

DTIs

Of the available DTIs, argatroban has been used most frequently in treatment of suspected MCS device thrombosis.[363] Vigilant monitoring of aPTT or anti-Xa levels is recommended. Intensification of therapy to a higher target aPTT may be considered. ACT may also be monitored with a recommended target of at least 160−180 seconds. Because aPTT is nonlinear at concentrations that can be achieved on the ward, careful monitoring should occur in conjunction with close follow-up for bleeding complications.[219,363,394]

Thrombolytic Therapy

Although thrombolytic agents may be considered to dissolve clots in acute MCS devices, complications such as hemorrhagic stroke and other serious bleeding events remain high. In a case series of suspected Impella thrombosis, tissue plasminogen activator administration in the Impella purge solution (0.04 or 0.08 mg/mL tPA in sterile water) demonstrated success in five cases with resolution of high purge pressures and low purge flow rates and no major bleeding.[395] In the absence of controlled data with thrombolytics, device exchange should be considered a safe alternative.

HIT Before Acute MCS

HIT is a prothrombotic disorder that is the result of antibody formation to a complex of heparin and platelet factor 4 (PF4). The development of these antibodies follows a characteristic time course after heparin exposure, and the clinicopathologic diagnosis requires both specific clinical findings and laboratory test results. These antibodies can result in activation of platelets and resultant thrombosis with associated high morbidity and mortality. However, not all antibodies that are formed activate platelets or cause thrombin generation.

A drop in platelet count occurring 5−10 days after UFH exposure is the sine qua non of HIT. If HIT is suspected, the 4T score (Table 2.6) can be used to calculate the probability as low, intermediate or high. Other scoring systems, including the HIT Expert Probability Score, have also been proposed.[396] A low score is associated with a high negative predictive value but a high score is less predictive.[397] If the suspicion is of intermediate or high probability, the patient should be empirically treated, and an immunologic assay to detect heparin/PF4 IgG antibodies should be sent. If the immunoassay is positive, the functional serotonin release assay, which has approximately 90% specificity and sensitivity, should be checked. However, limited lab availability requiring send-out testing typically results in a long turnaround time and need to treat patients before results are available.

Patients with intermediate or high probability 4T scores should have all heparin products discontinued immediately, immunoassay testing sent, and initiation of an alternative anticoagulant such as a DTI (argatroban or bivalirudin) while awaiting test results. Alternative non-heparin anticoagulants should be used even if the patient does not have thrombosis, as the risk of thrombosis is approximately 50%, often with limb or life-threatening thrombotic events. Limited data support the use of fondaparinux and direct oral anticoagulants.[398] If HIT is confirmed, the patient can be transitioned to warfarin if on a DTI once the platelet count has recovered to baseline, or one of the alternative

Table 2.6 The Four T Score

	Score		
Variable	2	1	0
Thrombocytopenia (decrease from baseline)	>50% AND nadir ≥20,000	30%−50% OR nadir 10,000−19,000	<30% OR nadir ≤10,000
Timing of platelet count fall	5−10 days OR ≤1 day and heparin exposure within 30 days	>10 days OR ≤1 day and heparin exposure in past 30−100 days	≤4 days without recent heparin exposure
Thrombosis	New thrombosis, skin necrosis or systemic reaction to heparin bolus	Progressive or recurrent thrombosis or non-necrotizing skin lesions	None
Other cause of thrombocytopenia	None	Possible	Definite
Total score	6−8, high suspicion	4−5, intermediate suspicion	0−3, low suspicion

agents. Recognizing that fondaparinux has a long half-life of 17−20 hours, its use in patients at high risk of bleeding is concerning. Upfront treatment of HIT with a direct oral anticoagulant is limited to case series and appears to be confined to stable patients without thrombosis. Patients without thrombosis should be treated with anticoagulation for a minimum of 1 month, whereas those with thrombosis should be treated for a minimum of 3 months.

For patients with acute MCS requiring anticoagulation with heparin, the development of HIT can be challenging. Alternative anticoagulants can be used with temporary support devices despite limited data, but for patients who require surgery with cardiopulmonary bypass, the use of alternative agents is particularly problematic. Strategies to avoid the development of HIT, such as the use of DTI in durable LVAD patients who need parenteral anticoagulation and are awaiting heart transplant have been used at some institutions. Similarly, strategies to remove the heparin/PF4 antibodies with immediate preoperative plasmapheresis, or the use of high-dose IV immunoglobulin, have been reported in small series with apparent success.[399] Although 80% of patients will clear the antibody by 90 days, some patients can have the heparin/PF4 antibody persist for up to 1 year. The serotonin release assay will become negative before the ELISA-detectable PF4 antibody clears.

Antimicrobial Therapy

There are limited published data on the diagnosis and management of acute MCS device infections. Most practices are based on retrospective studies and meta-analyses of current literature, as well as expert opinion. The vast majority of the literature addresses infections related to ECMO circuits or durable MCS device infections, such as LVADs.

Definitions and Types of Infection

Unlike definitions developed to classify infections in patients with durable VADs,[400] there is no standardized classification of infections related to acute MCS devices. In a similar format, however, infections can be divided into MCS specific infections, MCS related infections, and non −MCS-related infections, with some differences (Table 2.7). The main difference is the fact that durable LVADs are always intracorporeal and long-term. Therefore, classifying infections in these patients is easier to standardize. In contrast, there are "grades" of acute MCS, varying significantly from minimal (IABP) to maximal (central, open chest) invasiveness.

- MCS-specific infections include those that are specific to patients with acute MCS devices, are related to the device hardware, and do not occur in non MCS patients. Examples include ECMO cannula infection or infection involving the surgical site where the device was inserted.
- MCS-related infections are those that can also occur in patients who do not have an MCS device, but have unique features specific to the presence of an MCS device (eg, blood stream infection, infective endocarditis).
- Nonacute MCS infections are those that are not affected by the presence of the device itself (eg, pneumonia, urinary tract infection, *Clostridium difficile* infection).

Table 2.7 Classification of LVAD and Acute MCS Device Infections

	LVAD	Acute MCS
Specific	Cannula Pump pocket Driveline	Cannula
Related	Endocarditis Bloodstream infection Mediastinitis	Endocarditis Bloodstream infection Mediastinitis*
Unrelated	Others (eg, pneumonia, UTI, *C difficile*)	Others (eg, pneumonia, UTI, *C difficile*)

LVAD, left ventricular assist device; MCS, mechanical circulatory support; UTI, urinary tract infection; *C. difficile*, *Clostridium difficile* infection.

*With central cannulation (eg, venoarterial extracorporeal membrane oxygenation, surgical CentriMag).

It can be hard to differentiate device related infections from the infections that occur owing to critical illness or ICU stay that may be related to the presence of multiple intravenous and/or intra-arterial lines and tubes.

Rates of Infection

Infection rates differ depending on the type of acute MCS device. For example, IABP infection rate is reported as less than 1%,[401] compared with 4%−18% in patients with ECMO support.[402,403] Infection is least with peripherally inserted devices that do not require surgical cut-down, increases if the insertion of the device requires surgical cut-down or graft conduit, and is highest in centrally placed devices requiring a sternotomy with or without an open chest. The presence of an oxygenator adds additional risk for development of infection, most likely owing to the large artificial contact surfaces between blood and exogenous material.[404] The risk of infection also increases with the duration of support (eg, risk is markedly higher with longer duration of ECMO support) and in patients with higher simplified acute physiology scores.[402,405]

Diagnosis of Infection

Diagnosis of infection in patients supported with an acute MCS device can be challenging, and clinicians should maintain a high level of alertness for subtle signs. As body temperature is controlled by the ECMO circuit, using fever as a marker for infection in this population is not helpful. Serial measures of white blood cells, C-reactive protein, and procalcitonin may be used, although the systemic

inflammatory response triggered by blood-prosthetic surface interaction can also cause biomarker release.[403] The diagnosis of acute MCS infection is usually based on careful review of the clinical scenario, evaluating the insertion site for presence of localized signs of infection and/or finding positive blood cultures during acute MCS support or within 48 hours of device discontinuation. It may be difficult to distinguish positive blood cultures that are due to the presence of an infected device vs another source of infection. Diagnosis can be confirmed by obtaining a culture of the explanted device cannula, keeping in mind that a negative culture of the cannula does not necessarily exclude a device related infection.[406]

Organisms

Coagulase-negative staphylococci are the most frequently reported organisms, followed by gram-negative bacteria such as *Pseudomonas* species. *Enterobacter* and *Acinetobacter* species are disproportionately more commonly reported causes of infection in ECMO patients compared with other patients in the surgical ICU.[405] Fungal infections, such as *Candida* are less common, but can be especially challenging to manage in the presence of an acute MCS device.[407,408]

Complications Related to Infection

Infectious complications during acute MCS are associated with increased morbidity and mortality. Nosocomial infections can increase the risk of death by 38% to 63% in patients on ECMO support.[409,410] The presence of a blood stream infection during ECMO support is an independent risk factor for adverse outcomes, with up to 3-fold increase in mortality.[411,412]

Antimicrobial Therapy

Periprocedural Prophylaxis. There are no data to support routine prophylactic antibiotic use in patients with acute MCS and no standardized approach to perioperative antibiotic prophylaxis (Table 2.8).[413] Among centers that use antimicrobial prophylaxis, the duration as well as choice of antibiotics varies from center to center. Most centers use first-generation cephalosporins or vancomycin, while the use of antifungal prophylaxis is rare.

The ELSO Infectious Disease Task Force recommends following standard principles of surgical prophylaxis, with use of a single dose of antibiotics, and at the most 24 hours of duration, with either open or percutaneous cannulation. Exceptions include patients who require transthoracic cannulation owing to increased risk of mediastinitis. In choosing a prophylactic regimen, multiple factors, such as how long the chest is expected to stay open, the circumstances under which the chest was opened, the likelihood of contamination (opened in the operating room vs urgently in the ICU), preexisting skin colonization or infections (methicillin-resistant *S aureus*, fungal), as well as overall immune status of the patient, should be considered.[414]

Empiric Treatment. When choosing empiric antimicrobial therapy for acute MCS, consideration should be given to covering the most common organisms grown from blood cultures in such patients, such as coagulase-negative *Staphylococcus, S aureus, Pseudomonas* species, other gram-negatives, *S aureus*, and *C albicans*. Prophylactic antifungal therapy should be considered in high-risk patients owing to the high mortality risk of such infections.

Targeted Treatment. There are no specific antibiotic recommendations to guide therapy in patients with acute MCS devices and infection. The choice of therapy should be based on usual principles for that particular infection. It should also be recognized that achieving therapeutic

Table 2.8 Recommendations for the Management of Infection with Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
Management of infection with acute MCS via peripheral cannulation		
For percutaneous devices, routine antibiotic prophylaxis is not recommended.	I	C
For surgical cut-down without a graft, routine antibiotic prophylaxis is not recommended.	I	C
For surgical cut-down with a graft, periprocedural antibiotic prophylaxis (eg, cefazolin or vancomycin) should be considered.	II	C
Infection of percutaneous devices should be managed as a central line infection. A surgical cut-down with or without a graft should be managed as a surgical site infection.	I	C
Management of infection with acute MCS via central cannulation		
For tunneled devices, routine periprocedural antibiotic prophylaxis (eg, cefazolin or vancomycin) should be administered. Infection should be managed as a tunneled central line infection, and wound infection managed as a surgical site infection.	I	C
In the setting of a sternotomy, routine periprocedural antibiotic prophylaxis (eg, cefazolin or vancomycin) should be administered. For open chests, postprocedural antibiotic prophylaxis should be administered according to the institution's open chest protocol. Management of infection should be individualized based on extent, severity and pathogen identified.	II	C

MCS, mechanical circulatory support.

concentrations of certain antibiotics may be challenging owing to high volume of distribution on ECMO, and doses have to be adjusted accordingly.

For infections in patients with peripherally inserted acute MCS devices, duration of treatment should follow guidelines for treatment of central line associated infections.[415] Patients with centrally placed acute MCS devices or devices that require an open chest need to be evaluated and treated based on the extent and severity of infection. Continued positive blood cultures despite appropriate antibiotic therapy warrants further diagnostics to evaluate an unidentified source of infection, or consideration of exchange of the whole acute MCS device owing to concern for an acute MSC device-specific infection.[414]

Role of Surgical Intervention

Removal of the device when possible is the best treatment approach, especially if complications associated with the presence of acute MCS are present, such as severe sepsis, septic emboli, suppurative thrombophlebitis, or persistent bacteremia for more than 3 days. Certain types of infection, such as *S aureus, Pseudomonas*, nontuberculous *mycobacteria* or fungi also warrant device removal, if possible, or at least site relocation.[416] The role of antimicrobials for secondary prophylaxis if blood cultures clear but the device is maintained has not yet been studied.

Prevention of Infection

The ELSO Infectious Disease Task Force recommends that an ECMO circuit be treated as a protected central line. Chlorhexidine as a solution of choice for disinfection is also recommended. Application of guidelines for prevention of ventilator associated pneumonia, early shift to enteral nutrition (EN), avoiding and removing unnecessary central lines and invasive devices, and avoiding insertion of long-term intravenous access during ECMO support, are also recommended as preventive measures.

Other Resources

- Plavix [package insert]. Bridgewater, NJ: Bristol-Myers Squibb; 2019.
- Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2019.
- Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019.
- Integrelin [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2019.
- Aggrastat [package insert]. Westpoint, NJ: Merck & Co., Inc.; 1998.
- Reopro [package insert]. Indianapolis, IN: Eli Lilly and Company; 1997.
- Pradaxa [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2018.
- Xarelto [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011.
- Eliquis [package insert]. Princeton, New Jersey: Bristol-Myers Squibb Company; 2019.
- Savaysa [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; 2019.
- Kengreal [package insert]. Cary, NC; Chiesi USA, Inc.; 2020

Task Force 3: Specific Patient Populations

Task Force 1 described a general framework for patient and device selection when managing cardiogenic or pulmonary shock with acute MCS and outlined standard periprocedural and postimplantation care. However, the population of patients presenting with CS is heterogenous. A range of patient characteristics, comorbidities and specific shock etiologies may alter the risks and benefits of acute MCS strategies or necessitate additional management considerations beyond the standard MCS critical care approach. Recognition of these features enables clinicians to tailor CS management to the individual patient and optimize outcomes. Women, adults with congenital heart disease, frail and/or elderly patients, and patients with cachexia, malnutrition, or obesity who require acute MCS for the management of CS would each benefit from further research to refine best clinical practices.

Women

Sex-based differences in patient presentation, management and outcomes have been observed in many CV conditions, including for patients with CS (Table 3.1). The epidemiology is best described in CS secondary to AMI, where women tend to present at a later age and with a higher comorbidity burden, for example more often with diabetes and renal dysfunction.[2,417,418] Some studies have described poorer outcomes for women with AMI-CS.[12,419] Disparities in management have been observed whereby women presenting with AMI-CS are less likely to receive early coronary revascularization than men.[12,419] There are also data suggesting underuse of acute MCS for women with CS, with for example 43% vs 55% ($P < .001$) IABP deployment in women vs men presenting with STEMI and CS in an NIS cohort.[12] There are limited prospective sex-specific data regarding the safety and efficacy of acute MCS, although some registry data suggest poorer outcomes with MCS deployment in women. However, the literature mostly indicates that outcomes for women are at least equivalent to those for men.[2,65,74,417,420,421]

The apparent underuse of acute MCS in women with CS may be secondary to delays in recognition and management of AMI and CS, and potentially to concerns around suitability of MCS for female patients.[422] Sex-specific device safety and efficacy data are sparse and although encouraged by the US Food and Drug Administration (and should be encouraged by other regulatory bodies internationally), are not currently mandated before device approval. The tendency for smaller body size and smaller arterial caliber raises concerns regarding the risks of major bleeding and

Table 3.1 Recommendations for Women and Acute MCS

Recommendation	Class of Recommendation	Level of Evidence
Women requiring acute MCS may be at increased risk of access site complications and limb ischemia owing to smaller caliber vessels, and active mitigation of these potential complications should be sought during MCS deployment and management. Alternative peripheral access techniques may be necessary to improve flow and/or access.	II	C
Women with severe peripartum cardiomyopathy and CS should receive prompt deployment of acute MCS, mostly as a bridge to myocardial recovery, and, managed in conjunction with maternal–fetal medicine specialists.	I	C

CS, cardiogenic shock; MCS, mechanical circulatory support.

peripheral vascular complications in women receiving MCS. The potential for limb ischemia is a major limitation of more novel MCS strategies such as percutaneous subclavian artery IABP placement, and operators may be concerned that women are at greater risk of such injuries. IABP sizing can also pose a challenge in female patients, with height incompletely predicting optimal device length to avoid complications such as mesenteric or renal arterial compromise.[423,424]

In the case of peripheral VA-ECMO deployment, the smaller arterial caliber of women further increases the importance of antegrade perfusion cannulas at the femoral artery access site to prevent distal ischemia.[208] Patients may require Dacron grafts anastomosed to the axillary artery or the femoral artery to permit cannula connections to the graft for initiation of ECMO. Considering these sex-specific concerns in MCS deployment techniques, it is essential that future device clinical trials are adequately powered to determine safety and efficacy in women, thus providing an opportunity to recognize and mitigate any disparities in adverse event profiles.

A particularly important subgroup of patients is those presenting with CS secondary to peripartum cardiomyopathy, defined as the onset of HF within the last month of pregnancy or up to 5 months postpartum with an LVEF of less than 45% and no other cardiomyopathy etiology.[425] Despite the acuity of many presentations, the majority of patients experience partial or complete myocardial recovery.[426] It is however imperative to adequately support the patient at the time of presentation as a small proportion of cases will require acute MCS mostly as a bridge to recovery, and a few may require bridge to durable support and possible transplantation.

The European Society of Cardiology published guidelines on the management of acute severe peripartum cardiomyopathy that include consideration of 2.5 mg bromocriptine twice daily in patients requiring acute MCS.[427] No preference between devices is stipulated in the European Society of Cardiology guidance, beyond use of VA-ECMO if respiratory support is required. There is limited data indicating good CS outcomes with the use of early acute MCS support and bromocriptine.[428] MCS choices can become particularly complex when CS presents before labor. An assisted vaginal delivery is often preferred by obstetricians, owing to its lower physiological demands for mother and neonate compared with a cesarean delivery. However, the requirement for the lithotomy position during a vaginal delivery contraindicates femoral vessel access for MCS. Anticoagulation increases the risk of uterine bleeding after either a vaginal or cesarean delivery and therefore should be minimized early post partum.

Patients of Minority Race or Ethnic Groups

There are few data on the incidence, management, and outcomes of CS with respect to race and ethnicity, but available US data raise the possibility of disparities in MCS deployment. Among patients with AMI-CS, NIS data from 2003 to 2010 showed a higher incidence of shock in patients of Asian/Pacific Islander race, but lower rates of both early mechanical revascularization and IABP support among African American patients (IABP use in 47.3% of African American patients vs 49.9% of White patients; adjusted odds ratio, 0.85; 95% confidence interval, 0.81 −0.90; $P < .001$).[12] In-hospital mortality was highest in patients with Hispanic ethnicity. In an NIS ADHF-CS cohort, there was a similar incidence of shock between racial groups and a higher mortality rate in Whites.[15] A real-world registry of 270 patients admitted across 16 US cardiac ICUs for CS described non-White race for 35.7% of patients who did not receive MCS, vs 25.2% of patients receiving IABP support only, vs only 18.0% of patients receiving advanced MCS support (defined as all acute MCS devices other than IABP).[429] Cultural differences by race and ethnicity surrounding patient and next of kin decision-making in the critical care setting are incompletely understood, especially with respect to acute MCS.[430]

Patients with ACHD

Growing evidence is justifying the expansion of MCS use in patients with ACHD (Table 3.2). Although patients with ACHD with durable MCS have longer length of stay, they have similar rates of adverse events, readmissions, functional status, and quality of life outcomes compared with patients without ACHD. Specifically, for LVADs, survival in patients with ACHD is equal to patients without ACHD.[431] Two main patient cohorts exist in ACHD: Fontan patients and non-Fontan patients. Non-Fontan patients

Table 3.2 Recommendations for Patients With ACHD

Recommendation	Class of Recommendation	Level of Evidence
Patients with non-Fontan ACHD, including those with systemic RV failure, should receive similar forms of acute MCS as patients without ACHD.	II	C
In patients with Fontan ACHD, central VA-ECMO cannulation is superior to peripheral cannulation to drain venous return from aortopulmonary collaterals, decompress the ventricle, and improve lung resuscitation.	II	C
In Fontan patients requiring mechanical circulatory support, acute MCS can be used before durable MCS to allow for assessment of neurologic status, and ensure that flow through the Fontan and pulmonary circulations would provide adequate inflow for a durable VAD.	II	C
In Fontan patients, IABP or Impella should be used with caution especially if there is a Damus Kaye Stansel connection as experience with both is limited.	II	C

ACHD, adult congenital heart disease; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; RV, right ventricular; VAD, ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

with ACHD are often grouped with non-ACHD adults as their physiology is not critically different and survival after transplantation is equivalent.[432]

Frail and/or Elderly Patients

Among an aging population, an increasing proportion of patients considered for MCS will be elderly and/or have a high comorbidity burden.[433] The ELSO registry assessed in-hospital survival between 1992 and 2015 for elderly patients (defined as patients ≥70 years of age) undergoing VA-ECMO for CS. Survival to hospital discharge was 31% in the elderly patient group compared with 43% in younger adults ($P < .001$). Elderly patients had a higher rate of multiorgan failure and decreased survival, but a subset of patients 70 years of age and older with fewer comorbidities and a reversible etiology of CS can experience better outcomes.[434]

Frailty is a state of increased vulnerability to stress related to diminished homeostatic capacity across multiple physiologic systems and can be characterized by sarcopenia, reduced energy expenditure, and weight loss, usually occurring in the presence of chronic comorbidities. Frailty is common in older adults and was demonstrated by Fried and colleagues to contribute to increased risks of falls, disability, hospitalization, and mortality.[435] Patients with chronic HF and precardiac surgery are increasingly assessed for frailty, but there is limited data specific to CS.[436] For patients receiving a durable LVAD, frailty is associated with prolonged intubation, hospital length of stay, and long-term (but not short-term) mortality.[437] Among patients receiving transcatheter aortic valve replacement, the Hospital Frailty Risk Score was associated with short- and long-term mortality, longer length of stay, and all-cause rehospitalization.[438] Multiple other tools have been used to quantify frailty, including the Fried index derived from the Cardiovascular Health Study and the Study of Osteoporotic Fractures metric.[439] Handgrip strength may be a reasonable screening tool for conscious patients who have stabilized during an acute presentation. Although there is no CS-specific data, handgrip strength correlates with outcomes in patients with other CV diseases.[440] Gender-specific handgrip strength thresholds for sarcopenia are less than 27 kg for men and less than 16 kg for women.[441]

For patients with advanced HF, the HF-dependent component of frailty can reasonably be expected to improve after LVAD or transplantation, especially with the support of a multidisciplinary rehabilitation team. However, it remains uncertain whether patients in CS with frailty can be expected to achieve similar functional recoveries after an acute MCS bridge either to recovery or durable LVAD support.

Malnutrition and cardiac cachexia, which is a complex metabolic wasting syndrome characterized by unintentional edema-free weight loss, anorexia, inflammation and abnormal biochemistry, occurs in at least 10%−20% of patients with chronic HF and adversely affects prognosis.[442−446] The prevalence and prognostic implications of malnutrition and cachexia in CS are not well-described, although the critical care literature has established poor nutritional status as a strong mortality risk factor.[447,448] A lower body mass index (BMI) is associated with higher mortality after heart transplantation, and therefore it is important to recognize severe malnutrition and/or cachexia while considering prognosis and destination after acute MCS.[449]

Patients admitted with CS meeting cachexia criteria (unintentional weight loss of >7.5% over prior 6−12 months or a BMI of <18.5 kg/m^2) or with a positive malnutrition screen (eg, a Nutrition Risk in the Critically Ill [NUTRIC] score of ≥5) could particularly benefit from registered dietician nutritionist (RDN) consultation (Table 3.3).[450] It has not yet been established whether aggressive nutritional support aids cachexia reversal during CS, but it is considered reasonable to address protein−calorie inadequacy during the critical care admission, especially for patients requiring optimization preoperatively to transition from acute to durable MCS.[451,452]

The Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition guidelines for nutrition support therapy in critically ill patients offer useful

Table 3.3 Recommendations for Patients With Malnutrition and Cachexia

Recommendation	Class of Recommendation	Level of Evidence
In all patients, particularly for those with cachexia or a positive malnutrition screen, nutrition consultation is recommended.	I	C
In patients with evidence of malnutrition, it is reasonable to increase protein−calorie intake once CO is supported, especially during a preoperative optimization phase for transition from acute to durable MCS and/or transplantation.	II	C

CO, cardiac output; MCS, mechanical circulatory support.

recommendations.[451,453] The use of enteral nutrition (EN) increases mesenteric oxygen demand and thus EN should not be started for patients with CS until gastrointestinal perfusion has been stabilized by MCS deployment.[454] Once the CO is appropriately supported, EN can be instituted at a low rate ("trophic" feeding, <500 kcal/day) within 24−48 hours of intensive care admission. Vasopressor or paralytic medications are not contraindications to EN initiation and trophic EN can improve gut perfusion and integrity in patients with a vasopressor requirement.

These society guidelines recommend advancing EN to goal over the first week of admission once the biomarkers of tissues perfusion (eg, lactic acid levels) have normalized, vasopressors have been minimized and paralytics discontinued, with a goal of 25−50 kcal/kg/d. For patients not meeting these EN goals for more than 7 days and/or who are unable to receive 60% of caloric needs with EN, parenteral nutrition is an option. Use of parenteral nutrition sooner than 7 days is limited to patients who are particularly high risk (eg, NUTRIC score of ≥5) or unable to tolerate EN, but not within 48 hours of admission. Nutrition goals specific to patients with CS, and the usefulness of early EN in preventing bacterial translocation and intestinal complications for patients with MCS, should be prospectively examined in future clinical trials.

Patients with Obesity

Recent clinical trials of interventions for chronic HF have typically included at least 50% of patients who meet BMI criteria for obesity (≥30 kg/m^2) (Table 3.4).[455] The ELSO registry does not collect BMI data, but the weight of patients surviving to hospital discharge was lower than those who did not survival to discharge (77 ± 19 kg vs 80 ± 24 kg; $P < .001$) in an ELSO cohort.[103] There may, however, be an obesity survival paradox for patients presenting with CS, at least within the BMI range of 30.0−39.9 kg/m^2: among a 54,044-patient US sample of AMI-CS between 2005 and 2014, the adjusted odds ratio for in-hospital mortality for patients with less severe obesity (BMI of 30 to <40 kg/m^2) was 0.82 (95% confidence interval, 0.76−0.90), whereas patients with severe obesity (BMI of ≥40 kg/m^2) had higher mortality (1.17; 95% confidence interval, 1.05−1.32) compared with non-obese patients.[456] This mirrors experience with durable LVADs.[457] Outcomes for patients with obesity who receive acute MCS are less clear, but the reported experience with percutaneous cannulation for ECMO in patients with obesity has been reassuring. A German cohort of patients with BMI of greater than 35 kg/m^2 supported by peripherally cannulated VV- or VA-ECMO had comparable outcomes to patients without obesity, with 74% of VV patients and 52% of VA patients successfully weaning from support, and only 3% of patients requiring a surgical intervention for limb ischemia, with bleeding in 5% and wound infection in 2%.[458]

Despite reassuring outcomes reported from an experienced center, in practice the potential for cannulation site complications remains a major concern when managing patients with obesity in CS. Femoral access may be more challenging to obtain swiftly in a patient with excess adiposity and significant cannulation site bleeding may not be recognized promptly. Obesity is generally associated with a higher comorbidity burden that may also impact CS management, and patients with a BMI of more than 35 kg/m^2 may be ineligible for heart transplantation, thus affecting MCS strategy plans.[459]

Table 3.4 Recommendations for Acute MCS in Patients with Obesity

Recommendation	Class of Recommendation	Level of Evidence
Patients with obesity may be ineligible for transplantation or durable MCS based on institutional guidelines.	II	C
In patients with obesity, axillary or central cannulation may be more appropriate than femoral cannulation in cases where the femoral vessels are poorly accessible.	II	C

MCS, mechanical circulatory support.

Table 3.5 Recommendations for Acute MCS in Myocarditis

Recommendation	Class of Recommendation	Level of Evidence
Acute MCS should be considered as bridge to recovery or transplantation in hemodynamically unstable patients with fulminant myocarditis.	II	C
Patients should be referred to specialized centers for timely endomyocardial biopsy and appropriate treatment.	I	C
For patients who received an endomyocardial biopsy while on acute MCS, it is reasonable to discontinue anticoagulation for 6−24 hours to decrease the risk of post-biopsy cardiac tamponade.	II	C
Diagnostic workup and treatment specific to the myocarditis diagnosis (eg, giant cell myocarditis, checkpoint inhibitor myocarditis) should be initiated as soon as possible, irrespective of the use of MCS.	I	C

MCS, mechanical circulatory support

Special Considerations by Acute MCS Indication

Among patients hospitalized for myocarditis, approximately 2%−6% present with fulminant myocarditis and severe clinical instability including CS and ventricular arrhythmias (Table 3.5).[460] Despite limited data, acute MCS can be valuable as a bridge to recovery or transplantation in hemodynamically unstable patients with fulminant myocarditis, with the device selection dependent upon patient-specific criteria (eg, predominant LV or RV failure).[461] Survival to discharge was 61% in an ELSO series of 150 patients with acute myocarditis supported by VA-EMCO. Importantly, such patients require prompt referral to specialized centers to allow for timely endomyocardial biopsy and treatment initiation. Endomyocardial biopsy should be performed as soon as possible in all patients with suspected myocarditis and CS, and, if the initial findings are inconclusive but clinical suspicion remains high, should be repeated.[461] Specific immunosuppressive therapy should be considered and used where indicated, at least as an initial trial while determining myocardial response, to try to promote cardiac recovery.[461]

Postcardiotomy shock is a life-threatening entity that occurs infrequently after elective cardiac surgery, but is associated with significant morbidity and mortality. It is defined as acute HF after open heart surgery which leads to an inability to wean from cardiopulmonary bypass or leads to an acute decompensation in the early postoperative course. It is one of the most common indications for MCS and is associated with an in-hospital mortality of up to 50%.[462] Prompt initiation of MCS leads to the greatest chance of survival to discharge (Table 3.6). The use of an IABP alone offers limited benefit in cases where the inotrope requirement is high. Despite lack of guidelines, VA-ECMO has become the first line therapy for postcardiotomy shock.[180] A recent report found the use of a concurrent IABP with VA-ECMO to be an independent protective factor for in-hospital mortality.[463] Central and peripheral VA-ECMO cannulation appear to have similar results. There is growing evidence that other modalities of temporary MCS may offer a survival advantage in patients with postcardiotomy shock.[464] Durable MCS is rarely used as an initial therapy for postcardiotomy shock.

Almost 50% of patients treated with MCS devices had prior CPR, which is associated with worse outcomes.[465] Furthermore, there is an increasing use of eCPR; an early observational study has reported an association with improved outcomes in selected patients (Table 3.7).[466] Although overall survival to hospital discharge post-eCPR has been in the region of 30%, at present there is insufficient evidence to recommend a widespread adoption of this approach.[54] However, eCPR might be feasible in tertiary care centers with an established VA-ECMO program, usually restricted to younger patients with a witnessed cardiac arrest, short no-flow time, a primary rhythm that may be cardioverted, and/or a reversible etiology. Centers should provide an on-call, interdisciplinary eCPR team (eg, anesthesiology, cardiac surgery, cardiology, intensivist and perfusionist) and a dedicated ICU. For postresuscitation patients supported by VA-ECMO, serial neurologic

Table 3.6 Recommendations for Postcardiotomy Shock

Recommendation	Class of Recommendation	Level of Evidence
Patients who are unable to be weaned from cardiopulmonary bypass or who develop refractory shock shortly after separation should be considered for acute MCS.	I	C
The use of an IABP alone is of limited value in refractory postcardiotomy shock but may add value in combination with VA-ECMO.	II	B

IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Table 3.7 Recommendations for VA-ECMO–assisted Resuscitation and Postresuscitated Patients

Recommendation	Class	Level of Evidence
VA-ECMO–assisted resuscitation can be considered for selected patients treated at centers with sufficient experience in the use of MCS.	II	C
Centers providing VA-ECMO–assisted resuscitation should provide an on-call, interdisciplinary team and a dedicated cardiac intensive care unit.	II	C
Postresuscitation patients on VA-ECMO should undergo serial neurologic assessment	I	C

MCS, mechanical circulatory support; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

assessment is warranted to detect potentially fatal complications (eg, intracranial hemorrhage, hypoxic brain injury) as early as possible. Additionally, serial measurement of brain-specific biomarkers such as neuron-specific enolase might add useful information to identify patients with likely neurologic impairment.[467] In patients on VA-ECMO with serious neurologic complications, further decision-making should be made in close discussion with the patients' next of kin/health care proxies and should ideally include clinicians with palliative care expertise (see Task Force 4 for details).

Task Force 4: Goals of Care and Role of Palliative Care, Social Work, and Ethics

Shared Decision-making and Informed Consent Setting

Decision-making for acute MCS is complex (Table 4.1). These decisions frequently involve a variety of complex options, the potential to create indefinite dependence on a temporary treatment, a high degree of uncertainty in outcomes, the potential for significant suffering, the inability to engage an unconscious patient, and a strong emotional state of the people involved, and are further complicated by the rapidity with which many of the decisions must be made and revisited. These decisions are not simple weighing of length of life vs quality of life; rather, they are better framed as a high-risk, high-reward situation. Patients with life-threatening cardiopulmonary illness can be exposed to invasive interventions, often preventing death through a prolonged period of critical illness. The hope is that with stabilization these patients will either recover—which is often only partial and can leave patients with significant limitations in health status—or bridge to longer-term treatment strategies such as heart transplantation or durable LVAD—which also come with their own tradeoffs. But there is also the third outcome of worsening complications and patient death. Therefore, engagement of patients and families through expectation setting and shared decision-making has the potential to alter the course of care, diminish suffering, avoid adversarial relationships, lower decisional regret, and limit disagreements over eventual withdrawal of support if some situations eventually become futile.

Shared decision-making and informed consent are central to medical decision-making in acute MCS.[468] They require that clinicians, patients, and families share information with each other and work toward decisions about treatment that are medically reasonable and best aligned with patients' values, goals, and preferences. In the setting of acute MCS, clinicians may argue that they know best how to implement temporary support to stabilize patients. However, the ethical principle of autonomy recognizes the rights of patients to choose their therapies, if possible, from among reasonable available options, and this can and should occur even in the setting of acute MCS. In some emergency situations, this may not be feasible such as acute decline in clinical situation or patient consciousness. Informed consent includes not only the procedural details but also comprehension of the benefits and risks of the offered therapy and available alternatives, including continuation and withdrawal of ongoing treatments.[469]

Informed consent and shared decision-making work to uphold the principle of patient-centered care, 1 of the 6 pillars of health care quality identified by the Institute of Medicine.[470] The implication is that therapies with expected benefit and recommended by guidelines should be offered but need to be discussed among the range of potential strategies, paying attention to how the various options align with individual patient preferences. For a recently healthy patient with an acute event resulting in cardiopulmonary collapse, initiation of extracorporeal life support (ECLS) is often the obvious immediate option for most patients. Similarly, for patients who develop progressive multiorgan failure or catastrophic events (eg, major stroke) in the setting of preexisting multimorbidity and frailty, withdrawal of care may be the appropriate option. For most of these decisions, patients have the right to choose what is done to them from among medically reasonable options, including the choice to forego care.[471,472]

Setting Expectations

As discussed in Task Force 1, assessment is fundamental to the process of implementing acute MCS. Similarly, anticipation is a central tenet of decision-making, particularly in the setting of hemodynamically unstable patients with high rates of morbidity and early mortality. Each patient is unique, and each clinical situation is dynamic, such that risk models and care algorithms only provide a starting point from which to tailor care. This uncertainty should not deter discussions with patients and families, but rather should be acknowledged as an inherent part of decisions regarding future care with ranges of expected outcomes for each option.

Table 4.1 Recommendations for the Goals of Care and Role of Palliative Care, Social Work, and Ethics

Recommendation	Class of Recommendation	Level of Evidence
In patients for whom acute MCS is considered, shared decision-making and informed consent of the patient or healthcare proxy should be used.	I	C
Setting expectations for acute MCS should be done before implantation if possible, or as soon as possible thereafter.	I	C
Iterative discussions about options should be held at scheduled time points, or with changes in clinical status.	I	C
If durable MCS or organ transplant is being considered during a period of acute MCS, use of decision aids or open discussion of risks and benefits may help families assess preferences and goals of treatment options.	II	B
Palliative care consultation is recommended in patients with acute MCS to assist with symptom management, goals of care discussions, and complex decision-making.	I	C
Psychosocial evaluations should be used in acute MCS to guide decision-making regarding durable MCS or organ transplantation.	I	C
Exchange to a durable MCS device should preferably be made with primary person informed consent.	I	C
If the medical condition changes so that bridging options are no longer viable, then the decision to withdraw or discontinue acute MCS support is a clinical one that is ethically supported.	I	C
Withdrawal of acute MCS should be done following a transparent discussion with the patient (if possible), the family and the medical team.	I	C
Patients may request withdrawal or discontinuation of acute MCS at any time.	I	C
The acute MCS care team should be aware of the local legal statutes regarding discontinuation and withdrawal when placing short-term assist devices.	I	C
In complex patient care scenarios with an ethical question, an ethics consultation may be reasonable.	II	C
The use of acute MCS in the setting of public health emergencies, such as H1N1, SARS, and COVID-19 should follow similar ethical guidelines as acute MCS in other clinical settings.	I	C

COVID-19, coronavirus disease 2019; MCS, mechanical circulatory support; SARS, severe acute respiratory syndrome.

The initial decision to institute acute MCS is challenging. Not only is it often rushed, but application of the acute MCS can create indefinite dependence on devices that are designed to be used temporarily. Therefore, even in the most emergent situations, every effort should be made to allow patients or their designated proxies to be aware of plans to initiate acute MCS to stabilize a patient, with efforts by the medical team to learn about any previously unknown contraindications or care directives that would preclude or complicate the treatment. It should also be recognized that the public knowledge of ECLS and MCS in general may be lacking and that there may be a significant amount of therapeutic misperception about what MCS can achieve.[473,474]

Clear rules with hard cutoffs to acute MCS initiation usually find exceptions. Therefore, guidelines have generally suggested parameters but rejected absolutes. A commonly encountered example is the desire to clarify decision-making through the application of an upper age cutoff for ECLS. Chronological age should always be supplemented with additional information about the patient; although increasingly advanced age is associated with significantly worse outcomes, such that many use age more than 65 years as a relative contraindication to VA-ECMO, and at some point age above some threshold—75−80 years—becomes dominant.[475−477]

After the initiation of acute MCS, the series of options that may be presented to patients is also often complex, and may change frequently with the clinical situation, requiring major decision-making on the part of the patient and family. Common scenarios arising after initial stabilization with ECLS include initiation of continuous renal replacement therapy (creating further dependence on a temporary device), surgery to address bleeding, additional surgery for reconfiguration of support devices and attachments, and decisions about how to bridge to longer-term support options that may be altered by changing status and information. Examples of the clinical trajectory that impact ongoing decision-making include some of the following: worsening HF or fibrotic stage ARDS that make recovery less likely, transfusion-related sensitization that raises the risks and may decrease the likelihood of organ transplant, and prolonged anuria or RV failure closing options for durable LVAD. As a result, the temporary "bridging" nature of acute MCS often evolves from bridge to bridge, bridge to recovery, bridge to transplant, bridge to LVAD, and bridge to withdrawal.

How to Discuss Options

Given the dynamic nature of critical illness, one of the arguments for acute MCS is to allow time to engage patients and

families. Good shared decision-making involves an iterative approach that respects the dynamic nature of cardiopulmonary shock.

Research has shown that most patients and families want accurate and honest conversations with clinicians.[478,479] However, these complex conversations face potential barriers. Difficult decisions about life and family stimulate powerful and complex emotions that may prevent processing of important information. Attention to informational preferences, learning styles, health literacy, anxiety and depression, cognitive limitations, cultural and religious differences, and language barriers are critical to facilitate informed discussions.[468,480] Family and caregiver dynamics, particularly with regard to surrogate decision-making, can further complicate the goal of matching therapy to patient values and preferences. Conflict can arise when an intervention desired by the patient or family is not aligned with medical realities or the patient's stated goals.

To navigate these barriers, clinicians must be highly skilled in communication. Early elicitation of values, goals, and preferences is necessary to guide future discussions of possible therapeutic options and decision-making. Specific skills and tools that clinicians can integrate into their practice include the Ask-Tell-Ask format for communicating difficult information, the N-U-R-S-E mnemonic (**N**aming, **U**nderstanding, **R**especting, **S**upporting, **E**xploring) for dealing with complex emotions, and decision aids for enhancing the communication of difficult quantitative information and integration of patient values, goals, and preferences.[481,482] These tools can help frame the conversations to focus on what is meaningful to the patient (VitalTalk.org, TheConversationProject.org). The "Best Case, Worst Case" approach[483] using scenario planning is one that can be particularly powerful in both outlining major options while also capturing uncertainty; it also uses storytelling around possible outcome states that capture a range of potential patient experiences that go beyond survival statistics (Fig. 4.1).[484] These skills are not innate and can be learned; education is important.[485,486]

Decision Aids

Decision aids are tools that help patients and caregivers become involved in decision-making by providing information about the options and outcomes and by assisting patients in clarifying their personal values. Decision aids come in various forms including booklets, pamphlets, videos, and web-based systems (see http://decisionaid.ohri.ca/) and are designed to complement, not replace, a clinical encounter and dynamic discussion. They can be conceptualized broadly as either aids to assist the patient during or independently from the face-to-face encounter. Decision aids attempt to present probabilities of the risks and benefits in ways that patients can understand, including side-by-side comparisons of options. The concept of "gisting" what is most important to patients is integrated into decision aid design. A fundamental aspect of decision aids that goes beyond a mere informational tool is that they explicitly work to clarify patient values. Substantial evidence suggests that decision aids help patients to make better decisions.[487–490] An LVAD decision aid has been shown to improve decision quality for patients with advanced HF, one-quarter of whom were making the decision while in the ICU.[491,492]

Palliative Care

Engagement of formal palliative care specialists can be helpful in identifying goals of treatment, and setting expectations; although, 1 randomized trial of palliative care consultation with families of patients with chronic critical illness in the ICU did not demonstrate benefit in the anxiety and depression score for the surrogate decision-makers.[493] In contrast, a palliative-care trained social worker-led intervention in recently hospitalized patients with advanced HF, including a structured evaluation of prognostic understanding, end-of-life preferences, symptom burden, and quality of life followed by communication of this information to treating clinicians, improved documented goals of care and prognostic estimates by patients for their own survival.[494]

Palliative care is specialized medical care for individuals living with a serious illness. The primary goals of palliative care are to provide relief from the symptoms and stress of illness and to improve quality of life for patients and families. Palliative care can begin at diagnosis and continue through the end-of-life and is often provided alongside disease modifying treatment. Palliative care is sometimes delivered by palliative care interdisciplinary teams, which can work alongside the patient's primary clinical teams to provide care. The availability of specialty palliative care teams varies by location.[495] Primary palliative care refers to palliative care delivered by clinicians who are not palliative care specialists, such as cardiologists or internists. More complex aspects of serious illness treatment, such as complex symptom management and challenging goals of care discussions, can benefit from the involvement of palliative care specialty teams or ethics consultation services. Hospice is a specific type of palliative care provided when a patient is terminally ill with limited life expectancy and life-prolonging strategies are no longer the primary focus of care. Hospice care can be provided in the hospital, at home, in a hospice facility, or in a skilled nursing facility. In the United States, hospice care is usually paid for by the patient's medical insurance and is subject to more rules and restrictions than other types of palliative care. Some therapies for end-stage HF such as continuous inotropes, may not be possible with all hospice agencies and this is important to know when having discussions with patients and families about their treatment options.[496] In patients with acute MCS who decline or are not candidates for durable MCS, but are able to have acute MCS removed, inpatient hospice or even home hospice may be an option.

Although palliative care specialist involvement is recommended in durable MCS, there are limited data on its effectiveness in improving patient outcomes. Single center, observational reports have suggested that palliative care

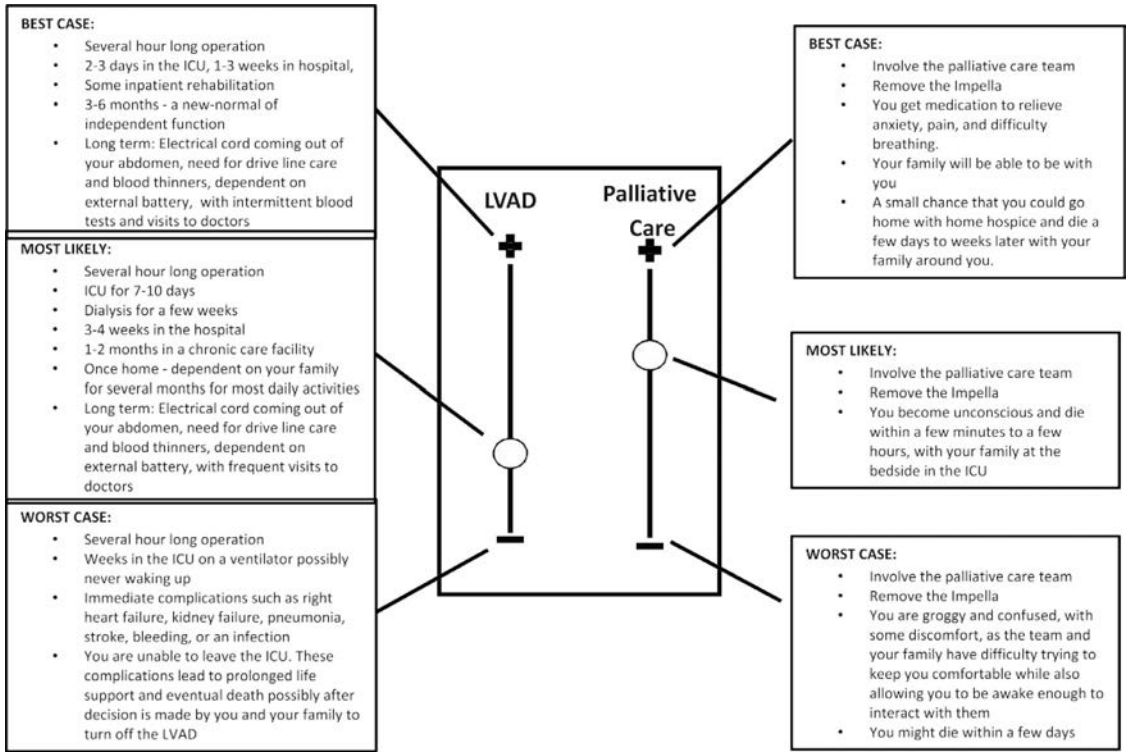

Fig. 4.1 Best case and worst case scenarios to be used in dialog between patient, family, and clinicians during medical decision-making. The best case/worst case handwritten graphic is tailored to the specific patient and their current situation, highlighting reasonable medical options side by side and then the expected range of outcomes based on currently available data and clinician experience. The best and worst outcomes are drawn initially at the same level but can be adjusted to reflect the patient's stated values of each outcome after discussion with the patient.[483,484,543] (adapted from[484]). The example presented here could represent a 78-year-old patient with chronic heart failure and significant comorbidity progressing to cardiogenic shock who has been stabilized on acute MCS with a decision to be made regarding transition to long-term durable LVAD support or to a comfort measures approach. For an explanatory video, see: https://www.youtube.com/watch?v=FnS3K44sbu0. LVAD, left ventricular assist device; MCS, mechanical circulatory support.

specialists can be integrated into MCS teams and may improve implementation of advance care planning.[497–499] There are even fewer and only retrospective data on involvement of palliative care teams in patients requiring acute MCS. Palliative care teams may be used in sicker patients.[500,501] One single center study suggested that palliative care teams were consulted in 48% of patients receiving acute MCS, and were more often involved in patients with prolonged ICU stays and MCS duration.[500] There are data on palliative care involvement in patients with advanced HF and those critically ill in the ICU that may be relevant to patients with acute MCS. In a randomized trial in caregivers for chronic critically ill patients on ventilators in the ICU, the use of palliative care-led informational and emotional support meetings compared with usual care did not reduce anxiety or depression symptoms and may have increased post-traumatic stress disorder symptoms.[493] In patients with advanced HF not receiving MCS, palliative care involvement has been shown in limited populations to improve patient satisfaction, symptom burden, and quality of life.[502,503] Most notably, the Palliative Care in Heart Failure trial randomized 150 patients with advanced HF and high estimated mortality to usual care with palliative care intervention vs usual care alone. Patients randomized to receive the palliative care intervention had more improvement in depression, anxiety, and quality of life scores with no difference in hospitalization or mortality compared with usual care alone.[502]

There are many ways that palliative care teams can provide support to patients and families in the setting of acute MCS, including addressing complex symptom needs, assisting with clarifying patient preferences and complex decision-making, and providing emotional and spiritual support. Palliative care clinicians have expertise in the management of a multitude of symptoms common in patients with advanced HF considering MCS, such as pain, refractory dyspnea, and depression. In the setting of acute MCS, they can assist ICU and MCS teams in treating these complex symptoms in the context of HF and multimorbidity. They are also able to assess the psychosocial needs of patients and families. The interdisciplinary palliative care team often includes individuals such as social workers and chaplains that can help to provide an extra layer of support to loved ones who may be struggling to cope.

Furthermore, palliative care clinicians are communication experts. Early in the process of acute MCS, these skills can be helpful in *preparing patients and families for likely clinical scenarios, setting expectations, and eliciting preferences for care*. In the setting of durable MCS, this is often referred to as preparedness planning,[504] and includes delineation of goals of care and review of quality of life preferences before durable MCS implantation. In the setting of

acute MCS, preimplantation palliative care consultation may not be possible if decompensation occurs suddenly. However, palliative care teams can still assist with eliciting preferences for care after acute MCS is in place through discussions with patients and/or surrogate decision-makers. If a patient's condition worsens despite acute MCS, palliative care teams can help MCS teams, patients, and families to make difficult choices about whether to pursue additional interventions. When the patient is approaching the end of life, palliative care teams can help to navigate the transition to comfort-focused care and withdrawal of MCS support if indicated.

Psychosocial Evaluations

Since the initial use of cardiac assist devices, candidate evaluation has included both assessments of medical and psychosocial factors. The psychosocial evaluation is typically completed by a master's prepared social worker. A recent International Society for Heart and Lung Transplantation consensus document details content of the psychosocial evaluation for durable MCS.[505] This process is also needed for patients with acute MCS being considered for transition to durable MCS. The domains explored are the same as the evaluation for heart transplant candidacy but also include a focus with the MCS patient on knowledge about and ability to operate the device. Patients need to demonstrate a capacity to care for their device and have a social support system that is available, reliable, and helpful. However, the group of patients with acute MCS, who are critically ill and possibly newly diagnosed with cardiac disease, may not be able to be as involved in the assessment process. During this urgent evaluation, the ability to assess the patient's cognitive status and determine their ability to care for a longer term device can be challenging. In these situations, the evaluator must turn to the patient's support system to provide knowledge about the patient's functioning and collateral medical information.

Key areas to focus on in the urgent psychosocial evaluation include past treatment adherence, mental health history and current status, past and current use of substances/alcohol/nicotine products, cognitive status, and social support.[459] MCS patients with histories of non-adherence with care recommendations are at greater risk for postimplant complications and this should be considered in discussions of goals of implantation, that is, bridge to recovery vs bridge to durable MCS.[506,507] Prior history of medication compliance and psychiatric mood disorders and substance use disorders are reasonable to incorporate into decisions about transitioning acute MCS to more durable support or transplantation.[505–513] Similarly, incorporation of the patient's social support system which will provide both practical and emotional support is important.

Although there is a small amount of literature for MCS patients, for transplant patients, helpful and reliable supports are associated with better outcomes both pre and post-transplant and also with increased adherence, longer survival time and lower risk of substance use disorder relapse, lower risk of mental health issues and increased quality of life.[514,515] When evaluated, but especially at times of medical crisis, it may be difficult for the patient and family/supports to process the extensive information about LVAD and achieve a clear understanding of the complexities of care. The patient and family may feel desperate, and any treatment option may seem possible and positive when they are facing near imminent death. They are often not able to have in-depth discussions about the treatment and are unable to meet other patients with LVADs to learn more about MCS from a patient-perspective. Nonetheless, it will be important to recognize the value of psychosocial assessment in setting expectations of the implantation, and in trying to avoid psychosocial settings which have been associated with increased complication rates for durable MCS. This is increasingly important when there is consideration to change from acute MCS to a durable device.[513,516]

Importance of Primary Person Consent

Although urgent acute MCS may be implanted without a long preexisting period of disease, it is nonetheless important for health care providers to recognize that living with durable MCS is challenging and is something that would not be acceptable to all people. There is a significant morbidity associated with VAD implantation, and because of the high intensity medical treatment that is necessary, and the changes in body morphology, patients need to be involved in plans for exchange.[517] Therefore, in general, acute MCS should be used in place of durable MCS until a patient is able to provide informed consent.

Ethics of Acute MCS Withdrawal

If support was initiated for the purpose of bridging therapy to transplant or durable VAD, and that is no longer an option, then the decision to discontinue therapy should be made on clinical criteria. This is not a patient or surrogate decision.[471] Although the decision should be made with input from family, surrogate decision-makers, palliative care, and VAD coordinators, continued support on acute MCS without an end point should be avoided. For some people, discussion about withdrawal of support or end-of-life decisions is viewed as disrespectful. In these settings, use of structured interview tools might help clinicians.

Fewer than 50% of patients present with advance directives,[518,519] and fewer still with specific data regarding acute MCS to help guide clinical care.[520] For medical teams, defending autonomy is a principle, just as it is essential to prepare to declare futility. Communicating with stressed family members to set limits for therapies requires specialized skills and attitudes. Fewer than 50% of patients are involved in decision-making in these circumstances.[518,521,522] It is important to prepare a plan for situations in which acute MCS is no longer beneficial for the patient. The process of turning off the devices must be coordinated by an interdisciplinary team; involving palliative care services reduces costs and shortens the stay in

intensive care.[517,523,524] Talking in detail with the patient in the context of possible complications and futility, before the establishment of support is a measure that can be considered. Patients feel grateful for the opportunity to discuss these options. The information must be transmitted by the attending physician and involve the team, including nursing.[525,526] It is also important to continue these discussions with family members. Family members who have to partake in end-of-life decision-making without guidance from advance directives can experience post-traumatic stress symptoms.[527] The process of deactivating acute MCS should be approached in a similar fashion as ventilator withdrawal.[528–530]

Discussion for Withdrawal of Acute MCS

Withdrawal of acute MCS—if, when, and how—can be challenging. This may be most pronounced when patients are well supported by temporary ECLS but medical realities make more durable treatment options problematic.[531] Delineation of the purpose of acute MCS is central to discussions about exchange or withdrawal. Recognizing the problems with longer term use of ECLS, opening up discussions around ECLS and engaging in shared decision-making can be seen as counterproductive. A survey[532] found that physicians, especially those who self-reported as knowledgeable about VA-ECMO, expressed a desire to retain decisional authority for VA-ECMO. The authors argue this reflects physicians' concern for an inability to convey medical complexity, stewardship of resources, and efforts to avoid futility and usefulness disputes. However, shared decision-making asks clinicians and patients to go beyond such questions, recognizing that clinicians are relatively expert in the medical aspects while patients are experts in their values, goals, and preferences. Therefore, the locus of control is shared: it can sometimes be dominated by medical realities that make VA-ECMO inappropriate even when survival is the primary goal; and at other times can be dominated by a chronically ill patient's desire to avoid further suffering even when VA-ECMO may have a reasonable chance of restoring a patient back to prior health.

Patient's Request for Withdrawal of Acute MCS

It is ethically acceptable to comply with a patient's (or surrogate's) request to discontinue acute MCS. It is important to identify early the symptoms of depression, and to treat them, considering that a decision to turn off a device can be taken under deep states of depression and is not advisable.[526] Patients' rights to self-determination and autonomy should also extend to a respect for their religious beliefs and practices. Given the penetration of these technologies, the implantation of acute devices will occur in patients of many religious faiths, which may have clearly expressed directives on how to consider discontinuation; however, there is also confusion as to what a particular religious faith might expect. Many religions support withdrawal of support if the patient finds the medical situation to be burdensome. Involvement of a religious leader of the same faith (such as a priest, imam, rabbi, or elder) can be useful in understanding choices regarding end-of-life decisions.[533] For many religions, suicide and euthanasia are not acceptable; therefore, a discussion of discontinuation should be had using language that clearly focuses on medical appropriateness, and clinical facts, rather than on patient choice.[480,533,534] As religiousness and spirituality comprise one of the core domains of palliative care, use of palliative care can also help incorporate patient and family discussion. This factor is of particular importance in the discussion of withdrawal of support because most religions are supportive of advance care planning and discussion about preparation for death.[529,535] If there are language barriers, use of a trained medical interpreter is essential and should not be substituted. If a decision is made to withdraw acute MCS, the use of a decommission checklist is suggested (Table 4.2).

Legal Considerations for Acute MCS Withdrawal

In the United States and Western Europe, discontinuation of MCS is seen as allowing the process of natural death, and as a move that respects patient autonomy in some cases and recognizes futility in others. The right of adults to refuse life support treatment is ethical.[472,523,524] It is also legally supported in the United States and numerous Western countries. However, in some regions such as in Japan, there are legal restrictions about the discontinuation of life sustaining treatment.[536–539] Unlike the United States or Europe, there are few guidelines available for circulatory support in regions, such as South America, the Middle East, and East Asia. Legal resources are a last resort if there are different opinions regarding the decision to turn off the device.

The Role of Ethics Consultation

The grieving of the family can be manifested through conflict in the middle of the discussion about the futility of treatment. It is important to maintain direct communication and to avoid inconsistencies in messages to the family.[471] Involvement of an ethics consultation service or committee can help with clarification of patient preferences and with the moral distress of health care providers. Potential scenarios in which ethics consultation can be sought are described in Table 4.3.

Public Health Emergencies

ECMO support in the setting of acute respiratory failure may be terminally discontinued if patient survival is highly unlikely, or there is no possibility of durable device implantation or transplantation. During public health emergencies, the appropriateness of acute MCS should be governed by medical judgement, but may be affected by allocation criteria for scarce resources.[124,540–542]

Table 4.2 Acute MCS Decommission Checklist[528–530]

Notification of team	Family meeting	Team meeting	Discontinuation steps
Clinicians involved in the patient's care (eg, HF, interventional cardiologists, surgeon, palliative care provider, intensivists, social worker, VAD coordinator)	Review the clinical course and goal for comfort, or adherence to patient preferences	Determine time for deactivation	1. Identify a lead person to oversee deactivation
Chaplains, clinical ethicists, other religious or spiritual support	Outline process for deactivation, setting expectations including possibility of prolonged period before death.	Review all orders for anxiolytics, sedation and analgesia	2. Make sure all people required to be present are there
	Determine who will be present, and the need for any religious rites	Create a schedule for discontinuation of other life-sustaining therapies, and deactivation of any other devices, such as pacemakers or implantable cardioverter-defibrillators	3. Remind family of possible signs, symptoms and again of the uncertainty in the timing of death
	Discuss other life sustaining therapies in use that may need deactivation (eg, renal replacement, artificial nutrition and hydration, mechanical ventilation)		4. Administer medications for comfort
	If appropriate discuss decisions regarding organ or tissue donation		5. Turn off the monitors and silence alarms
	Document meeting in the medical record		6. Discontinue support

HF, heart failure; MCS, mechanical circulatory support; VAD, ventricular assist device.

Table 4.3 Clinical Scenarios for which Ethics Consultation can be Considered

Clinical Scenario	Role of Ethics Consultant
Decisions based on interpretation of religious tenets	Clarification about interpretation of religious texts can be useful to guide decision-making. Defining care as "extraordinary" or "heroic" can help with decision about withdrawal or ongoing support
Disagreement in goals of care	Alignment of how patients lived with expectations of outcomes may help surrogate decision-makers understand implications of their decisions
Limitations of escalation of care	Providing support for professional medical judgement and appropriate limitations of care

Disclosures

See Appendix 1.

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Supplementary materials

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